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Novel peptide and pharmaceutical composition for treatment of eye diseases comprising same novel peptide as active ingredient

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(56) Related Art
WO 2017/018613 A1
US 6037135 A
CHAE EUN KIM ET AL, "Effects of chondrocyte-derived extracellular matrix in a dry eye mouse model", MOLECULAR VISION, (2015-10-26), vol. 21, pages 1210 - 1223

(12) 특허협력조약에 의하여 공개된 국제출원

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(81) 지정국 (별도의 표시가 없는 한, 가능한 모든 종류의 국내 권리의 보호를 위하여): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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(54) **Title:** NOVEL PEPTIDE AND PHARMACEUTICAL COMPOSITION FOR TREATMENT OF EYE DISEASES COMPRISING SAME NOVEL PEPTIDE AS ACTIVE INGREDIENT

(54) **발명의 명칭:** 신규한 펩타이드 및 이를 유효성분으로 포함하는 안구질환 치료용 약학 조성물

도 1

No	AA Lot Number	BB Peptide Name	CC Sequence	MW	DD Purity (%)	EE Amount (mg)	FF Solubility (0.5mg/ml)
1	K161388	YDE-001	GG OGQEGLAGPK (O : Hydroxyproline)	969.1	>99.7%	5.0mg 10.0mg	Water
2	K161389	YDE-002	HH OGQNGLAGPK (O : Hydroxyproline)	984.0	>99.7%	5.0mg 10.0mg	Water
3	K161390	YDE-003	II OGQQGLAGPK (O : Hydroxyproline)	983.1	>99.7%	5.0mg 10.0mg	Water
4	K161392	YDE-004	JJ OGQHGLAGPK (O : Hydroxyproline)	977.1	>99.7%	5.0mg 10.0mg	Water
5	K161393	YDE-005	KK OGQKGLAGPK (O : Hydroxyproline)	968.1	>99.5%	5.0mg 10.0mg	Water
6	K161394	YDE-006	LL OGQSGLAGPK (O : Hydroxyproline)	927.0	>98.8%	5.0mg 10.0mg	Water
7	K161395	YDE-007	MM OGQTGLAGPK (O : Hydroxyproline)	941.0	>98.9%	5.0mg 10.0mg	Water
8	K161396	YDE-008	NN OGQAGLAGPK (O : Hydroxyproline)	911.0	>98.8%	5.0mg 10.0mg	Water
9	K161397	YDE-009	OO OGQVGLAGPK (O : Hydroxyproline)	939.1	>98.1%	5.0mg 10.0mg	Water
10	K161398	YDE-010	PP OGQIGLAGPK (O : Hydroxyproline)	953.1	>99.0%	5.0mg 10.0mg	Water
11	K161399	YDE-011	QQ OGQLGLAGPK (O : Hydroxyproline)	953.1	>98.3%	5.0mg 10.0mg	Water
12	K161400	YDE-012	RR OGQRGLAGPK (O : Hydroxyproline)	997.1	>98.9%	5.0mg 10.0mg	Water
13	K161401	YDE-013	SS OGQSGLAGPK (O : Hydroxyproline)	927.0	>98.7%	5.0mg 10.0mg	Water
14	K161402	YDE-014	TT OGQTGLAGPK (O : Hydroxyproline)	941.0	>98.5%	5.0mg 10.0mg	Water
15	K161403	YDE-015	UU OGQVLAGPK (O : Hydroxyproline)	897.1	>99.1%	5.0mg 10.0mg	Water
16	K161404	YDE-016	VV OGQDILAGPK (O : Hydroxyproline)	1011.1	>95.6%	5.0mg 10.0mg	Water
17	K161405	YDE-017	WW OGQDLLAGPK (O : Hydroxyproline)	1011.1	>98.0%	5.0mg 10.0mg	Water
18	K161406	YDE-018	XX OGQDALAGPK (O : Hydroxyproline)	969.1	>98.8%	5.0mg 10.0mg	Water
19	K161407	YDE-019	YY OGQDFLAGPK (O : Hydroxyproline)	1045.2	>99.6%	5.0mg 10.0mg	Water
20	K161408	YDE-020	ZZ OGQDYLAGPK (O : Hydroxyproline)	1061.2	>99.7%	5.0mg 10.0mg	Water
21	K161409	YDE-021	AAA OGQDWLAGPK (O : Hydroxyproline)	1094.2	>98.3%	5.0mg 10.0mg	Water
22	K161410	YDE-022	BBB OGQDHLAGPK (O : Hydroxyproline)	1035.3	>98.3%	5.0mg 10.0mg	Water
23	K161411	YDE-023	CCC OGQDSLAGPK (O : Hydroxyproline)	985.1	>98.5%	5.0mg 10.0mg	Water
24	K161412	YDE-024	DDD OGQDTLAGPK (O : Hydroxyproline)	999.1	>98.9%	5.0mg 10.0mg	Water
25	K161413	YDE-025	EEE OGQ(D-Sar-LAGPK (Sar : me-Gly) (D : Hydroxyproline)	969.1	>95%	5.0mg 10.0mg	Water
26	K161414	YDE-026	FFF OGQS*GLAGPK (S* : homo-Ser) (O : Hydroxyproline)	941.1	>95%	5.0mg 10.0mg	Water
27	K161415	YDE-027	GGG OGQD*GLAGPK (D* : D(OMe)) (O : Hydroxyproline)	969.1	>95%	5.0mg 10.0mg	water
28	K161416	YDE-028	HHH OGQN*GLAGPK (N* : N(NMe)) (O : Hydroxyproline)	968.1	>95%	5.0mg 10.0mg	Water

AA ... Lot number
BB ... Peptide name
CC ... Sequence
DD ... Purity (%)
EE ... Amount (mg)
FF ... Solubility (0.5 mg/ml)
GG ... OGQEGLAGPK (O: Hydroxyproline)
HH ... OGQNGLAGPK (O: Hydroxyproline)
II ... OGQQGLAGPK (O: Hydroxyproline)
JJ ... OGQHGLAGPK (O: Hydroxyproline)
KK ... OGQKGLAGPK (O: Hydroxyproline)
LL ... OGQSGLAGPK (O: Hydroxyproline)
MM ... OGQTGLAGPK (O: Hydroxyproline)
NN ... OGQAGLAGPK (O: Hydroxyproline)
OO ... OGQVGLAGPK (O: Hydroxyproline)
PP ... OGQIGLAGPK (O: Hydroxyproline)
QQ ... OGQLGLAGPK (O: Hydroxyproline)
RR ... OGQFGLAGPK (O: Hydroxyproline)
SS ... OGQYGLAGPK (O: Hydroxyproline)
TT ... OGQWGLAGPK (O: Hydroxyproline)
UU ... OGQDVLAGPK (O: Hydroxyproline)
VV ... OGQDILAGPK (O: Hydroxyproline)
WW ... OGQDLLAGPK (O: Hydroxyproline)
XX ... OGQDALAGPK (O: Hydroxyproline)
YY ... OGQDFLAGPK (O: Hydroxyproline)
ZZ ... OGQDYLAGPK (O: Hydroxyproline)
AAA ... OGQDWLAGPK (O: Hydroxyproline)
BBB ... OGQDHLAGPK (O: Hydroxyproline)
CCC ... OGQDSLAGPK (O: Hydroxyproline)
DDD ... OGQDTLAGPK (O: Hydroxyproline)
EEE ... OGQD-Sar-LAGPK (Sar : me-Gly) (O: Hydroxyproline)
FFF ... OGQS*GLAGPK (S* : homo-Ser) (O: Hydroxyproline)
GGG ... OGQD*GLAGPK (D* : D(OMe)) (O: Hydroxyproline)
HHH ... OGQN*GLAGPK (N* : N(NMe)) (O: Hydroxyproline)
III ... Water

(57) **Abstract:** The present invention relates to a novel peptide and a pharmaceutical composition for treatment of eye diseases comprising the novel peptide as an active ingredient. When the novel peptide of the present invention is applied to an eye, the amount of tear secretion is increased and a damaged cornea is healed such that the novel peptide may be effectively used as a therapeutic agent for eye diseases.

(57) **요약서:** 본 발명은 신규한 펩타이드 및 이를 유효성분으로 포함하는 안구질환 치료용 약학 조성물에 관한 것이다. 본 발명의 신규한 펩타이드를 안구에 점안할 경우 눈물 분비량을 증가시키고, 손상된 각막을 회복시키므 안구질환 치료제로서 유용하게 사용될 수 있다.

[다음 쪽 계속]

(84) 지정국 (별도의 표시가 없는 한, 가능한 모든 종류의 역내 권리의 보호를 위하여): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), 유라시아 (AM, AZ, BY, KG, KZ, RU, TJ, TM), 유럽 (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

공개:

— 국제조사보고서와 함께 (조약 제21조(3))

— 청구범위 보정 기한 만료 전의 공개이며, 보정서를 접수하는 경우 그에 관하여 별도 공개함 (규칙 48.2(h))

— 명세서의 서열목록 부분과 함께 (규칙 5.2(a))

SPECIFICATION

[Title of the Invention]

NOVEL PEPTIDE AND PHARMACEUTICAL COMPOSITION FOR TREATING AN EYE DISEASE COMPRISING THE SAME AS AN ACTIVE PHARMACEUTICAL INGREDIENT

Technical Field

The present invention relates to novel peptides and pharmaceutical compositions for treating eye diseases that comprises the same as an active pharmaceutical ingredient.

Background Art

Dry eye syndrome or keratoconjunctivitis sicca may be defined, in a broad sense, as damage to the ocular surface due to tear secretion disorders (Joossen C *et al.*, *Exp. Eye Res.*, 146:172-8, 2016). Dry eye syndrome is known to cause tear secretion disorders and damage and discomfort to the eyeball due to a combination of various factors. Although the onset of dry eye syndrome is closely related to age, the incidence thereof is increasing in younger age groups due to a long-term exposure to a dry environment as the use of contact lenses, computers, and smart devices (Stern ME *et al.*, *Int. Rev. Immunol.*, 32: 19-41, 2013).

Specifically, dry eye syndrome reduces the mucus secretion of the corneal and conjunctival epithelia and that of the mucus-secreting goblet cells, resulting in a sharp decrease in the lubrication of the eyeball. In addition, dry eye syndrome causes damage to the corneal surface, thereby increasing the penetration of a fluorescein dye into the cornea. These symptoms of dry eye syndrome can be evaluated as changes in the tear secretion through the Schirmer test, which uses cobalt chloride paper. Further, the damage to the cornea that may accompany dry eye syndrome can be easily evaluated using a general fluorescent dye and a slit-lamp fluorophotometer.

In the meantime, most of the treatments for dry eye syndrome are confined to

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symptom therapies, the treatment efficiency of which is often very low. Currently, artificial tears are the first choice for the treatment of dry eye syndrome. Since artificial tears as a representative symptom therapy merely supplement the insufficient tears; moreover, they suffer from the disadvantage that they need to be administered to the eyes frequently (Kim CS *et al., Nutrients* 8. pii: E750, 2016). Sodium hyaluronate and eye drops derived from autologous serum have been developed and used in patients suffering from dry eye syndrome. In addition, such synthetic compounds as rebamipide (OPC-127959) and diquafosol sodium, which promote the secretion of tears and mucus, have been developed and used. Long-term use of these drugs, however, may give rise to various side effects such as ocular hyperemia and corneal calcification (Bemauer *Wet al., Br. J. Ophthalmol.,* 90:285-8, 2006). Therefore, there has been a demand for the development of a safe and effective therapeutic agent for treating dry eye syndrome.

Any discussion of the prior art throughout the specification should in no way be considered as an admission that such prior art is widely known or forms part of common general knowledge in the field.

Unless the context clearly requires otherwise, throughout the description and the claims, the words “comprise”, “comprising”, and the like are to be construed in an inclusive sense as opposed to an exclusive or exhaustive sense; that is to say, in the sense of “including, but not limited to”

[Disclosure of the Invention]

It is an object of the present invention to overcome or ameliorate at least one of the disadvantages of the prior art, or to provide a useful alternative.

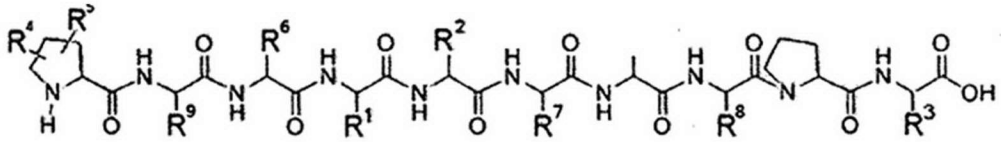
Therefore, the present inventors have endeavored to develop safe and effective therapeutic agents for treating an eye disease and, as a result, completed the present invention by way of synthesizing new peptides, administering them to the eyes of rats with dry eye syndrome, and confirming the eye protection effect through the Schirmer test and the fluorescent dye deposition test.

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One aspect of the present invention provides a compound represented by Formula 1.

In a further aspect, the present invention relates to a compound represented by Formula 1:

[Formula 1]



wherein R1 to R3 are each independently hydrogen, substituted or unsubstituted C1-6 alkyl, substituted or unsubstituted C1-10 alkoxy, substituted or unsubstituted C1-10 haloalkyl, substituted or unsubstituted C2-10 alkenyl, substituted or unsubstituted C2-10 alkynyl, substituted or unsubstituted C1-10 alkylene, substituted or unsubstituted C1-10 alkenylene, substituted or unsubstituted C1-10 alkynylene, substituted or unsubstituted C5-12 aryl, substituted or unsubstituted C7-12 arylalkyl, substituted or unsubstituted C5-14 arylalkynyl, substituted or unsubstituted C8-16 arylalkenyl, substituted or unsubstituted C3-10 heteroalkyl, substituted or unsubstituted C3-10 cycloalkyl, substituted or unsubstituted C3-10 heterocycloalkyl, or substituted or unsubstituted C5-12 heteroaryl, the heteroalkyl, heterocycloalkyl, or heteroaryl containing at least one of N, O, and S,

R4 and R5 are each independently hydrogen, substituted or unsubstituted C1-6 alkyl, -X2, -Rb, -O-, =O, -CH2ORb, or -ORb;

provided that at least one of R4 or R5 is not H;

X2 is F, Cl, Br, or I,

Rb is H, substituted or unsubstituted C1-6 alkyl, substituted or unsubstituted C5-12 aryl, substituted or unsubstituted C7-12 arylalkyl, or substituted or unsubstituted heterocycle,

R6 is hydrogen, unsubstituted C1-6 alkyl, or C1-6 alkyl substituted with -C(=O)NH2,

R7 is hydrogen or C1-6 alkyl, and

R8 and R9 are hydrogen or unsubstituted C1-6 alkyl

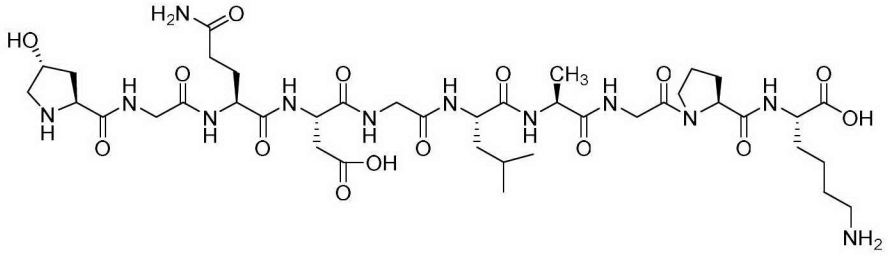
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wherein when a group is substituted, unless otherwise indicated, the substituent is selected from X1, -Ra, -O-, =O, -ORa, -SRa, -S-, -N(Ra)2, -N+(Ra)3, =NRa, -C(X1)3, -CN, -OCN, -SCN, -N=C=O, -NCS, -NO, -NO2, =N-OH, =N2, -N3, -NHC(=O)Ra, -C(=O)Ra, -C(=O)NRaRa, -S(=O)2O-, -S(=O)2OH, -S(=O)2Ra, -OS(=O)2ORa, -S(=O)2NRa, -S(=O)Ra, -OP(=O)(ORa)2, -C(=O)Ra, alkylene-C(=O)Ra, -C(=S)Ra, -C(=O)ORa, alkylene-C(=O)ORa, -C(=O)O-, alkylene-C(=O)O-, -C(=S)ORa, -C(=O)SRa, -C(=S)SRa, -C(=O)NRaRa, alkylene-C(=O)NRaRa, -C(=S)NRaRa, and -C(-NRa)NRaRa;

wherein X1 is F, Cl, Br, or I, and

Ra is hydrogen, C1-6 alkyl, C5-12 aryl, C7-12 arylalkyl, or heterocycle,

further wherein the compound is not:



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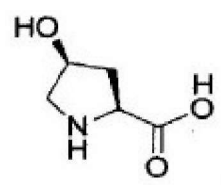
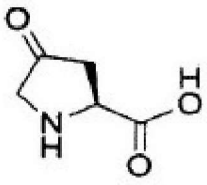
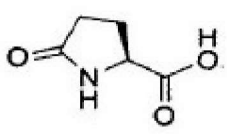
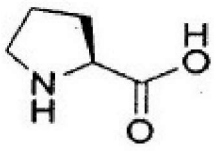
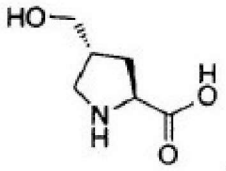
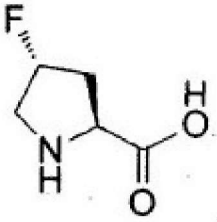
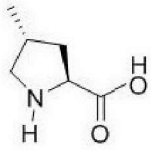
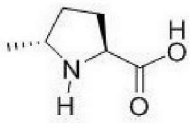
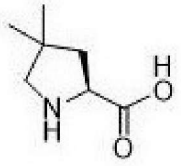
In a further aspect, the present invention relates to a peptide having an amino acid sequence represented by HyP-Gly-Gln-Xaa^1-Gly-Leu-Ala-Gly-Pro-Lys, wherein Xaa^1 is selected from Glu, Asn, Gln, His, Lys, Ser, Thr, Ala, Val, Ile, Leu, Phe, Tyr, Trp, homo-Ser, Asp(Me), and Asn(Me), preferably wherein Xaa^1 is selected from Glu, Asn, Gln, Asn, Gln, His, Lys, Ser, Thr, Ala, Val, Leu, Phe, Tyr, Trp, and homo-Ser.

In a yet a further aspect, the present invention relates to a peptide having an amino acid sequence represented by HyP-Gly-Gln-Asp-Xaa^2-Leu-Ala-Gly-Pro-Lys, wherein Xaa^2 is selected from Val, Ile, Leu, Ala, Phe, Tyr, Trp, Ser, Thr, and (N-Me)Gly.

In still a further aspect, the present invention relates to a peptide having an amino acid sequence represented by HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Xaa^3, wherein Xaa^3 is selected from Tyr, Leu, Glu, Gln, Ala, and Nle(6-OH).

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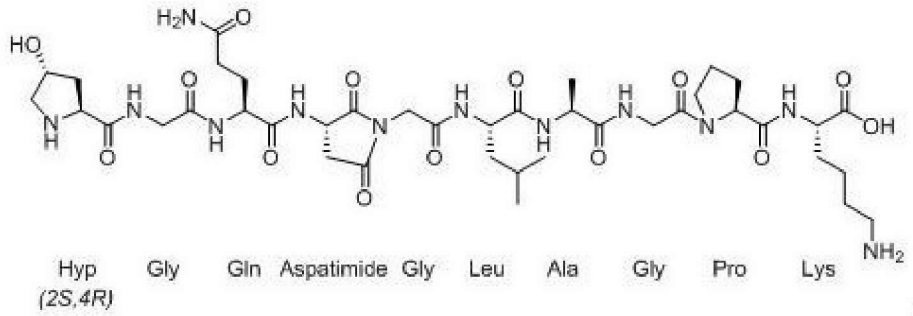
In another aspect, the present invention relates to a peptide having an amino acid sequence represented by PD-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, wherein PD is any one selected from the following formulae:


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, and

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In a further aspect, the present invention relates to a peptide having any one amino acid sequence selected from the group consisting of Ala-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, Hyp-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Ala-Lys, HyP-Gly-Gln-Leu-Gly-Leu-Ala, HyP-Gly-Gln-Glu-Gly-Lys-Gly, HyP-Gly-Gln-Leu-Gly-Leu, $_{D}$-HyP(2R, 4S)-Gly-$_{D}$-Gln-$_{D}$-Leu-Gly-$_{D}$-Leu, HyP-Gly-Gln-Leu-Gly, HyP-Gly-Gln-$_{D}$-Leu-Gly, and $_{D}$-HyP(2R, 4S)-Gly-Gln-Leu-Gly.

In a yet a further aspect, the present invention relates to A compound represented by Formula 8 or Formula 10:

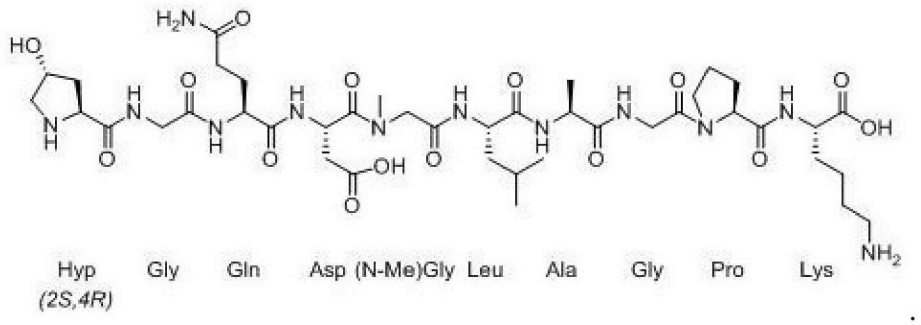
[Formula 8]



;

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[Formula 10]



.

In another aspect, the present invention relates to use of a compound according to the invention, or the peptide according to the invention, in the manufacture of a medicament for treating an eye disease, wherein the eye disease is selected from retinopathy, keratitis, dry-macular degeneration, wet-macular degeneration, dry eye syndrome, keratoconjunctivitis sicca and keratoconjunctival epithelium disorder.

In yet another aspect, the present invention relates to a method for treating an eye disease in a subject comprising administering a compound according to the invention, or the peptide according to the invention, to the subject, wherein the eye disease is selected from retinopathy, keratitis, dry-macular degeneration, wet-macular degeneration, dry eye syndrome, keratoconjunctivitis sicca and keratoconjunctival epithelium disorder.

Further, another aspect of the present invention provides a peptide having an amino acid sequence represented by HyP-Gly-Gln-Xaa-Gly-Leu-Ala-Gly-Pro-Lys.
In addition, still another aspect of the present invention provides a peptide having an amino acid sequence represented by HyP-Gly-Gln-Asp-Xaa-Leu-Ala-Gly-Pro-Lys.

Further, still another aspect of the present invention provides a peptide having an amino acid sequence represented by HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro•
Xaa.

In addition, still another aspect of the present invention provides a peptide having an amino acid sequence represented by PD-Gly-Gln-Leu-Gly-Leu-Ala-Gly• Pro-Lys.

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Further, still another aspect of the present invention provides a peptide having any one amino acid sequence selected from the group consisting of Ala-Gly-Gln• Leu-Gly-Leu-Ala-Gly-Pro-Lys, Hyp-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Ala-Lys, HyP-Gly-Gln-Leu-Gly-Leu-Ala, HyP-Gly-Gln-Glu-Gly-Leu-Gly, HyP-Gly-Gln•Leu-Gly-Leu, HyP(2R, 4$S)-Gly-Gln-pLeu-Gly--Leu, HyP-Gly-Gln-Leu-Gly, HyP-Gly-Gln-pLeu-Gly, and p HyP(2R, 4S)-Gly-Gln-Leu-Gly.

In addition, still another aspect of the present invention provides a compound represented by Formula 8.

Further, still another aspect of the present invention provides a compound represented by Formula 10.

In addition, still another aspect of the present invention provides a pharmaceutical composition for treating an eye disease, which comprises the compound or the peptide as an active pharmaceutical ingredient.

Further, still another aspect of the present invention provides a method for treating an eye disease, which comprises administering the compound or the peptide to a subject.

Effects of the Invention

When a novel peptide of the present invention is administered to the eye, it can increase the amount of tear secretion and recovers promotes recovery of the damaged cornea. Hence, they can be advantageously used as therapeutic agents for treating eye diseases.

Brief Description of the Drawings

Fig. 1 is a diagram showing the sequence and characteristics of the peptides prepared according to an embodiment of the present invention.

Fig. 2 is a diagram showing a process for synthesizing the peptides prepared according to an embodiment of the present invention.

Fig. 3 is a diagram showing a purification procedure of the peptides prepared according to an embodiment of the present invention.

Fig. 4 is a diagram confirming the purity of YDE-001 prepared according to an embodiment of the present invention through HPLC.

Fig. 5 is a diagram confirming the purity of YDE-002 prepared according to an embodiment of the present invention through HPLC.

Fig. 6 is a diagram confirming the purity of YDE-003 prepared according to an embodiment of the present invention through HPLC.

Fig. 7 is a diagram confirming the purity of YDE-004 prepared according to an embodiment of the present invention through HPLC.

Fig. 8 is a diagram confirming the purity of YDE-005 prepared according to an embodiment of the present invention through HPLC.

Fig. 9 is a diagram confirming the purity of YDE-006 prepared according to an embodiment of the present invention through HPLC.

Fig. 10 is a diagram confirming the purity of YDE-007 prepared according to an embodiment of the present invention through HPLC.

Fig. 11 is a diagram confirming the purity of YDE-008 prepared according to an embodiment of the present invention through HPLC.

Fig. 12 is a diagram confirming the purity of YDE-009 prepared according to an embodiment of the present invention through HPLC.

Fig. 13 is a diagram confirming the purity of YDE-010 prepared according to an embodiment of the present invention through HPLC.

Fig. 14 is a diagram confirming the purity of YDE-011 prepared according to an embodiment of the present invention through HPLC.

Fig. 15 is a diagram confirming the purity of YDE-012 prepared according to an embodiment of the present invention through HPLC.

Fig. 16 is a diagram confirming the purity of YDE-013 prepared according to

an embodiment of the present invention through HPLC.

Fig. 17 is a diagram confirming the purity of YDE-014 prepared according to an embodiment of the present invention through HPLC.

Fig. 18 is a diagram confirming the purity of YDE-015 prepared according to an embodiment of the present invention through HPLC.

Fig. 19 is a diagram confirming the purity of YDE-016 prepared according to an embodiment of the present invention through HPLC.

Fig. 20 is a diagram confirming the purity of YDE-017 prepared according to an embodiment of the present invention through HPLC.

Fig. 21 is a diagram confirming the purity of YDE-018 prepared according to an embodiment of the present invention through HPLC.

Fig. 22 is a diagram confirming the purity of YDE-019 prepared according to an embodiment of the present invention through HPLC.

Fig. 23 is a diagram confirming the purity of YDE-020 prepared according to an embodiment of the present invention through HPLC.

Fig. 24 is a diagram confirming the purity of YDE-021 prepared according to an embodiment of the present invention through HPLC.

Fig. 25 is a diagram confirming the purity of YDE-022 prepared according to an embodiment of the present invention through HPLC.

Fig. 26 is a diagram confirming the purity of YDE-023 prepared according to an embodiment of the present invention through HPLC.

Fig. 27 is a diagram confirming the purity of YDE-024 prepared according to an embodiment of the present invention through HPLC.

Fig. 28 is a diagram confirming the purity of YDE-025 prepared according to an embodiment of the present invention through HPLC.

Fig. 29 is a diagram confirming the purity of YDE-026 prepared according to an embodiment of the present invention through HPLC.

Fig. 30 is a diagram confirming the purity of YDE-027 prepared according to an embodiment of the present invention through HPLC.

Fig. 31 is a diagram confirming the purity of YDE-028 prepared according to an embodiment of the present invention through HPLC.

Fig. 32 is a diagram confirming the purity of YDE-029 prepared according to an embodiment of the present invention through HPLC.

Fig. 33 is a diagram confirming the purity of YDE-030 prepared according to an embodiment of the present invention through HPLC.

Fig. 34 is a diagram confirming the purity of YDE-031 prepared according to an embodiment of the present invention through HPLC.

Fig. 35 is a diagram confirming the purity of YDE-032 prepared according to an embodiment of the present invention through HPLC.

Fig. 36 is a diagram confirming the purity of YDE-033 prepared according to an embodiment of the present invention through HPLC.

Fig. 37 is a diagram confirming the purity of YDE-034 prepared according to an embodiment of the present invention through HPLC.

Fig. 38 is a diagram confirming the purity of YDE-035 prepared according to an embodiment of the present invention through HPLC.

Fig. 39 is a diagram confirming the purity of YDE-036 prepared according to an embodiment of the present invention through HPLC.

Fig. 40 is a diagram confirming the purity of YDE-037 prepared according to an embodiment of the present invention through HPLC.

Fig. 41 is a diagram confirming the purity of YDE-038 prepared according to an embodiment of the present invention through HPLC.

Fig. 42 is a diagram confirming the purity of YDE-039 prepared according to an embodiment of the present invention through HPLC.

Fig. 43 is a diagram confirming the purity of YDE-040 prepared according to an embodiment of the present invention through HPLC.

Fig. 44 is a diagram confirming the purity of YDE-041 prepared according to an embodiment of the present invention through HPLC.

Fig. 45 is a diagram confirming the purity of YDE-042 prepared according to an embodiment of the present invention through HPLC.

Fig. 46 is a diagram confirming the purity of YDE-043 prepared according to an embodiment of the present invention through HPLC.

Fig. 47 is a diagram confirming the purity of YDE-044 prepared according to

an embodiment of the present invention through HPLC.

Fig. 48 is a diagram confirming the purity of YDE-045 prepared according to an embodiment of the present invention through HPLC.

Fig. 49 is a diagram confirming the purity of YDE-047 prepared according to an embodiment of the present invention through HPLC.

Fig. 50 is a diagram confirming the purity of YDE-048 prepared according to an embodiment of the present invention through HPLC.

Fig. 51 is a diagram confirming the purity of YDE-049 prepared according to an embodiment of the present invention through HPLC.

Fig. 52 is a diagram confirming the purity of YDE-050 prepared according to an embodiment of the present invention through HPLC.

Fig. 53 is a diagram confirming the purity of YDE-051 prepared according to an embodiment of the present invention through HPLC.

Fig. 54 is a diagram confirming the purity of YDE-052 prepared according to an embodiment of the present invention through HPLC.

Fig. 55 is a diagram confirming the purity of YDE-053 prepared according to an embodiment of the present invention through HPLC.

Fig. 56 is a diagram confirming the purity of YDE-054 prepared according to an embodiment of the present invention through HPLC.

Fig. 57 is a diagram confirming the purity of YDE-055 prepared according to an embodiment of the present invention through HPLC.

Fig. 58 is a diagram confirming the purity of YDE-056 prepared according to an embodiment of the present invention through HPLC.

Fig. 59 is a diagram confirming the purity of YDE-057 prepared according to an embodiment of the present invention through HPLC.

Fig. 60 is a diagram confirming the purity of YDE-058 prepared according to an embodiment of the present invention through HPLC.

Fig. 61 is a diagram confirming the purity of YDE-059 prepared according to an embodiment of the present invention through HPLC.

Fig. 62 is a diagram confirming the purity of YDE-060 prepared according to an embodiment of the present invention through HPLC.

Fig. 63 is a diagram confirming the purity of YDE-064 prepared according to an embodiment of the present invention through HPLC.

Fig. 64 is a diagram confirming the purity of YDE-066 prepared according to an embodiment of the present invention through HPLC.

Fig. 65 is a diagram confirming the purity of YDE-072 prepared according to an embodiment of the present invention through HPLC.

Fig. 66 is a diagram confirming the purity of YDE-073 prepared according to an embodiment of the present invention through HPLC.

Fig. 67 is a diagram confirming the purity of YDE-074 prepared according to an embodiment of the present invention through HPLC.

Fig. 68 is a diagram confirming the purity of YDE-075 prepared according to an embodiment of the present invention through HPLC.

Fig. 69 is a diagram confirming the molecular weight of YDE-001 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 70 is a diagram confirming the molecular weight of YDE-002 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 71 is a diagram confirming the molecular weight of YDE-003 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 72 is a diagram confirming the molecular weight of YDE-004 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 73 is a diagram confirming the molecular weight of YDE-005 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 74 is a diagram confirming the molecular weight of YDE-006 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 75 is a diagram confirming the molecular weight of YDE-007 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 76 is a diagram confirming the molecular weight of YDE-008 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 77 is a diagram confirming the molecular weight of YDE-009 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 78 is a diagram confirming the molecular weight of YDE-010 prepared

according to an embodiment of the present invention through Ion-Mass.

Fig. 79 is a diagram confirming the molecular weight of YDE-011 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 80 is a diagram confirming the molecular weight of YDE-012 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 81 is a diagram confirming the molecular weight of YDE-013 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 82 is a diagram confirming the molecular weight of YDE-014 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 83 is a diagram confirming the molecular weight of YDE-015 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 84 is a diagram confirming the molecular weight of YDE-016 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 85 is a diagram confirming the molecular weight of YDE-017 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 86 is a diagram confirming the molecular weight of YDE-018 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 87 is a diagram confirming the molecular weight of YDE-019 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 88 is a diagram confirming the molecular weight of YDE-020 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 89 is a diagram confirming the molecular weight of YDE-021 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 90 is a diagram confirming the molecular weight of YDE-022 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 91 is a diagram confirming the molecular weight of YDE-023 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 92 is a diagram confirming the molecular weight of YDE-024 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 93 is a diagram confirming the molecular weight of YDE-025 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 94 is a diagram confirming the molecular weight of YDE-026 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 95 is a diagram confirming the molecular weight of YDE-027 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 96 is a diagram confirming the molecular weight of YDE-028 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 97 is a diagram confirming the molecular weight of YDE-029 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 98 is a diagram confirming the molecular weight of YDE-030 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 99 is a diagram confirming the molecular weight of YDE-031 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 100 is a diagram confirming the molecular weight of YDE-032 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 101 is a diagram confirming the molecular weight of YDE-033 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 102 is a diagram confirming the molecular weight of YDE-034 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 103 is a diagram confirming the molecular weight of YDE-035 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 104 is a diagram confirming the molecular weight of YDE-036 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 105 is a diagram confirming the molecular weight of YDE-037 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 106 is a diagram confirming the molecular weight of YDE-038 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 107 is a diagram confirming the molecular weight of YDE-039 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 108 is a diagram confirming the molecular weight of YDE-040 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 109 is a diagram confirming the molecular weight of YDE-041 prepared

according to an embodiment of the present invention through Ion-Mass.

Fig. 110 is a diagram confirming the molecular weight of YDE-042 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 111 is a diagram confirming the molecular weight of YDE-043 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 112 is a diagram confirming the molecular weight of YDE-044 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 113 is a diagram confirming the molecular weight of YDE-045 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 114 is a diagram confirming the molecular weight of YDE-047 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 115 is a diagram confirming the molecular weight of YDE-048 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 116 is a diagram confirming the molecular weight of YDE-049 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 117 is a diagram confirming the molecular weight of YDE-050 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 118 is a diagram confirming the molecular weight of YDE-051 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 119 is a diagram confirming the molecular weight of YDE-052 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 120 is a diagram confirming the molecular weight of YDE-053 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 121 is a diagram confirming the molecular weight of YDE-054 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 122 is a diagram confirming the molecular weight of YDE-055 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 123 is a diagram confirming the molecular weight of YDE-056 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 124 is a diagram confirming the molecular weight of YDE-057 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 125 is a diagram confirming the molecular weight of YDE-058 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 126 is a diagram confirming the molecular weight of YDE-059 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 127 is a diagram confirming the molecular weight of YDE-060 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 128 is a diagram confirming the molecular weight of YDE-064 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 129 is a diagram confirming the molecular weight of YDE-066 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 130 is a diagram confirming the molecular weight of YDE-072 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 131 is a diagram confirming the molecular weight of YDE-073 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 132 is a diagram confirming the molecular weight of YDE-074 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 133 is a diagram confirming the molecular weight of YDE-075 prepared according to an embodiment of the present invention through Ion-Mass.

Fig. 134 is a photograph showing a procedure of extraorbital lacrimal gland excision.

Fig. 135 is a diagram showing a change in the body weight of a rat model whose eyes have been administered with YDE-001 to YDE-028.

Fig. 136 is a diagram showing a change in the body weight of a rat model whose eyes have been administered with YDE-029 to YDE-043.

Fig. 137 is a photograph showing a procedure of administering an agent to the eyes of a rat model.

Fig. 138 is a photograph showing a procedure of measuring the amount of tear secretion of a rat model using cobalt chloride paper.

Fig. 139 is a photograph showing the results of measuring the amount of tear secretion of a rat model whose eyes have been administered with YDE-001 to YDE-028 using cobalt chloride paper.

Fig. 140 is a diagram showing the changes in the amount of tear secretion of a rat model whose eyes have been administered with YDE-001 to YDE-028.

Fig. 141 is a photograph showing the results of measuring the amount of tear secretion of a rat model whose eyes have been administered with YDE-029 to YDE-043 using cobalt chloride paper.

Fig. 142 is a diagram showing the changes in the amount of tear secretion of a rat model whose eyes have been administered with YDE-029 to YDE-043.

Fig. 143 is a photograph showing a procedure of administering a fluorescent substance to the eyes of a rat model for confirming damage to the cornea thereof.

Fig. 144 is a photograph showing the results of measuring damage to the cornea of a rat model whose eyes have been administered with YDE-001 to YDE-028 using a fluorescent substance.

Fig. 145 is a diagram showing the permeability of a fluorescence dye to confirm the recovery of corneal damage of a rat model whose eyes have been administered with YDE-001 to YDE-028.

Fig. 146 is a photograph showing the results of measuring damage to the cornea of a rat model whose eyes have been administered with YDE-029 to YDE-043 using a fluorescent substance.

Fig. 147 is a diagram showing the permeability of a fluorescence dye to confirm the recovery of corneal damage of a rat model whose eyes have been administered with YDE-029 to YDE-043.

FIG. 148 is a diagram showing the cell growth rate after 48 hours from the treatment of hEGF on human corneal epithelial cells of plate No. 1.

FIG. 149 is a diagram showing the cell growth rate after 48 hours from the treatment of hEGF on human corneal epithelial cells of plate No. 2.

FIG. 150 is a diagram showing the cell growth rate after 48 hours from the treatment of hEGF on human corneal epithelial cells of plate No. 3.

FIG. 151 is a diagram showing the cell growth rate after 48 hours from the treatment of hEGF on human corneal epithelial cells of plate No. 4.

FIG. 152 is a diagram showing the cell growth rate after 72 hours from the treatment of hEGF on human corneal epithelial cells of plate No. 1.

FIG. 153 is a diagram showing the cell growth rate after 72 hours from the treatment of hEGF on human corneal epithelial cells of plate No. 2.

FIG. 154 is a diagram showing the cell growth rate after 72 hours from the treatment of hEGF on human corneal epithelial cells of plate No. 3.

FIG. 155 is a diagram showing the cell growth rate after 48 hours from the treatment of hEGF on human corneal epithelial cells of plate No. 4.

FIG. 156 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72 hours from the treatment of YY-101 on human corneal epithelial cells.

FIG. 157 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72 hours from the treatment of YY-102 on human corneal epithelial cells.

FIG. 158 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72 hours from the treatment of YDE-011 on human corneal epithelial cells.

FIG. 159 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72 hours from the treatment of YDE-038 on human corneal epithelial cells.

FIG. 160 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72 hours from the treatment of YDE-042 on human corneal epithelial cells.

FIG. 161 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72 hours from the treatment of YDE-043 on human corneal epithelial cells.

FIG. 162 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72 hours from the treatment of YDE-044 on human corneal epithelial cells.

FIG. 163 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72 hours from the treatment of YDE-045 on human corneal epithelial cells.

FIG. 164 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72 hours from the treatment of YDE-049 on human corneal epithelial cells.

FIG. 165 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72 hours from the treatment of YDE-054 on human corneal epithelial cells.

FIG. 166 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72 hours from the treatment of YDE-057 on human corneal epithelial cells.

FIG. 167 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72 hours from the treatment of YDE-058 on human corneal epithelial cells.

FIG. 168 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72

hours from the treatment of YDE-059 on human corneal epithelial cells.

FIG. 169 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72 hours from the treatment of YDE-060 on human corneal epithelial cells.

FIG. 170 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72 hours from the treatment of YDE-072 on human corneal epithelial cells.

FIG. 171 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72 hours from the treatment of YDE-073 on human corneal epithelial cells.

FIG. 172 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72 hours from the treatment of YDE-074 on human corneal epithelial cells.

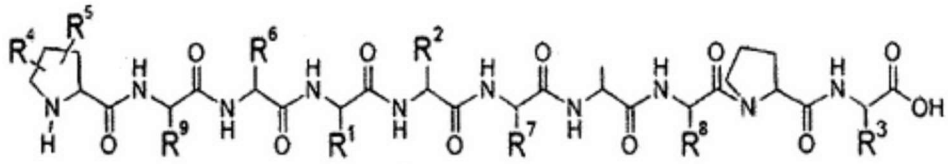
FIG. 173 is a diagram showing the cell growth rate after (a) 48 hours or (b) 72 hours from the treatment of YDE-075 on human corneal epithelial cells.

Detailed Description of the Invention

Hereinafter, the present invention will be described in detail.

An aspect of the present invention provides a compound represented by Formula 1.

[Formula 1]



In the above formula,

R^1 to R^3 are each independently hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{1-10} alkoxy, substituted or unsubstituted C_{1-10} haloalkyl, substituted or unsubstituted C_{2-10} alkenyl, substituted or unsubstituted C_{2-10} alkynyl, substituted or unsubstituted C_{1-10} alkylene, substituted or unsubstituted C_{1-10} alkenylene, substituted or unsubstituted C_{1-10} alkynylene, substituted or unsubstituted C_{5-12} aryl, substituted or unsubstituted C_{7-12} arylalkyl, substituted or unsubstituted C_{5-14} arylalkynyl, substituted or unsubstituted C_{8-16} arylalkenyl, substituted or unsubstituted C_{3-10} heteroalkyl, substituted or unsubstituted C_{3-10} cycloalkyl, substituted or unsubstituted C_{3-10} heterocycloalkyl, or substituted or

unsubstituted C_{5-12} heteroaryl, the heteroalkyl, heterocycloalkyl, or heteroaryl containing at least one of N, O, and S,

the substitution refers to a substitution with one or more non-hydrogen substituents, each non-hydrogen substituent being selected from the group consisting of $-X_1$, $-R_a$, $-O^-$, $=O$, $-OR_a$, $-SR_a$, $-S^-$, $-N(R_a)_2$, $-N^+(R_a)_3$, $=NR_a$, $-C(X_1)_3$, -CN, -OCN, -SCN, -N=C=O, -NCS, -NO, $-NO_2$, =N-OH, $=N_2$, $-N_3$, $-NHC(=O)R_a$, $-C(=O)R_a$, $-C(=O)NR_aR_a$, $-S(=O)_2O^-$, $-S(=O)_2OH$, $-S(=O)_2R_a$, $-OS(=O)_2OR_a$, $-S(=O)_2NR_a$, $-S(=O)R_a$, $-OP(=O)(OR_a)_2$, $-C(=O)R_a$, alkylene-$C(=O)R_a$, $-C(=S)R_a$, $-C(=O)OR_a$, alkylene-$C(=O)OR_a$, $-C(=O)O^-$, alkylene-C(=O)O-, $-C(=S)OR_a$, $-C(=O)SR_a$, $-C(=S)SR_a$, $-C(=O)NR_aR_a$, alkylene-$C(=O)NR_aR_a$, $-C(=S)NR_aR_a$, and $-C(-NR_a)NR_aR_a$, each X_1 is independently selected from F, Cl, Br, or I, each R_a is independently selected from hydrogen, C_{1-6} alkyl, C_{5-12} aryl, C_{7-12} arylalkyl, or heterocycle,

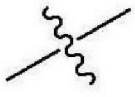
R^4 and R^5 are each independently hydrogen, substituted or unsubstituted C_{1-6} alkyl, $-X_2$, $-R_b$, $-O^-$, $=O$, $-CH_2OR_b$, or $-OR_b$, X_2 is F, Cl, Br, or I, and R_b is H, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{5-12} aryl, substituted or unsubstituted C_{7-12} arylalkyl, or substituted or unsubstituted heterocycle,

R^6 is hydrogen or substituted or unsubstituted C_{1-6} alkyl, the substituent being $-C(=O)NH_2$,

R^7 is hydrogen or C_{1-6} alkyl, and

R^8 and R^9 are each independently hydrogen or unsubstituted C_{1-6} alkyl.

In the definition of R_b, the substitution refers to a substitution with the non-hydrogen substituent.

According to the convention used in the art,  in the formulae herein is used to denote a bond, where a moiety or a substituent is attached to the nucleus or the backbone structure.

"Alkyl" is a hydrocarbon having primary, secondary, tertiary, and/or cyclic carbon atoms. For example, an alkyl group may have 1 to 20 carbon atoms (i.e., C_1-C_{20} alkyl), 1 to 10 carbon atoms (i.e., C_1-C_{10} alkyl), or 1 to 6 carbon atoms (i.e., C_1-

C_6 alkyl). Examples of a suitable alkyl group include methyl (Me, $-CH_3$), ethyl (Et, $-CH_2CH_3$), 1-propyl (n-Pr, n-propyl, $-CH_2CH_2CH_3$), 2-propyl (i-Pr, i-propyl, $-CH(CH_3)_2$), 1-butyl (n-Bu, n-butyl, $-CH_2CH_2CH_2CH_3$), 2-methyl-1-propyl (i-Bu, i-butyl, $-CH_2CH(CH_3)_2$), 2-butyl (s-Bu, s-butyl, $-CH(CH_3)CH_2CH_3$), 2-methyl-2-propyl (t-Bu, t-butyl, $-C(CH_3)_3$), 1-pentyl (n-pentyl, $-CH_2CH_2CH_2CH_2CH_3$), 2-pentyl ($-CH(CH_3)CH_2CH_2CH_3$), 3-pentyl ($-CH(CH_2CH_3)_2$), 2-methyl-2-butyl ($-C(CH_3)_2CH_2CH_3$), 3-methyl-2-butyl ($-CH(CH_3)CH(CH_3)_2$), 3-methyl-1-butyl ($-CH_2CH_2CH(CH_3)_2$), 2-methyl-1-butyl ($-CH_2CH(CH_3)CH_2CH_3$), 1-hexyl ($-CH_2CH_2CH_2CH_2CH_2CH_3$), 2-hexyl ($-CH(CH_3)CH_2CH_2CH_2CH_3$), 3-hexyl ($-CH(CH_2CH_3)(CH_2CH_2CH_3)$), 2-methyl-2-pentyl ($-C(CH_3)_2CH_2CH_2CH_3$), 3-methyl-2-pentyl ($-CH(CH_3)CH(CH_3)CH_2CH_3$), 4-methyl-2-pentyl ($-CH(CH_3)CH_2CH(CH_3)_2$), 3-methyl-3-pentyl ($-C(CH_3)(CH_2CH_3)_2$), 2-methyl-3-pentyl ($-CH(CH_2CH_3)CH(CH_3)_2$), 2,3-dimethyl-2-butyl ($-C(CH_3)_2CH(CH_3)_2$), 3,3-dimethyl-2-butyl ($-CH(CH_3)C(CH_3)_3$), and octyl ($-(CH_2)_7CH_3$), but it is not limited thereto.

"Alkoxy" refers to a group having the formula -O-alkyl, wherein the alkyl group as defined above is attached to the parent compound via an oxygen atom. The alkyl moiety of the alkoxy group may have 1 to 20 carbon atoms (i.e., C_1-C_{20} alkoxy), 1 to 12 carbon atoms (i.e., C_1-C_{12} alkoxy), or 1 to 6 carbon atoms (i.e., C_1-C_6 alkoxy). Examples of a suitable alkoxy group include methoxy ($-O-CH_3$ or -OMe), ethoxy ($-OCH_2CH_3$ or -OEt), and t-butoxy ($-OC(CH_3)_3$ or -O-tBu), but it is not limited thereto.

"Haloalkyl" is an alkyl group in which at least one of the hydrogen atoms of the alkyl group as defined above is substituted by a halogen atom. The alkyl moiety of the haloalkyl group may have 1 to 20 carbon atoms (i.e., C_1-C_{20} haloalkyl), 1 to 12 carbon atoms (i.e., C_1-C_{12} haloalkyl), or 1 to 6 carbon atoms (i.e., C_1-C_6 haloalkyl). Examples of a suitable haloalkyl group include $-CF_3$, $-CHF_2$, $-CFH_2$, and $-CH_2CF_3$, but it is not limited thereto.

"Alkenyl" is a hydrocarbon having primary, secondary, tertiary, and/or cyclic carbon atoms, and having at least one unsaturated region, i.e., a carbon-carbon sp^2 double bond. For example, an alkenyl group may have 2 to 20 carbon atoms (i.e.,

C_2-C_{20} alkenyl), 2 to 12 carbon atoms (i.e., C_2-C_{12} alkenyl), or 2 to 6 carbon atoms (i.e., C_2-C_6 alkenyl). Examples of a suitable alkenyl group include vinyl (-CH=CH_2), allyl (-CH_2CH=CH_2), cyclopentenyl (-C_5H_7), and 5-hexenyl (-$CH_2CH_2CH_2CH_2$CH=CH_2), but it is not limited thereto.

"Alkynyl" is a hydrocarbon having primary, secondary, tertiary, and/or cyclic carbon atoms, and having at least two unsaturated regions, i.e., one carbon-carbon sp triple bond. For example, an alkynyl group may have 2 to 20 carbon atoms (i.e., C_2-C_{20} alkynyl), 2 to 12 carbon atoms (i.e., C_2-C_{12} alkynyl), or 2 to 6 carbon atoms (i.e., C_2-C_6 alkynyl). Examples of a suitable alkenyl group include acetylenic (-C≡CH) and propargyl (-CH_2C≡CH), but it is not limited thereto.

"Alkylene" refers to a saturated hydrocarbon group that may be branched, straight, or cyclic and has two valencies derived by a removal of two hydrogen atoms from the same carbon atom or two different carbon atoms of a parent alkane. For example, an alkylene group may have 1 to 20 carbon atoms, 1 to 10 carbon atoms, or 1 to 6 carbon atoms. Examples of a typical alkylene radical include methylene (-CH_2-), 1,1-ethylene (-CH(CH_3)-), 1,2-ethylene (-CH_2CH_2-), 1,1-propylene (-CH(CH_2CH_3)-), 1,2-propylene (-CH_2CH(CH_3)-), 1,3-propylene (-$CH_2CH_2CH_2$-), and 1,4-butylene (-$CH_2CH_2CH_2CH_2$-), but it is not limited thereto.

"Alkenylene" refers to an unsaturated hydrocarbon group that may be branched, straight, and/or cyclic and has two valencies derived by a removal of two hydrogen atoms from the same carbon atom or two different carbon atoms of a parent alkene. For example, an alkenylene group may have 1 to 20 carbon atoms, 1 to 10 carbon atoms, or 1 to 6 carbon atoms. Examples of a typical alkenylene group include 1,2-ethylene (-CH=CH-), but it is not limited thereto.

"Alkynylene" refers to an unsaturated hydrocarbon group that is branched, straight, and/or cyclic and has two valencies derived by a removal of two hydrogen atoms from the same carbon atom or two different carbon atoms of a parent alkyne. For example, an alkynylene group may have 1 to 20 carbon atoms, 1 to 10 carbon atoms, or 1 to 6 carbon atoms. Examples of a typical alkynylene radical include acetylenylene (-C≡C-), propargylene (-CH_2C≡C-), and 4-pentynylene (-$CH_2CH_2CH_2$C≡C-), but it is not limited thereto.

"Aryl" refers to an aromatic hydrocarbon group derived by a removal of one hydrogen atom from the six carbon atoms of a parent aromatic ring system. For example, an aryl group may have 6 to 20 carbon atoms, 6 to 14 carbon atoms, or 6 to 12 carbon atoms. Examples of a typical aryl group include a radical derived from benzene (e.g., phenyl), substituted benzene, substituted or unsubstituted naphthalene, substituted or unsubstituted anthracene, substituted or unsubstituted biphenyl, and the like, but it is not limited thereto.

"Arylalkyl" refers to an acyclic alkyl group in which one hydrogen atom bonded to a carbon atom, typically a terminal or other sp3 carbon atom, is substituted by an aryl group. Examples of a typical arylalkyl group include benzyl, 2-phenylethan-1-yl, naphthylmethyl, 2-naphthylethane-1-yl, naphthobenzyl, 2-naphthophenylethane-1-yl, and the like (each of which is substituted or unsubstituted), but it is not limited thereto. An arylalkyl group may have 7 to 20 carbon atoms. For example, the alkyl moiety thereof may have 1 to 6 carbon atoms, and the aryl moiety thereof may have 6 to 14 carbon atoms.

"Arylalkenyl" refers to an acyclic alkenyl radical in which one of the hydrogen atoms bonded to a carbon atom, typically a terminal or sp3 carbon atom although an sp2 carbon atom is also available, is substituted with an aryl radical. The aryl moiety of the arylalkenyl may be, for example, any aryl group described herein, and the alkenyl moiety of the arylalkenyl may comprise, for example, any of the alkenyl groups described herein. An arylalkenyl group may have 8 to 20 carbon atoms. For example, the alkenyl moiety thereof may have 2 to 6 carbon atoms, and the aryl moiety thereof may have 6 to 14 carbon atoms.

"Cycloalkyl" refers to a saturated monocycle or polycycle that comprises only carbon atoms in the ring. A cycloalkyl group may have 3 to 7 carbon atoms as a monocycle, 7 to 12 carbon atoms as a bicycle, and up to about 20 carbon atoms as a polycycle. A monocyclic cycloalkyl has 3 to 6 ring atoms, more typically 5 or 6 ring atoms. A bicyclic cycloalkyl may have 7 to 12 ring atoms arranged in a bicyclo[4,5], [5,5], [5,6], or [6,6] system or 9 to 10 ring atoms arranged in a bicyclo[5,6] or [6,6] system or in a spiro-bonded ring. Non-limiting examples of a monocyclic cycloalkyl include cyclopropyl, cyclobutyl, cyclopentyl, and

cyclohexyl (each of which may be substituted or unsubstituted).

"Arylalkynyl" refers to an acyclic alkynyl group in which one of the hydrogen atoms bonded to a carbon atom, typically a terminal or other sp3 carbon atom, although an sp carbon atom may also be used, is substituted by an aryl group. The aryl moiety of the arylalkynyl may be, for example, any aryl group described herein, and the alkynyl moiety of the arylalkynyl may comprise, for example, any of the alkynyl groups described herein. An arylalkynyl group may have 8 to 20 carbon atoms. For example, the alkynyl moiety thereof may have 2 to 6 carbon atoms, and the aryl moiety thereof may have 6 to 14 carbon atoms.

The term "substituted" with respect to alkyl, alkylene, aryl, arylalkyl, heterocyclyl, and the like, for example, "substituted alkyl," "substituted alkylene," "substituted aryl," "substituted arylalkyl," "substituted heterocyclyl," and "substituted carbocyclyl (e.g., substituted cycloalkyl)," means that at least one hydrogen atom of the alkyl, alkylene, aryl, arylalkyl, heterocyclyl, or carbocyclyl (e.g., cycloalkyl) is each independently substituted by a non-hydrogen substituent. Examples of the typical substituent include -X, -R, $-O^-$, =O, -OR, -SR, $-S^-$, $-NR_2$, $-N^+R_3$, =NR, $-C(X)_3$, -CN, -OCN, -SCN, -N=C=O, -NCS, -NO, $-NO_2$, =N-OH, $=N_2$, $-N_3$, -NHC(=O)R, -C(=O)R, -C(=O)NRR, $-S(=O)_2O^-$, $-S(=O)_2OH$, $-S(=O)_2R$, $-OS(=O)_2OR$, $-S(=O)_2NR$, -S(=O)R, $-OP(=O)(OR)_2$, -C(=O)R, alkylene-C(=O)R, -C(S)R, -C(=O)OR, alkylene-C(=O)OR, $-C(=O)O^-$, alkylene-C(=O)O-, -C(=S)OR, -C(=O)SR, -C(=S)SR, -C(=O)NRR, alkylene-C(=O)NRR, -C(=S)NRR, and -C(=NR)NRR, wherein X is each independently halogen such as F, Cl, Br, or I, and R is independently H, alkyl, aryl, arylalkyl, or heterocycle, but it is not limited thereto. The alkylene, alkenylene, and alkynylene groups may also be similarly substituted.

Those skilled in the art will understand that when a moiety such as "alkyl," "aryl," "heterocyclyl," and the like is substituted with at least one substituent, they may optionally be referred to as a moiety of "alkylene," "arylene," "heterocyclylene," or the like (that is, at least one hydrogen atom of the parent "alkyl," "aryl," or "heterocyclyl" moiety is substituted by the substituent as described herein). If the moiety of "alkyl," "aryl," "heterocyclyl," or the like is described herein as "substituted" or depicted in the drawings as substituted (or

optionally substituted, for example, the number of substituents is 0 or a positive number), the term "alkyl," "aryl," "heterocyclyl," or the like should be understood to be interchangeable with "alkylene," "arylene," "heterocyclylene," or the like.

Those skilled in the art will recognize that the substituents and other moieties of the compound of Formula 1 should be selected so as to provide a compound that is sufficiently stable as a pharmaceutically useful compound that can be formulated into an acceptably stable pharmaceutical composition. The compound of Formula 1 having such stability is to be understood to fall within the scope of the present invention.

"Heteroalkyl" refers to an alkyl group in which at least one carbon atom is substituted by a heteroatom such as O, N, or S. For example, if a carbon atom of the alkyl group attached to a parent molecule is substituted by a heteroatom (e.g., O, N, or S), the resulting heteroalkyl group may be an alkoxy group (e.g., $-OCH_3$), an amine group (e.g., $-NHCH_3$, $-N(CH_3)_2$, or the like), or a thioalkyl group (e.g., $-SCH_3$), respectively. If a non-terminal carbon atom of the alkyl group that is not attached to a parent molecule is substituted by a heteroatom (e.g., O, N, or S), the resulting heteroalkyl group may be an alkyl ether (e.g., $-CH_2CH_2-O-CH_3$ or the like), an alkylamine (e.g., $-CH_2NHCH_3$, $-CH_2N(CH_3)_2$, or the like), or a thioalkyl ether (e.g., $-CH_2-S-CH_3$), respectively. If the terminal carbon atom of the alkyl group is substituted by a heteroatom (for example, O, N, or S), the resulting heteroalkyl group may be a hydroxyalkyl group (e.g., $-CH_2CH_2-OH$), an aminoalkyl group (e.g., $-CH_2NH_2$), or an alkylthiol group (e.g., $-CH_2CH_2-SH$), respectively. For example, a heteroalkyl group may have 1 to 20 carbon atoms, 1 to 10 carbon atoms, or 1 to 6 carbon atoms. A C_1-C_6 heteroalkyl group refers to a heteroalkyl group having 1 to 6 carbon atoms.

The term "heterocycle" or "heterocyclyl" used herein includes those described in the documents such as Paquette, Leo A., Principles of Modern Heterocyclic Chemistry (W. A. Benjamin, New York, 1968), specifically Chapters 1, 3, 4, 6, 7, and 9; The Chemistry of Heterocyclic Compounds, A Series of Monographs (John Wiley & Sons, New York, from 1950 to the present), specifically Volumes 13, 14, 16, 19, and 28; and J. Am. Chem. Soc. (1960) 82:5566, but it is not limited thereto.

In a specific embodiment of the present invention, "heterocycle" includes "carbocycle" as defined herein in which at least one (e.g., 1, 2, 3, or 4) carbon atom is substituted by a heteroatom (e.g., O, N, or S). The term "heterocycle" or "heterocyclyl" includes saturated, partially unsaturated, and aromatic rings (i.e., a heteroaromatic ring). Substituted heterocycle, for example, includes a heterocyclic ring substituted with any of the substituents disclosed herein, inclusive of a carbonyl group.

Examples of heterocycles include pyridyl, dihydropyridyl, tetrahydropyridyl(piperidyl), thiazolyl, tetrahydrothiophenyl, sulfur-oxidized tetrahydrothiophenyl, pyrimidinyl, furanyl, thienyl, pyrrolyl, pyrazolyl, imidazolyl, tetrazolyl, benzofuranyl, thianaphthalenyl, indolyl, indolenyl, quinolinyl, isoquinolinyl, benzimidazolyl, piperidinyl, 4-piperidinyl, pyrrolidinyl, 2-pyrrolidonyl, pyrrolinyl, tetrahydrofuranyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, decahydroquinolinyl, octahydroisoquinolinyl, azocynyl, triazinyl, 6H-1,2,5-thiadiazinyl, 2H,6H-1,5,2-dithiazinyl, thienyl, thianthrenyl, pyranyl, isobenzofuranyl, chromenyl, xanthenyl, phenoxatinyl, 2H-pyrrolyl, isothiazolyl, isoxazolyl, pyrazinyl, pyridazinyl, indolizinyl, isoindolyl, 3H-indolyl, 1H-indazoly, purinyl, 4H-quinolizinyl, phthalazinyl, naphthyridinyl, quinoxalinyl, quinazolinyl, cinnolinyl, phtheridinyl, 4aH-carbazolyl, carbazolyl, β-carbolinyl, phenanthridinyl, acridinyl, pyrimidinyl, phenanthrolinyl, phenazinyl, phenothiazinyl, furazanyl, phenoxazinyl, isochromanyl, chromanyl, imidazolidinyl, imidazolinyl, pyrazolidinyl, pyrazolinyl, piperazinyl, indolinyl, isoindolinyl, quinuclidinyl, morpholinyl, oxazolidinyl, benzotriazolyl, benzisoxazolyl, oxindolyl, benzoxazolinyl, isothinoyl, and bis-tetrahydrofuranyl (each of which may be substituted or unsubstituted), but it is not limited thereto.

As an example, a carbon-bonded heterocycle may be bonded at the 2, 3, 4, 5, or 6-position of pyrazine, at the 3, 4, 5, or 6-position of pyridazine, at the 2, 4, 5, or 6-position of pyrimidine, at the 2, 3, 5, or 6-position of pyrazine, at the 2, 3, 4, or 5-position of furan, tetrahydrofuran, thiofuran, thiophene, pyrrole, or tetrahydropyrrole, at the 2, 4, or 5-position of oxazole, imidazole, or thiazole, at the 3, 4, or 5-position of isoxazole, pyrazole, or isothiazole, at the 2 or 3-position of

aziridine, at the 2, 3, or 4-position of azetidine, at the 2, 3, 4, 5, 6, 7, or 8-position of quinoline, or at the 1, 3, 4, 5, 6, 7, or 8-position of isoquinoline, but it is not limited thereto. More typically, examples of a carbon-bonded heterocycle include 2-pyridyl, 3-pyridyl, 4-pyridyl, 5-pyridyl, 6-pyridyl, 3-pyridazinyl, 4-pyridazinyl, 5-pyridazinyl, 6-pyridazinyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 6-pyrimidinyl, 2-pyrazinyl, 3-pyrazinyl, 5-pyrazinyl, 6-pyrazinyl, 2-thiazolyl, 4-thiazolyl, and 5-thiazolyl (each of which may be substituted or unsubstituted).

As an example, a nitrogen-bonded heterocycle may be bonded at the 1-position of aziridine, azetidine, pyrrole, pyrrolidine, 2-pyrroline, 3-pyrroline, imidazole, imidazolidine, 2-imidazoline, 3-imidazoline, pyrazole, pyrazoline, 2-pyrazoline, 3-pyrazoline, piperidine, piperazine, indole, indoline, or 1H-indazole, at the 2-position of isoindole or isoindoline, at the 4-position of morpholine, and at the 9-position of carbazole or β-carboline (each of which may be substituted or unsubstituted), but it is not limited thereto. More typically, examples of a nitrogen-bonded heterocycle include 1-aziridinyl, 1-azetidyl, 1-pyrrolyl, 1-imidazolyl, 1-pyrazolyl, and 1-piperidinyl (each of which may be substituted or unsubstituted).

"Heterocyclylalkyl" refers to an acyclic alkyl radical in which one hydrogen atom bonded to a carbon atom, typically a terminal or sp3 carbon atom, is substituted by a heterocyclyl radical (i.e., a heterocyclyl-alkylene moiety). Examples of a typical heterocyclylalkyl group include heterocyclyl-CH_2-, 2-(heterocyclyl)ethan-1-yl, and the like, but it is not limited thereto. The "heterocyclyl" moiety thereof used herein includes those described in the document such as "Principles of Modern Heterocyclic Chemistry" and any heterocyclyl group described above. Those skilled in the art will understand that if the resulting group is chemically stable, the heterocyclyl group may be attached to the alkyl moiety of the heterocyclylalkyl through a carbon-to-carbon bond or a carbon-to-heteroatom bond. A heterocyclylalkyl group may have 2 to 20 carbon atoms. For example, the alkyl moiety of the heterocyclylalkyl group may have 1 to 6 carbon atoms, and the heterocyclyl moiety thereof may have 1 to 14 carbon atoms. Examples of the heterocyclylalkyl include a 5-membered heterocycle containing sulfur, oxygen, and/or nitrogen such as thiazolylmethyl, 2-thiazolylethan-1-yl, imidazolylmethyl,

oxazolylmethyl, thiadiazolylmethyl, and the like; and a 6-membered heterocycle containing sulfur, oxygen, and/or nitrogen such as piperidinylmethyl, piperazinylmethyl, morpholinylmethyl, pyridinylmethyl, pyridazylmethyl, pyrimidylmethyl, pyrazinylmethyl, and the like (each of which may be substituted or unsubstituted), but it is not limited thereto.

"Heterocyclylalkenyl" refers to an acyclic alkenyl radical in which one of the hydrogen atoms bonded to a carbon atom, typically a terminal or sp3 carbon atom (although an sp2 carbon atom may also be used), is substituted by a heterocyclyl radical (i.e., a heterocyclyl-alkenylene moiety). The heterocyclyl moiety of the heterocyclylalkenyl group includes those described in the document such as "Principles of Modern Heterocyclic Chemistry" and any heterocyclyl group described herein. The alkenyl moiety of the heterocyclylalkenyl group includes any alkenyl group described herein. Those skilled in the art will understand that if the resulting group is chemically stable, the heterocyclyl group may be attached to the alkenyl moiety of the heterocyclylalkenyl via a carbon-to-carbon bond or a carbon-to-heteroatom bond. A heterocyclylalkenyl group may have 3 to 20 carbon atoms. For example, the alkenyl moiety of the heterocyclylalkenyl group may have 2 to 6 carbon atoms, and the heterocyclyl moiety thereof may have 1 to 14 carbon atoms.

"Heterocyclylalkynyl" refers to an acyclic alkynyl radical in which one of the hydrogen atoms bonded to a carbon atom, typically a terminal or sp3 carbon atom (although an sp carbon atom may also be used), is substituted by a heterocyclyl radical (i.e., a heterocyclyl-alkynylene moiety). The heterocyclyl moiety of the heterocyclylalkynyl group includes those described in the document such as "Principles of Modern Heterocyclic Chemistry" and any heterocyclyl group described herein. The alkynyl moiety of the heterocyclylalkynyl group includes any alkynyl group described herein. Those skilled in the art will understand that if the resulting group is chemically stable, the heterocyclyl group may be attached to the alkynyl moiety of the heterocyclylalkynyl via a carbon-to-carbon bond or a carbon-to-heteroatom bond. A heterocyclylalkynyl group may have 3 to 20 carbon atoms. For example, the alkynyl moiety of the heterocyclylalkynyl group may have 2 to 6 carbon atoms, and the heterocyclyl moiety thereof may have 1 to 14 carbon atoms.

"Heteroaryl" refers to an aromatic heterocyclyl containing at least one heteroatom in the ring. Non-limiting examples of a suitable heteroatom that may be contained in the aromatic ring include oxygen, sulfur, and nitrogen. Non-limiting examples of a heteroaryl ring include all of those enumerated in the definition of "heterocyclyl" herein, inclusive of pyridinyl, pyrrolyl, oxazolyl, indolyl, isoindolyl, furinyl, furanyl, thienyl, benzofuranyl, benzothiophenyl, carbazolyl, imidazolyl, thiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, quinolyl, isoquinolyl, pyridazyl, pyrimidyl, pyrazyl, and the like (each of which may be substituted or unsubstituted).

"Carbocycle" or "carbocyclyl" refers to a saturated, partially unsaturated, or aromatic ring having 3 to 7 carbon atoms as a monocycle, 7 to 12 carbon atoms as a bicycle, and up to about 20 carbon atoms as a polycycle. A monocyclic carbocycle has 3 to 6 ring atoms, more typically 5 or 6 ring atoms. A bicyclic carbocycle has 7 to 12 ring atoms arranged in a bicyclo[4,5], [5,5], [5,6], or [6,6] system or 9 to 10 ring atoms arranged in a bicyclo[5,6] or [6,6] system. Examples of a monocyclic or bicyclic carbocycle include cyclopropyl, cyclobutyl, cyclopentyl, 1-cyclopent-1-enyl, 1-cyclopent-2-enyl, 1-cyclopent-3-enyl, cyclohexyl, 1-cyclohex-1-enyl, 1-cyclohex-2-enyl, 1-cyclohex-3-enyl, phenyl, and naphthyl (each of which may be substituted or unsubstituted).

"Acyl" refers to -C(=O)-alkyl, -C(=O)-carbocycle (which is substituted or unsubstituted), and -C(=O)-heterocycle (which is substituted or unsubstituted), wherein the alkyl, carbocycle, or heterocycle moiety is as defined herein. Non-limiting examples of "acyl" include $-C(=O)CH_3$, $-C(=O)CH_2CH_3$, $-C(=O)CH(CH_3)_2$, $-C(=O)C(CH_3)_3$, -C(=O)-phenyl (which is substituted or unsubstituted), -C(=O)-cyclopropyl (which is substituted or unsubstituted), -C(=O)-cyclobutyl (which is substituted or unsubstituted), -C(=O)-cyclopentyl (which is substituted or unsubstituted), -C(=O)-cyclohexyl (which is substituted or unsubstituted), and -C(=O)-pyridyl (which is substituted or unsubstituted).

"Arylheteroalkyl" refers to a heteroalkyl as defined herein, wherein a hydrogen atom (which may be attached to either a carbon atom or a heteroatom) is substituted by an aryl group as defined herein. If the resulting group is chemically stable, the aryl group may be attached to a carbon atom of the heteroalkyl group or

the heteroatom of the heteroalkyl group. For example, an arylheteroalkyl group may have a formula of -alkylene-O-aryl, -alkylene-O-alkylene-aryl, -alkylene-NH-aryl, -alkylene-NH-alkylene-aryl, -alkylene-S-aryl, -alkylene-S-alkylene-aryl, or the like. In addition, any alkylene moiety in the above formulae may be further substituted with any of the substituents defined or exemplified herein.

"Heteroarylalkyl" refers to an alkyl group as defined herein, wherein a hydrogen atom is substituted by a heteroaryl group as defined herein. Non-limiting examples of heteroarylalkyl include -CH_2-pyridinyl, -CH_2-pyrrolyl, -CH_2-oxazolyl, -CH_2-indolyl, -CH_2-isoindolyl, -CH_2-furinyl, -CH_2-furanyl, -CH_2-thienyl, -CH_2-benzofuranyl, -CH_2-benzothiophenyl, -CH_2-carbazolyl, -CH_2-imidazolyl, -CH_2-thiazolyl, -CH_2-isoxazolyl, -CH_2-pyrazolyl, -CH_2-isothiazolyl, -CH_2-quinolyl, -CH_2-isoquinolyl, -CH_2-pyridazyl, -CH_2-pyrimidyl, -CH_2-pyrazyl, -$CH(CH_3)$-pyridinyl, -$CH(CH_3)$-pyrrolyl, -$CH(CH_3)$-oxazolyl, -$CH(CH_3)$-indolyl, -$CH(CH_3)$-isoindolyl, -$CH(CH_3)$-furinyl, -$CH(CH_3)$-furanyl, -$CH(CH_3)$-thienyl, -$CH(CH_3)$-benzofuranyl, -$CH(CH_3)$-benzothiophenyl, -$CH(CH_3)$-carbazolyl, -$CH(CH_3)$-imidazolyl, -$CH(CH_3)$-thiazolyl, -$CH(CH_3)$-isoxazolyl, -$CH(CH_3)$-pyrazolyl, -$CH(CH_3)$-isothiazolyl, -$CH(CH_3)$-quinolyl, -$CH(CH_3)$-isoquinolyl, -$CH(CH_3)$-pyridazyl, -$CH(CH_3)$-pyrimidyl, -$CH(CH_3)$-pyrazyl, and the like.

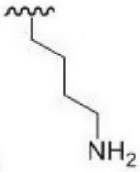
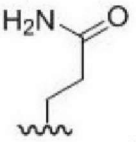
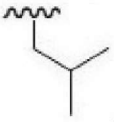
"Silyloxy" refers to the group -O-SiR_3, wherein R comprises alkyl, aryl (which is substituted or unsubstituted), heteroaryl (which is substituted or unsubstituted), or a combination thereof. Non-limiting examples of silyloxy include -O-$Si(CH_3)_3$, -O-$Si(CH_3)_2tBu$, -O-$Si(tBu)_2CH_3$, -O-$Si(tBu)_3$, -O-$Si(CH_3)_2Ph$, -O-$Si(Ph)_2CH_3$, and -O-$Si(Ph)_3$.

The term "optionally substituted" refers to a particular moiety (e.g., an optionally substituted aryl group) of the compound of Formula 1 that has one, two, or more substituents.

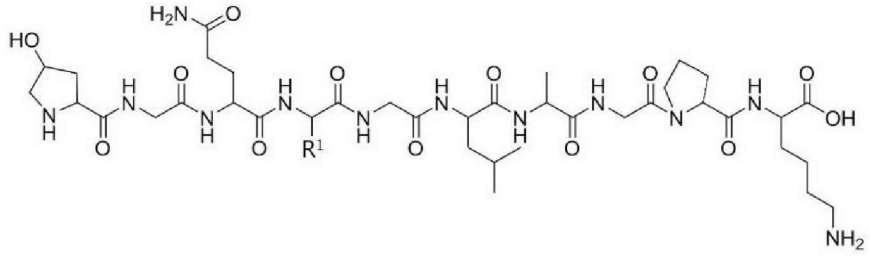
The term "ester thereof" refers to any ester of a compound wherein any -COOH functional group of the molecule is substituted to a -COOR functional group or any -OH functional group of the molecule is substituted to a -C(=O)OR. Here, the R moiety of the ester may be any carbon-containing group that forms a stable ester moiety, which includes, but is not limited to, alkyl, alkenyl, alkynyl, cycloalkyl,

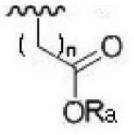
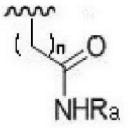
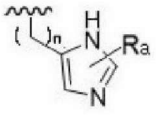
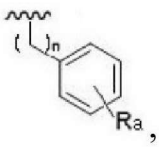
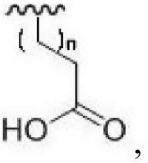
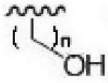
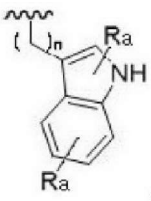
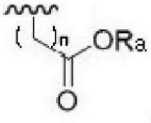
cycloalkylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, and substituted derivatives thereof. Examples of the ester may also include an ester such as those described above of a “tautomeric enol” as described below.

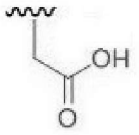
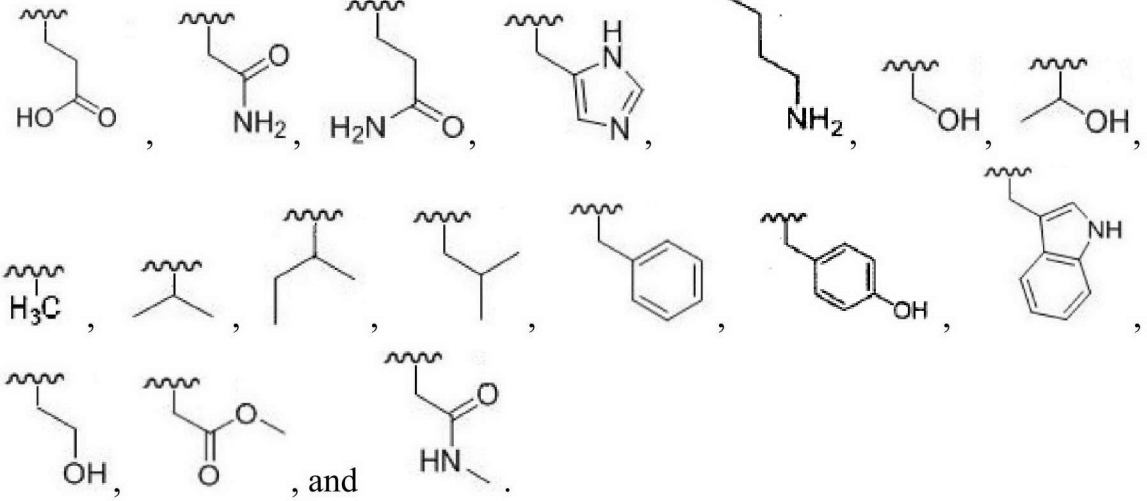
In the present invention, the compound represented by the above Formula 1 may be an optical isomer type L or D.

The compound represented by the above Formula 1 may be represented by Formula 1-1 when R^2 is H, R^3 is  , R^4 is -OH, R^5 is H, R^6 is  , R^7 is  , R^8 is H, and R^9 is H. Further, the compound represented by the following Formula 1-1 may be an optical isomer type L or D.

[Formula 1-1]

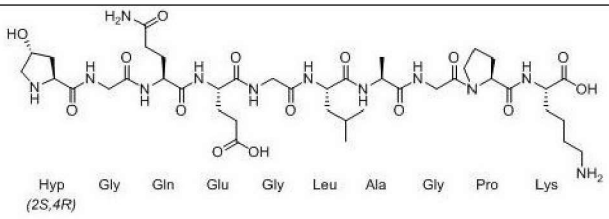
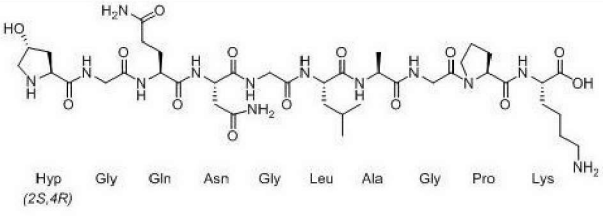
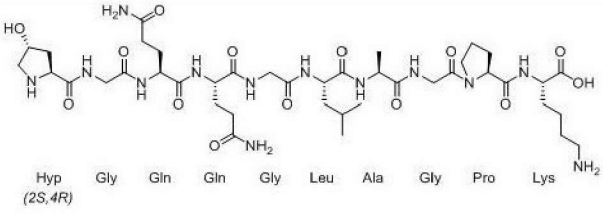


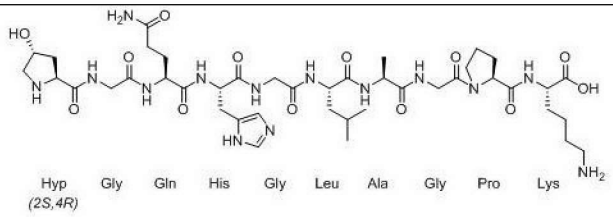
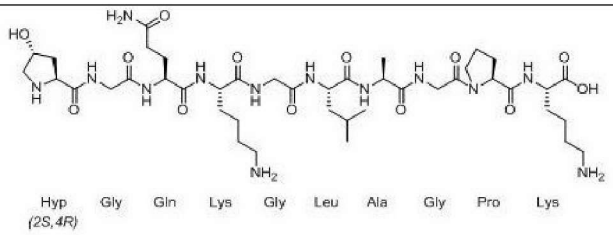
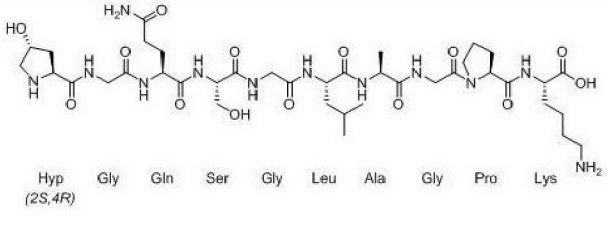
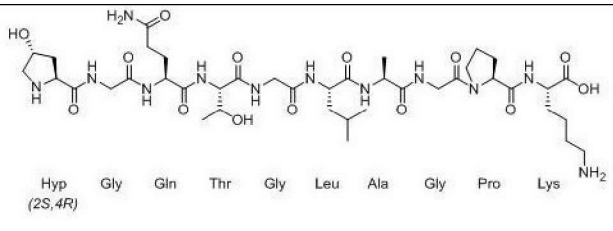
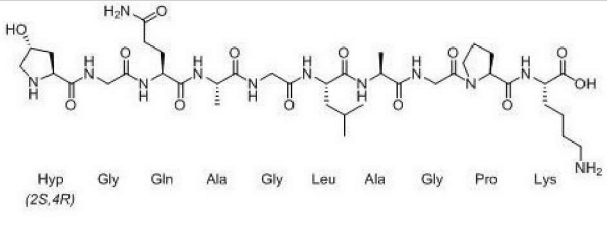
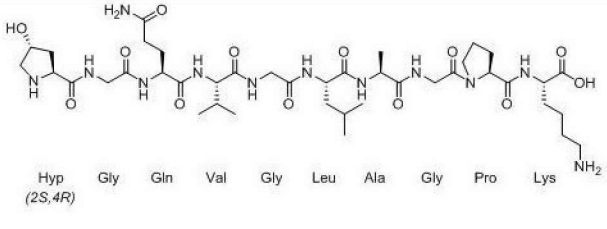
R^1 may be one selected from the group consisting of substituted or unsubstituted C_{1-6} alkyl,  ,  ,  ,  ,  ,  ,  ,  , and  . Here, n may be an integer of 1 to 10, but it is not limited thereto. R_a may be hydrogen or C_{1-6} alkyl.

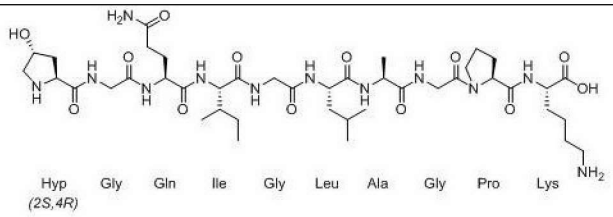
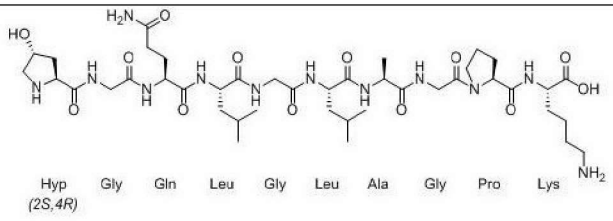
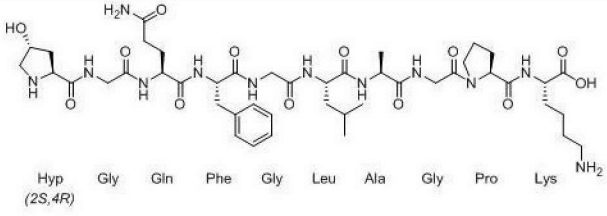
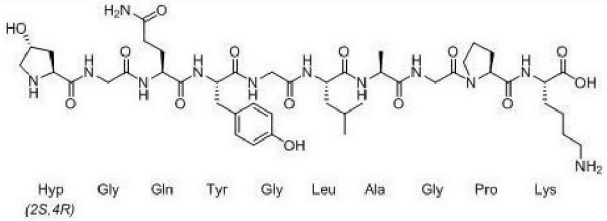
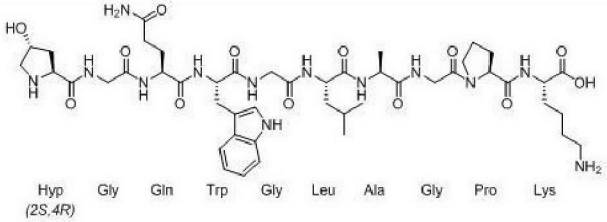
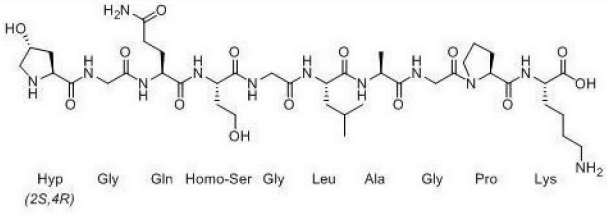
Specifically, R^1 may be one selected from the group consisting of  ,  , and .

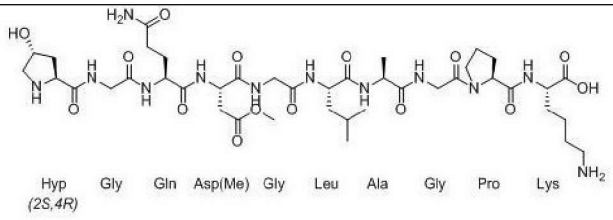
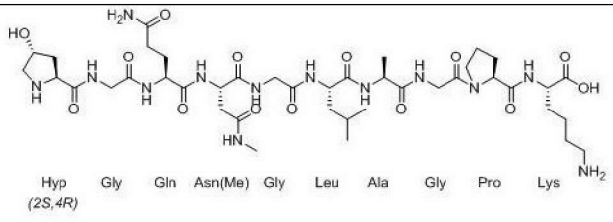
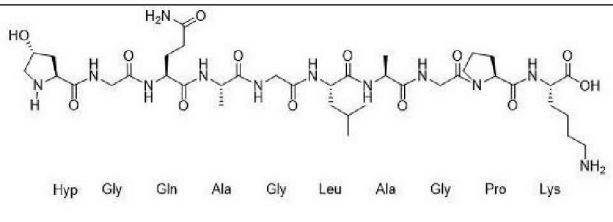
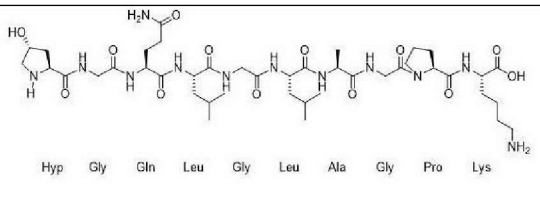
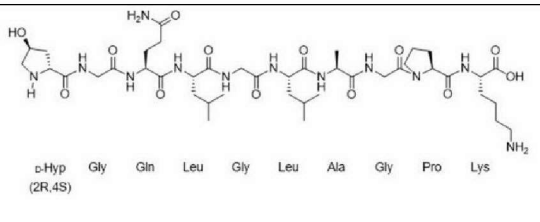
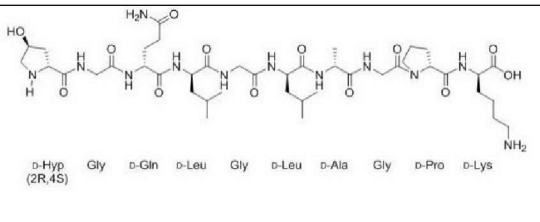
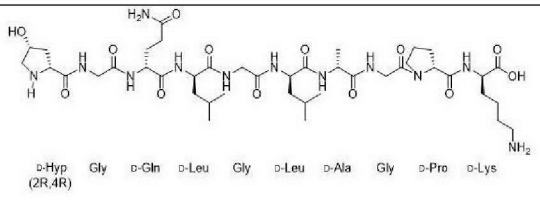
More specifically, the compound may be a compound described in Table 1 below.

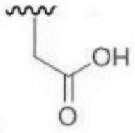
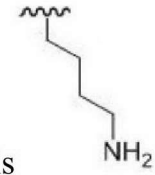
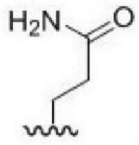
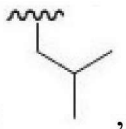
[Table 1]

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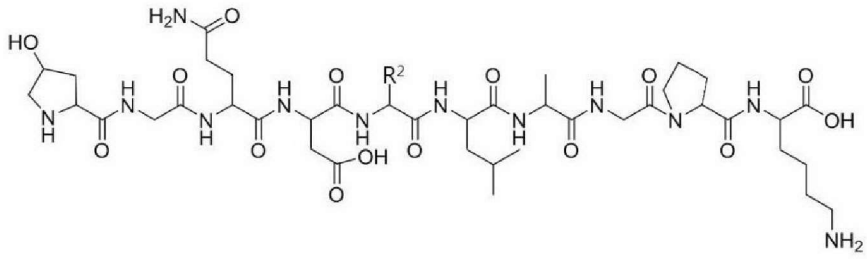
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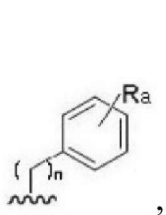
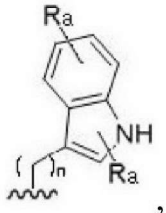
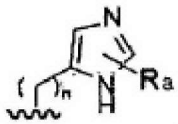
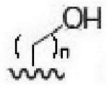
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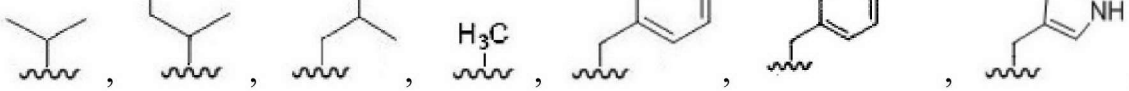
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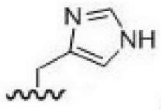
The compound represented by the above Formula 1 may be represented by Formula 1-2 when R^1 is  , R^3 is  , R^4 is -OH, R^5 is H, R^6 is  , R^7 is  , R^8 is H, and R^9 is H. Further, the compound represented by the following Formula 1-2 may be an optical isomer type L or D.

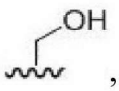
[Formula 1-2]

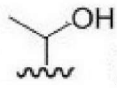


In addition, R^2 may be one selected from the group consisting of hydrogen, substituted or unsubstituted C_{1-6} alkyl,  ,  ,  , and  . Here, n may be an integer of 1 to 10, but it is not limited thereto. R_a may be hydrogen or C_{1-6} alkyl.

Specifically, R^2 may be one selected from the group consisting of  ,  ,

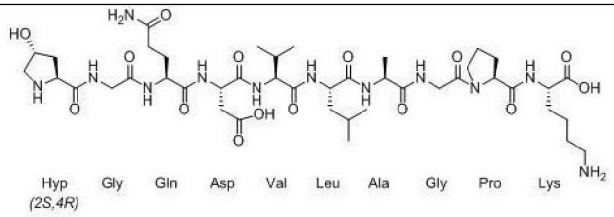
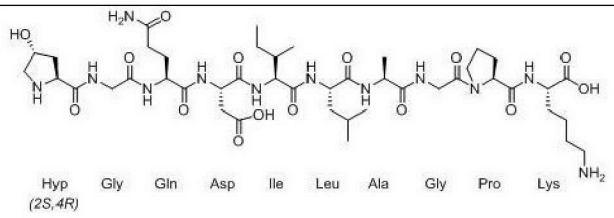
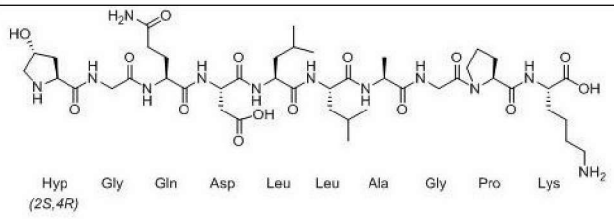
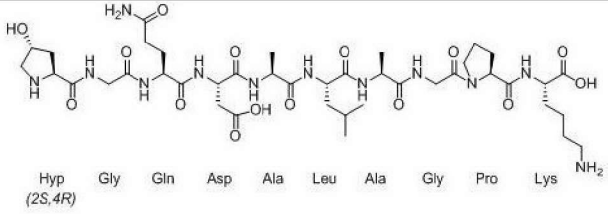
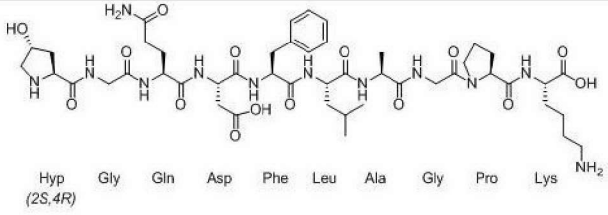


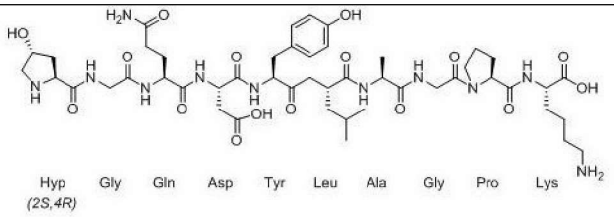
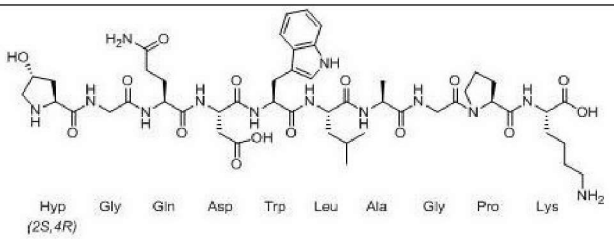
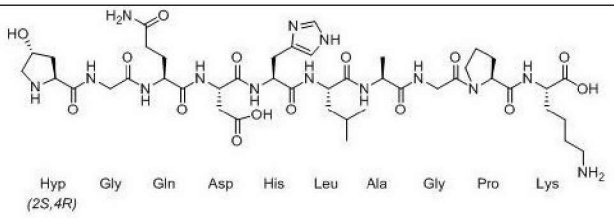
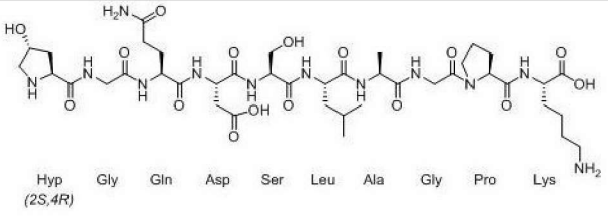
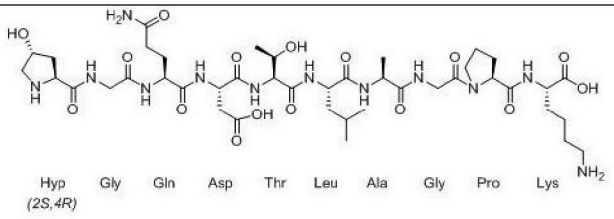
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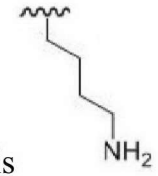
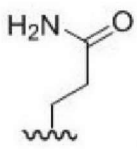
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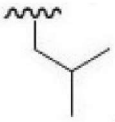
. More specifically, the compound may be a compound described in Table 2 below.

[Table 2]

YDE-015		SEQ ID NO: 21
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YDE-017		SEQ ID NO: 23
YDE-018		SEQ ID NO: 24
YDE-019		SEQ ID NO: 25

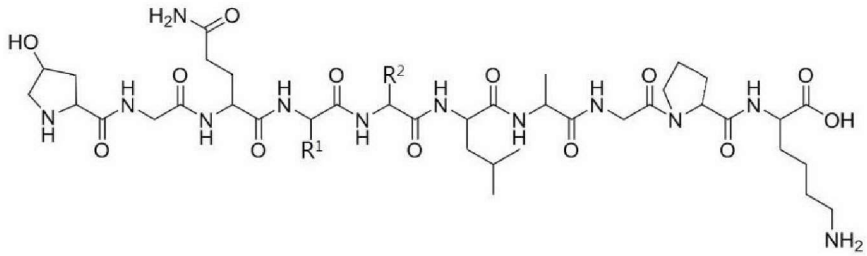
YDE-020		SEQ ID NO: 26
YDE-021		SEQ ID NO: 27
YDE-022		SEQ ID NO: 28
YDE-023		SEQ ID NO: 29
YDE-024		SEQ ID NO: 30

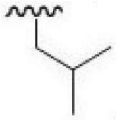
The compound represented by the above Formula 1 may be represented by Formula 1-3 when R^3 is  , R^4 is -OH, R^5 is H, R^6 is  , R^7 is



, R^8 is H, and R^9 is H. Further, the compound represented by the following Formula 1-3 may be an optical isomer type L or D.

[Formula 1-3]

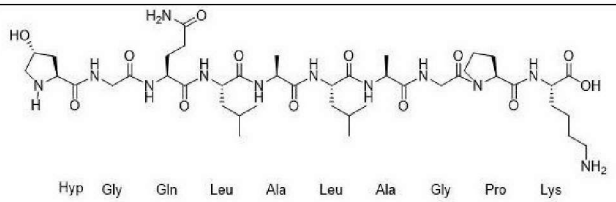


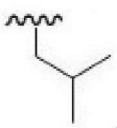
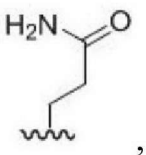
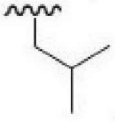
R^1 may be C_{1-6} alkyl. Specifically, R^1 may be  .

R^2 may be C_{1-6} alkyl. Specifically, R^2 may be  .

More specifically, the compound may be a compound described in Table 3 below.

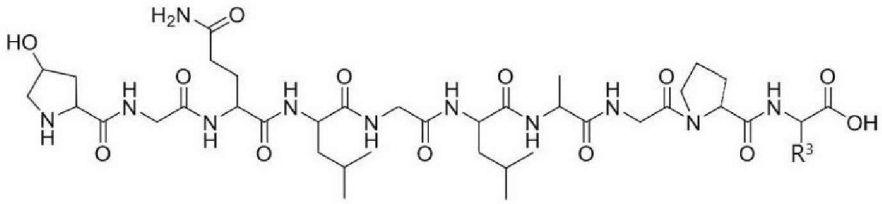
[Table 3]

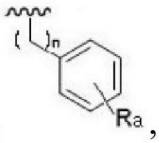
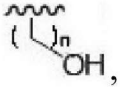
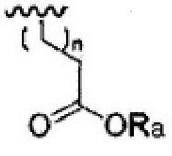
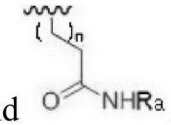
YDE-051		SEQ ID NO: 32

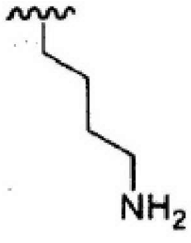
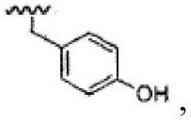
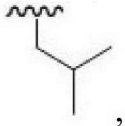
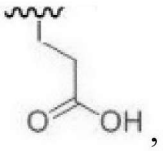
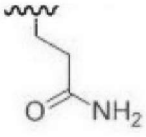
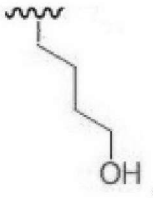
The compound represented by the above Formula 1 may be represented by Formula 1-4 when R^1 is  , R^2 is H, R^4 is -OH, R^5 is H, R^6 is  , R^7 is  , R^8 is H, and R^9 is H. Further, the compound represented by the following

Formula 1-4 may be an optical isomer type L or D.

[Formula 1-4]

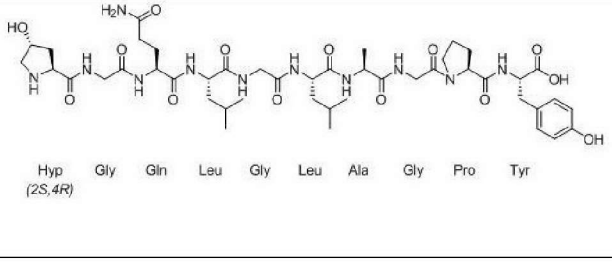


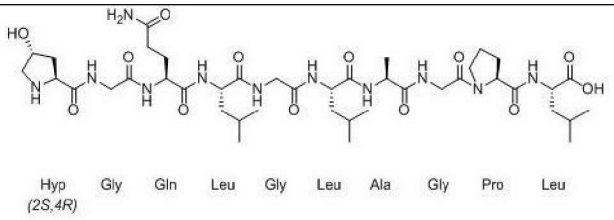
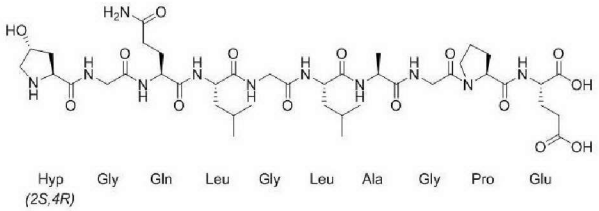
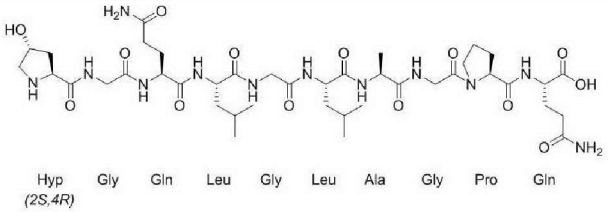
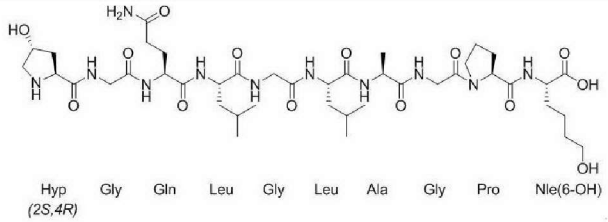
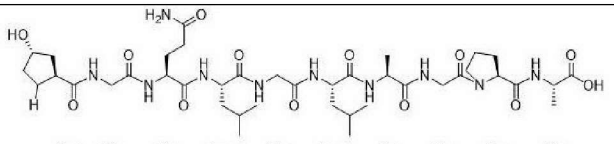
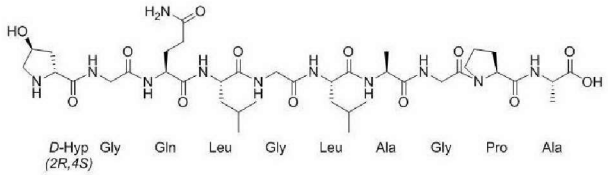
R^3 may be one selected from the group consisting of substituted or unsubstituted C_{1-6} alkyl,  ,  ,  , and  . Here, n may be an integer of 1 to 10, but it is not limited thereto. R_a may be hydrogen or C_{1-6} alkyl.

Specifically, R^3 may be one selected from the group consisting of,  ,  ,  ,  ,  , and  .

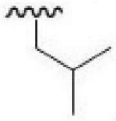
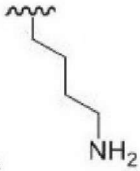
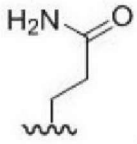
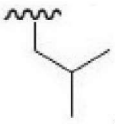
More specifically, the compound may be a compound described in Table 4 below.

[Table 4]

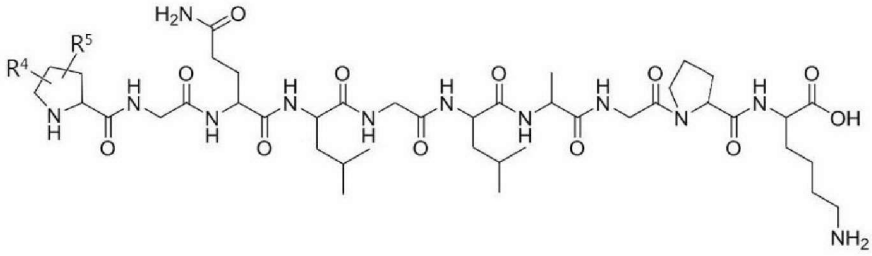
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YDE-031		SEQ ID NO: 35
YDE-032		SEQ ID NO: 36
YDE-033		SEQ ID NO: 37
YDE-056		SEQ ID NO: 38
YDE-073		SEQ ID NO: 39

The compound represented by the above Formula 1 may be represented by

Formula 1-5 when R^1 is  , R^2 is H, R^3 is  , R^6 is  , R^7 is  , R^8 is H, and R^9 is H. Further, the compound represented by the following Formula 1-5 may be an optical isomer type L or D.

[Formula 1-5]

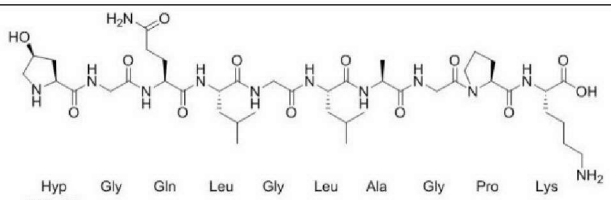


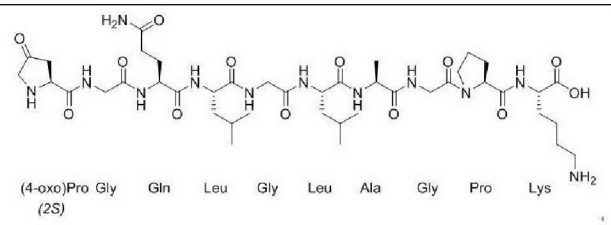
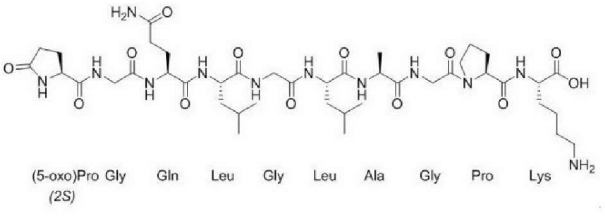
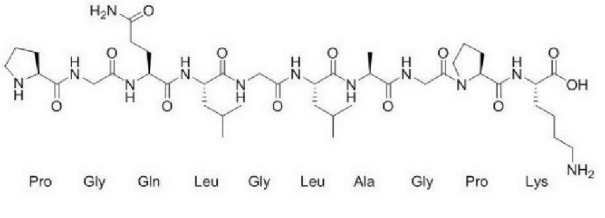
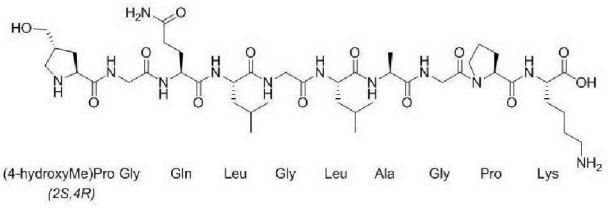
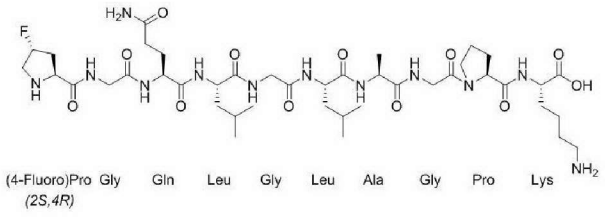
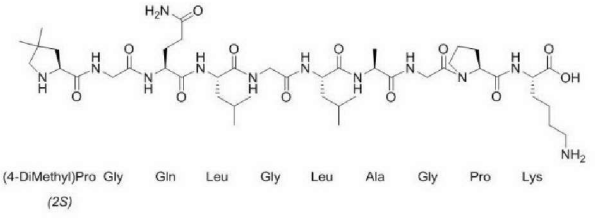
R^4 and R^5 may be each independently one selected from the group consisting of substituted or unsubstituted C_{1-6} alkyl, $-OR_b$, =O, $-CH_2OR_b$, and $-X_2$. Here, X_2 may be independently halogen such as F, Cl, Br, or I. R_b may be hydrogen or C_{1-6} alkyl.

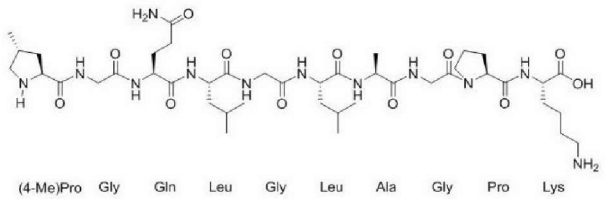
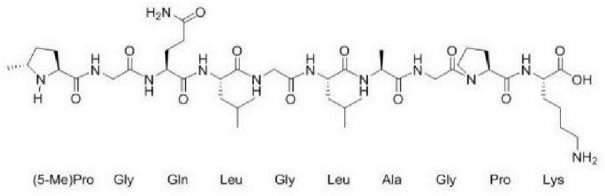
Specifically, R^4 may be one selected from the group consisting of H, -OH, =O, $-CH_2OR_b$, and F; in such event, R^5 may be H. Further, R^4 may be CH_3; in such event, R^5 may be CH_3.

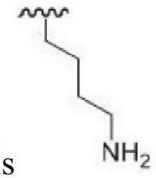
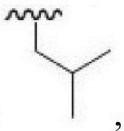
More specifically, the compound may be a compound described in Table 5 below.

[Table 5]

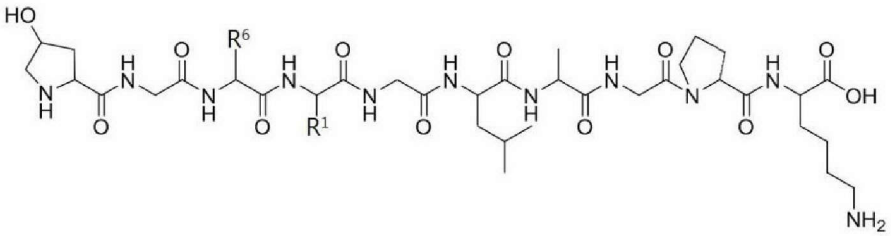
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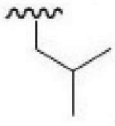
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YDE-036		SEQ ID NO: 41
YDE-037		SEQ ID NO: 42
YDE-038		SEQ ID NO: 43
YDE-039		SEQ ID NO: 44
YDE-040		SEQ ID NO: 45

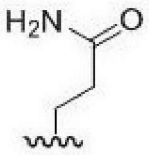
YDE-044		SEQ ID NO: 46
YDE-045		SEQ ID NO: 47

The compound represented by the above Formula 1 may be represented by Formula 1-6 when R^2 is H, R^3 is  , R^4 is -OH, R^5 is H, R^7 is  , R^8 is H, and R^9 is H. Further, the compound represented by the following Formula 1-6 may be an optical isomer type L or D.

[Formula 1-6]

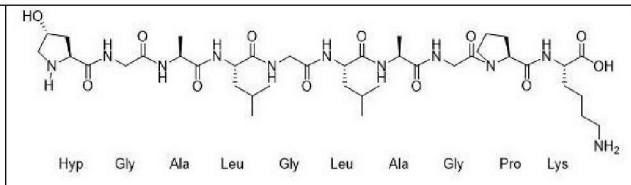


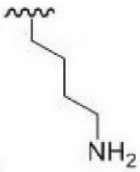
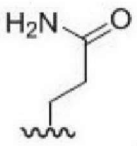
R^1 may be C_{1-6} alkyl. Specifically, R^1 may be  .

R^6 may be substituted or unsubstituted C_{1-6} alkyl, wherein the substituent may be $-C(=O)NH_2$. Specifically, R^6 may be  or  .

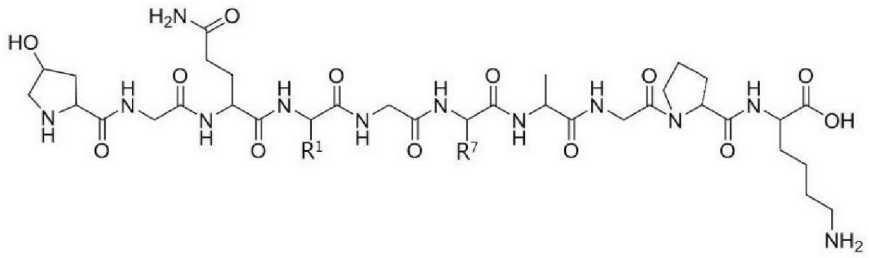
More specifically, the compound may be a compound described in Table 6 below.

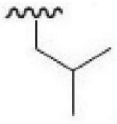
[Table 6]

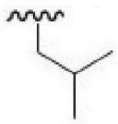
YDE-049		SEQ ID NO: 48

The compound represented by the above Formula 1 may be represented by Formula 1-7 when R^2 is H, R^3 is  , R^4 is -OH, R^5 is H, R^6 is  , R^8 is H, and R^9 is H. Further, the compound represented by the following Formula 1-7 may be an optical isomer type L or D.

[Formula 1-7]



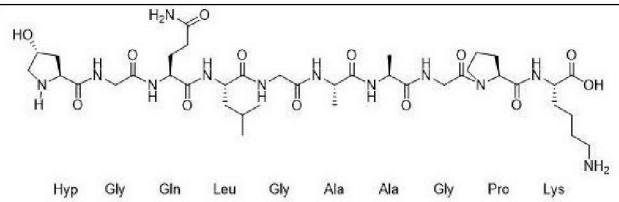
R^1 may be C_{1-6} alkyl. Specifically, R^1 may be  .

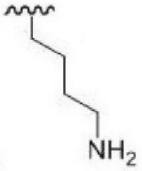
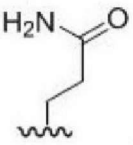
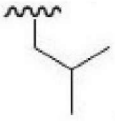
R^7 may be unsubstituted C_{1-6} alkyl. Specifically, R^7 may be  or  .

More specifically, the compound may be a compound described in Table 7

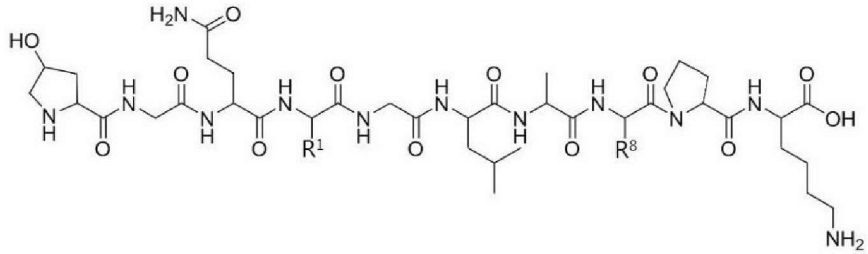
below.

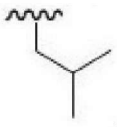
[Table 7]

YDE-052		SEQ ID NO: 49

The compound represented by the above Formula 1 may be represented by Formula 1-8 when R^2 is H, R^3 is  , R^4 is -OH, R^5 is H, R^6 is  , R^7 is  , and R^9 is H. Further, the compound represented by the following Formula 1-8 may be an optical isomer type L or D.

[Formula 1-8]

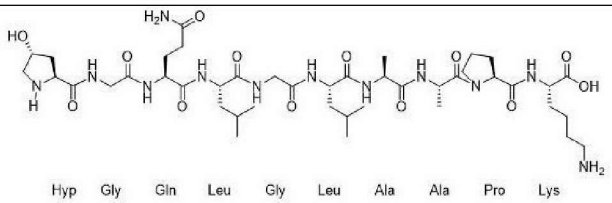


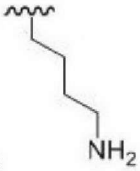
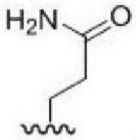
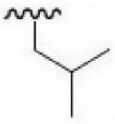
R^1 may be C_{1-6} alkyl. Specifically, R^1 may be  .

R^8 may be hydrogen or C_{1-6} alkyl. Specifically, R^8 may be  or  .

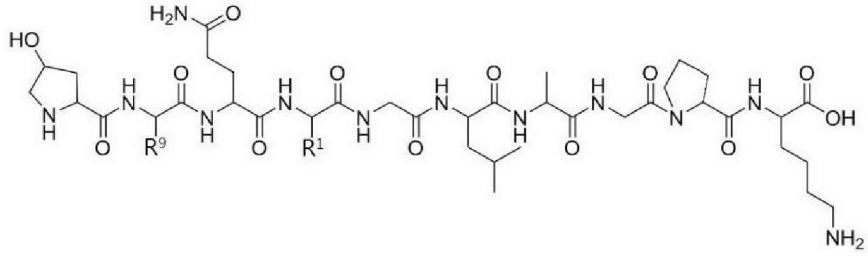
More specifically, the compound may be a compound described in Table 8 below.

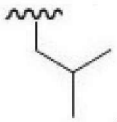
[Table 8]

YDE-054		SEQ ID NO: 50

The compound represented by the above Formula 1 may be represented by Formula 1-9 when R^2 is H, R^3 is  , R^4 is -OH, R^5 is H, R^6 is  , R^7 is  , and R^8 is H. Further, the compound represented by the following Formula 1-9 may be an optical isomer type L or D.

[Formula 1-9]

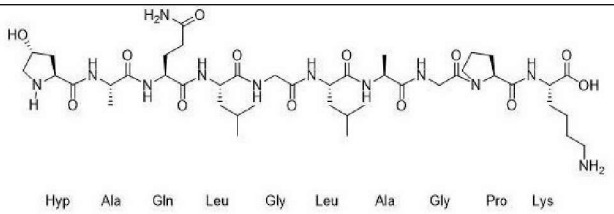
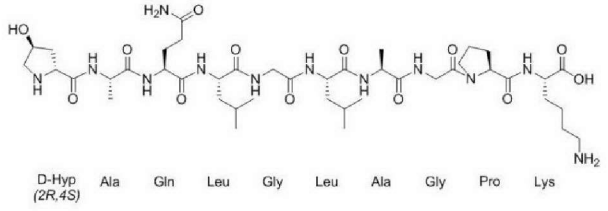


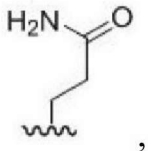
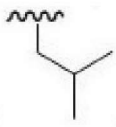
R^1 may be C_{1-6} alkyl. Specifically, R^1 may be  .

R^9 may be hydrogen or C_{1-6} alkyl. Specifically, R^9 may be  or  .

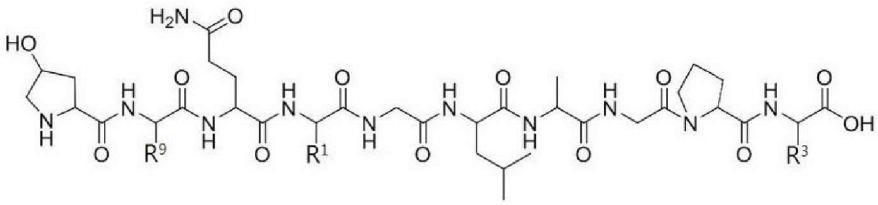
More specifically, the compound may be a compound described in Table 9 below.

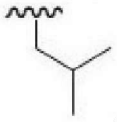
[Table 9]

YDE-048		SEQ ID NO: 51
YDE-072		SEQ ID NO: 53

The compound represented by the above Formula 1 may be represented by Formula 1-10 when R^2 is H, R^4 is -OH, R^5 is H, R^6 is  , R^7 is  , and R^8 is H. Further, the compound represented by the following Formula 1-10 may be an optical isomer type L or D.

[Formula 1-10]



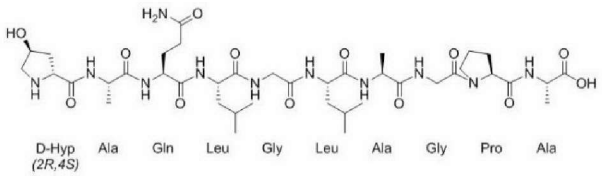
R^1 may be C_{1-6} alkyl. Specifically, R^1 may be  .

In such event, R^3 may be C_{1-6} alkyl. Specifically, R^3 may be  .

In such event, R^9 may be C_{1-6} alkyl. Specifically, R^9 may be  .

More specifically, the compound may be a compound described in Table 10 below.

[Table 10]

YDE-074		SEQ ID NO: 52

The compounds represented by the above Formulae 1-1 to 1-10 may be any one selected from the group consisting of HyP-Gly-Gln-Glu-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asn-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Gln-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-His-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Lys-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Ser-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Thr-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Ala-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Val-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Ile-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Phe-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Tyr-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Trp-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Ser(Homo)-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp(Me)-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asn(Me)-Gly-Leu-Ala-Gly-Pro-Lys, $_{D}$-HyP(2R, 4S)-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, $_{D}$-Hyp(2R,4S)-Gly-$_{D}$-Gln-$_{D}$-Leu-Gly-$_{D}$-Leu-$_{D}$-Ala-Gly-$_{D}$-Pro-$_{D}$-Lys, $_{D}$-Hyp(2R, 4R)-Gly-$_{D}$-Gln-$_{D}$-Leu-Gly-$_{D}$-Leu-$_{D}$-Ala-Gly-$_{D}$-Pro-$_{D}$-Lys,

HyP-Gly-Gln-Asp-Val-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Ile-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Leu-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Ala-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Phe-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Tyr-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Trp-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-His-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Ser-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Thr-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Leu-Ala-Leu-Ala-Gly-Pro-Lys,

HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Tyr, HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Leu, HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Glu, HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Gln, HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Nle(6-

OH), HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Ala, $_{D}$-HyP(2R, 4S)-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Ala,

Hyp(2S, 4S)-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, (4-oxo)Pro-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, (5-oxo)Pro-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, Pro-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, (4-hydroxyMe)Pro-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, (4-Fluoro)Pro-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, (4-Dimethyl)Pro-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, (4-Me)Pro-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, (5-Me)Pro-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys,

Hyp-Gly-Ala-Leu-Gly-Leu-Ala-Gly-Pro-Lys, Hyp-Gly-Gln-Leu-Gly-Ala-Ala-Gly-Pro-Lys, Hyp-Gly-Gln-Leu-Gly-Leu-Ala-Ala-Pro-Lys, Hyp-Ala-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, $_{D}$-Hyp(2R, 4S)-Ala-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys and $_{D}$-Hyp(2R, 4S)-Ala-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Ala.

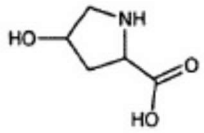
Another aspect of the present invention provides a peptide having an amino acid sequence represented by HyP-Gly-Gln-Xaa-Gly-Leu-Ala-Gly-Pro-Lys. Here, Xaa may be one selected from the group consisting of Glu, Asn, Gln, His, Lys, Ser, Thr, Ala, Val, Ile, Leu, Phe, Tyr, Trp, homo-Ser, Asp(Me), and Asn(Me).

The peptide may be a variant of a collagen type II α1-derived peptide. The collagen type II α1 may be isolated from the extracellular matrix derived from animal chondrocytes.

The term "peptide" used in the present invention refers to a compound in which two or more amino acids are linked by a peptide bond. Further, it is classified into dipeptide, tripeptide, tetrapeptide, and the like according to the number of constituent amino acids. An oligopeptide has about 10 or fewer peptide bonds, and a polypeptide has a plurality of peptide bonds. In addition, a peptide in the present invention includes a mutated peptide in which its amino acid residue is substituted.

The term "HyP" used in the present invention refers to an amino acid called hydroxyproline, in which a hydroxyl group (-OH) is bonded to the carbon atom at the 4-position of proline. HyP has a structure of $C_5H_9NO_3$ and may be represented by the following Formula 2.

[Formula 2]

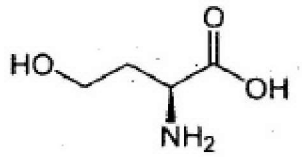


HyP may include all isomers. In addition, HyP may be an isomer represented by the stereochemistry of "2S,4R" unless otherwise specified.

The term "2S,4R" is represented by R and S that indicate a stereochemical configuration of a chiral molecule. A typical chiral molecule has a chiral center such as an asymmetric carbon atom. Since the chiral center has four different substituent groups (or substitution atoms), their priority is determined by a predetermined procedure. Once the order of the four substituents is determined by (1), (2), (3), and (4), the lowest order substituent (4) is placed farthest away from the eye direction, and the remaining substituents are arranged from the higher order to the lower order. R (or rectus in Latin, right) indicate the arrangement in which the sequence of (1) to (2) to (3) turns right. S (or sinister, left) indicates the arrangement in which this sequence turns left.

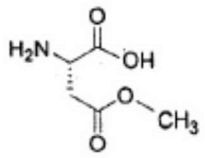
The term "homo-Ser" used in the present invention is called homoserine and refers to an α-amino acid having a hydroxyl group in the side chain. Homo-Ser is not an amino acid that constitutes a protein and is an intermediate present in the biosynthesis of threonine and methionine in microorganisms and plants. Homo-Ser may have the following Formula 3.

[Formula 3]



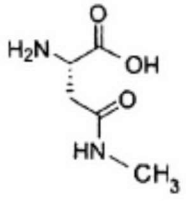
The term "Asp(Me)" used in the present invention indicates an amino acid in which the hydrogen atom of the hydroxyl group (OH) bonded to the carbon atom at the 4-position of aspartic acid is substituted by a methyl group (CH_3). Asp(Me) may have the following Formula 4.

[Formula 4]



The term “Asn(Me)” used in the present invention indicates an amino acid in which the hydrogen atom of the amine group (NH_2) bonded to the carbon atom at the 4-position of asparagine is substituted by a methyl group (CH_3). Asn(Me) may have the following Formula 5.

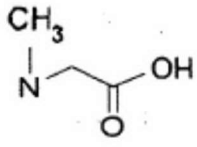
[Formula 5]



In addition, still another aspect of the present invention provides a peptide having an amino acid sequence represented by HyP-Gly-Gln-Asp-Xaa-Leu-Ala-Gly-Pro-Lys. Here, Xaa may be one selected from the group consisting of Val, Ile, Leu, Ala, Phe, Tyr, Trp, Ser, Thr, and (N-Me)Gly.

The term “(N-Me)Gly” used in the present invention indicates an amino acid in which the hydrogen atom of the amine group (NH_2) bonded to the carbon atom at the 2-position of glycine is substituted by a methyl group (CH_3). (N-Me)Gly may have the following Formula 6.

[Formula 6]

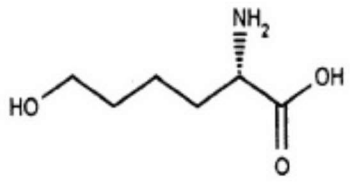


Still another aspect of the present invention provides a peptide having an amino acid sequence represented by HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Xaa. Here, Xaa may be one selected from the group consisting of Tyr, Leu, Glu, Gln, Ala, and Nle(6-OH).

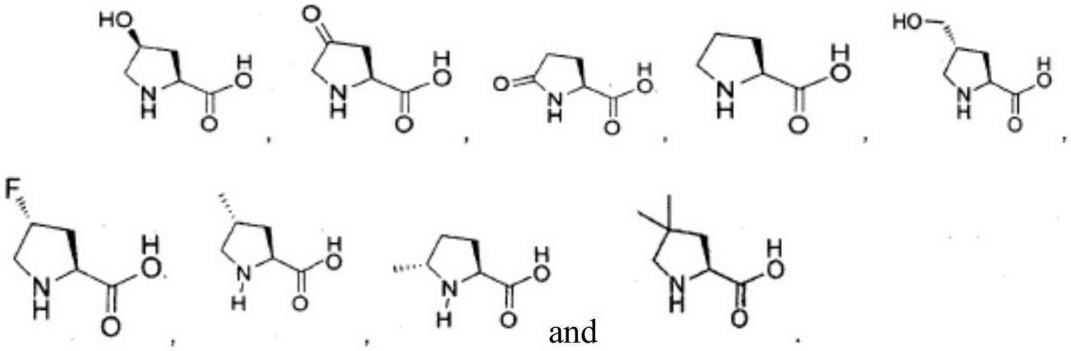
The term “Nle(6-OH)” used in the present invention refers to an amino acid in

which a hydroxyl group (-OH) is bonded to the carbon atom at the 6-position of norleucine. Nle(6-OH) has a structure of $C_5H_{11}NO_3$ and may be represented by the following Formula 7.

[Formula 7]



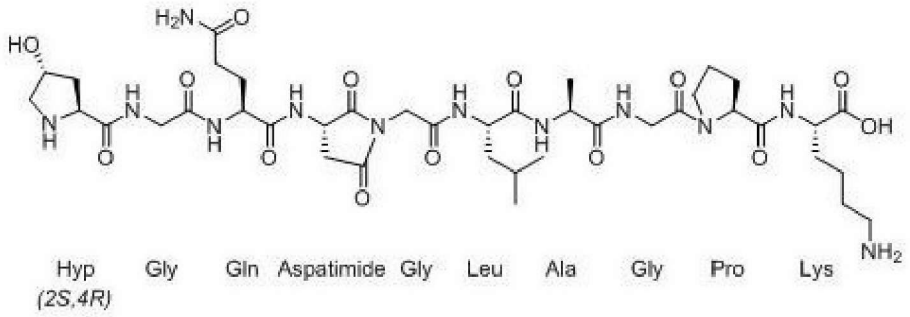
Still another aspect of the present invention provides a peptide having an amino acid sequence represented by PD-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys. Here, PD may be any one selected from the group consisting of the following formulae.



Still another aspect of the present invention provides a peptide having any one amino acid sequence selected from the group consisting of Ala-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys (SEQ ID NO: 54), Hyp-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Ala-Lys (SEQ ID NO: 55), HyP-Gly-Gln-Leu-Gly-Leu-Ala (SEQ ID NO: 56), HyP-Gly-Gln-Glu-Gly-Leu-Gly (SEQ ID NO: 57), HyP-Gly-Gln-Leu-Gly-Leu (SEQ ID NO: 58), $_D$-HyP(2R, 4S)-Gly-$_D$-Gln-$_D$-Leu-Gly-$_D$-Leu (SEQ ID NO: 59), HyP-Gly-Gln-Leu-Gly (SEQ ID NO: 60), HyP-Gly-Gln-$_D$-Leu-Gly (SEQ ID NO: 61), and $_D$-HyP(2R, 4S)-Gly-Gln-Leu-Gly (SEQ ID NO: 62).

Still another aspect of the present invention provides a compound represented by Formula 8.

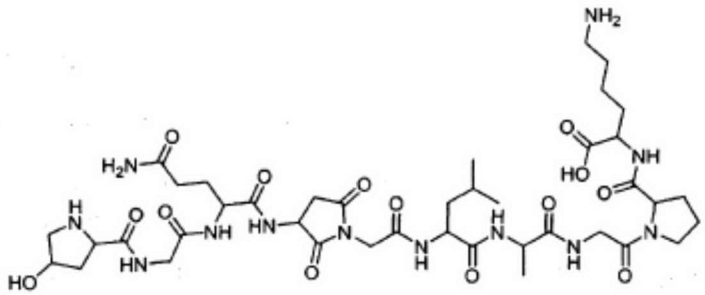
[Formula 8]



The compound represented by the above Formula 8 indicates a compound in which Asp is modified to Aspartimide by a dehydration condensation reaction of the hydroxyl group (-OH) bonded to the carbon atom at the 4-position of Asp in the amino acid sequence represented by HyP-Gly-Gln-Asp-Gly-Leu-Ala-Gly-Pro-Lys with the Asp-Gly peptide bond.

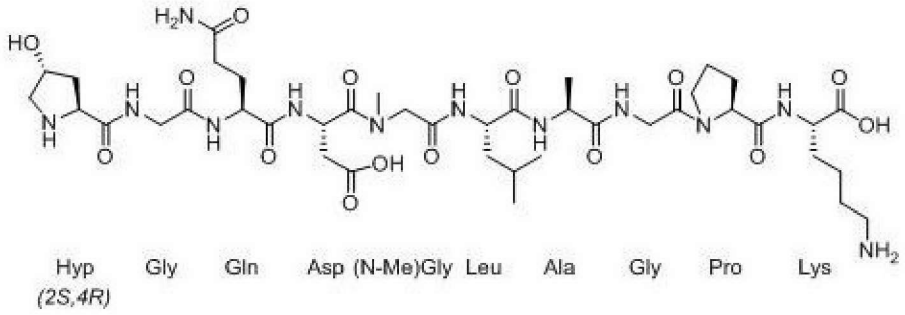
The modified compound may be a compound represented by the following Formula 9.

[Formula 9]



Still another aspect of the present invention provides a compound represented by Formula 10.

[Formula 10]



The compound represented by Formula 10 may be a compound represented by the amino acid sequence of SEQ ID NO: 31.

Further, the present invention provides a pharmaceutical composition for treating an eye disease, which comprises the compound or the peptide as an active pharmaceutical ingredient.

Specifically, the eye disease may be one selected from the group consisting of retinopathy, keratitis, dry-macular degeneration, wet-macular degeneration, dry eye syndrome, keratoconjunctival epithelium disorder, proliferative vitreoretinopathy, pigmentary retinopathy, diabetic retinopathy, retinopathy of prematurity, retinopathy of immaturity, proliferative retinopathy, ischemic retinopathy, epidemic keratoconjunctivitis, atopic keratitis, superior limbic keratitis, pterygium keratitis sicca, phlyctenular keratoconjunctivitis, scleritis, corneal transplant rejection, choroidal neovascularization, neovascular glaucoma, ischemic optic neuropathy, retrolental fibroplasias, diabetic macula, neovascular iris disease, erythrosis, myopia, Von Hippel-Lindau syndrome, ocular histoplasmosis, central retinal vein occlusion, Sjogren syndrome and Stevens-Johnson syndrome. Preferably, the eye disease may be one selected from the group consisting of retinopathy, keratitis, macular degeneration, dry eye syndrome and keratoconjunctival epithelium disorder.

The keratoconjunctival epithelium disorder may be due to post-operative surgery, drug, trauma or contact lens wear.

Specifically, the composition for treating an eye disease, which comprises the compound or the peptide as an active pharmaceutical ingredient, may further comprise at least one additive selected from the group consisting of a carrier, an excipient, a disintegrant, a sweetener, a coating agent, a swelling agent, a lubricant,

a slip agent, a flavor, an antioxidant, a buffer, a bacteriostat, a diluent, a dispersant, a surfactant, and a binder. Specifically, a formulation for parenteral administration may be a sterilized aqueous solution, a non-aqueous solution, a suspension, an emulsion, a lyophilized preparation, a suppository, or the like.

Still another aspect of the present invention provides a method for treating an eye disease, which comprises administering the compound or the peptide to a subject.

The dose of the compound or the peptide may be adjusted depending on such various factors as the kind of the disease, the severity of the disease, the kinds and amounts of the active pharmaceutical ingredient and other ingredients contained in the pharmaceutical composition, the type of the formulation, the age, body weight, general health condition, sex, and diet of the patient, the time and the route of administration, the duration of treatment, and the drugs concurrently used.

However, for the desired effect, the effective amount of the compound or the peptide contained in the pharmaceutical composition may be 0.0001 μg/day to 100 μg/day. In such event, the administration may be carried out once a day, or divided into several doses. Specifically, the concentration of the compound or the peptide contained in the pharmaceutical composition may be 1000 μM to 0.001 μM. Also, the concentration of the compound or the peptide contained in the pharmaceutical composition may be 100 μM to 0.005 μM or 50 μM to 0.02 μM.

In addition, if necessary, the concentration of the compound or the peptide contained in the pharmaceutical composition may be 30 μM to 1 μM. Further, the concentration of the compound or the peptide contained in the pharmaceutical composition may be 0.01 μM to 1 μM.

In addition, the subject may be a mammal, particularly a human. The administration route may be appropriately selected by a person skilled in the art in consideration of the administration method, the volume and viscosity of the body fluid, and the like. Specifically, the administration may be carried out through any one route selected from the group consisting of an application, intravenous, intraarterial, intraperitoneal, intramuscular, intrasternal, percutaneous, intranasal, inhalation, topical, rectal, oral, intraocular, and intradermal. In particular, it may

preferably be applied to the eye for use as an eye drop.

Still another aspect of the present invention provides the use of the compound or the peptides for the treatment of an eye disease.

Still another aspect of the present invention provides the use of the compound or the peptides for the preparation of a pharmaceutical composition for treating an eye disease.

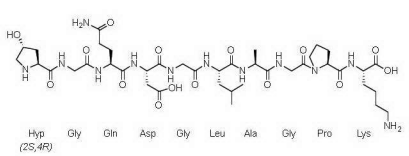
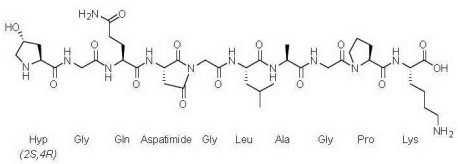
Hereinafter, the present invention is explained in more detail by the following working examples. However, the following working examples are intended to further illustrate the present invention. The scope of the present invention is not limited thereby.

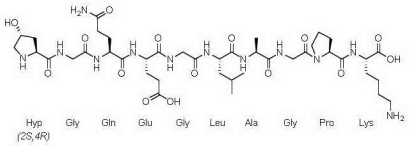
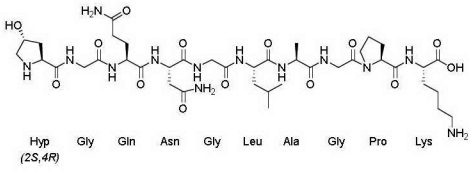
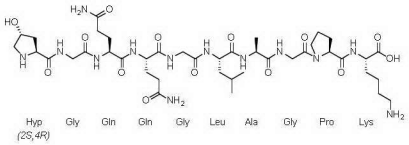
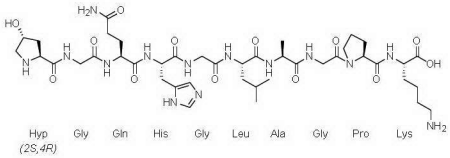
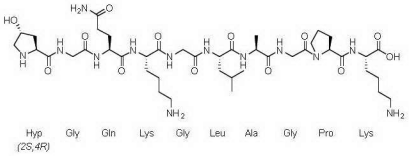
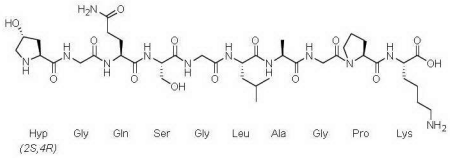
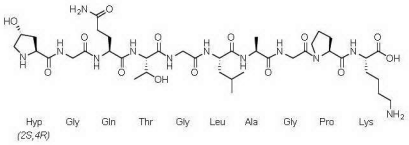
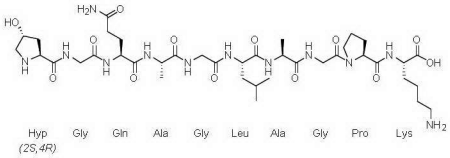
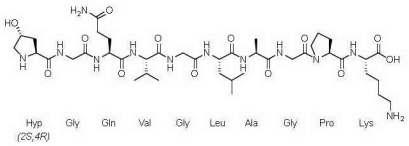
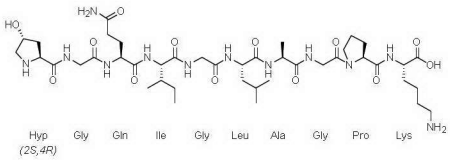
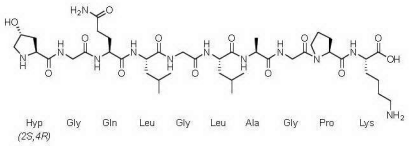
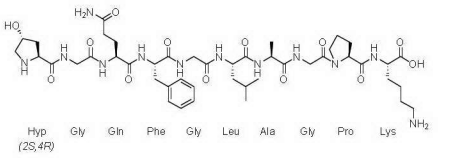
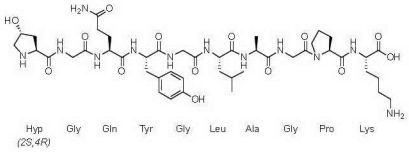
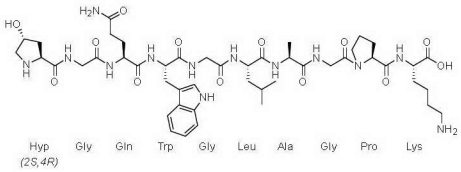
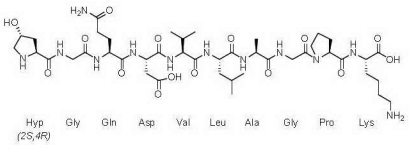
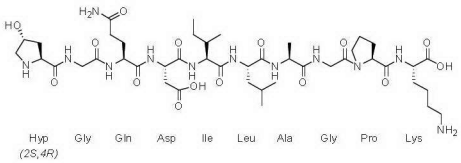
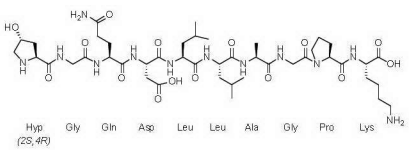
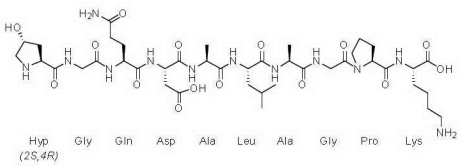
Working Example 1: Preparation of YDE derivatives

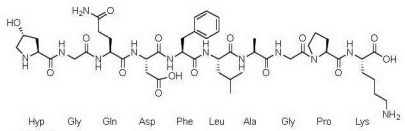
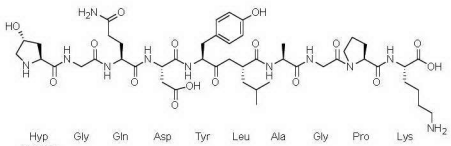
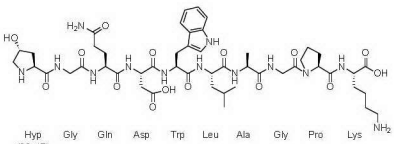
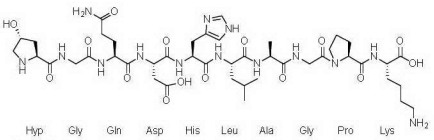
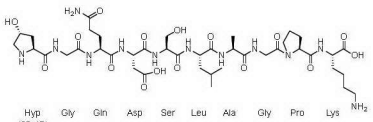
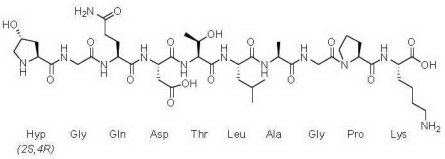
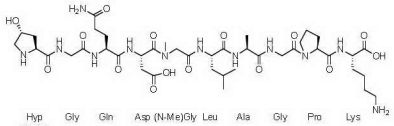
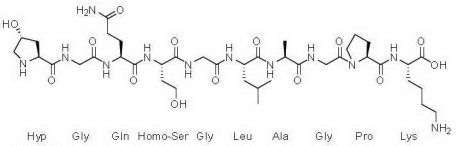
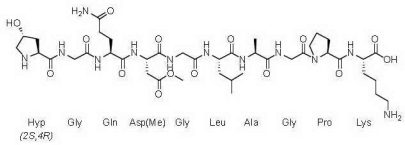
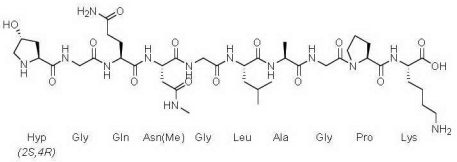
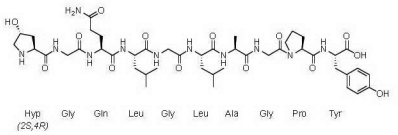
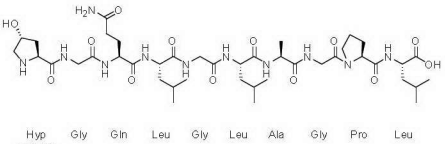
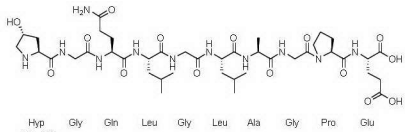
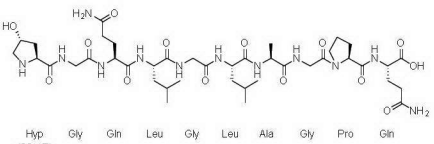
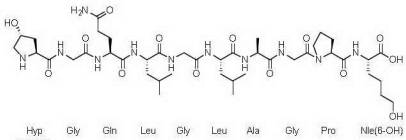
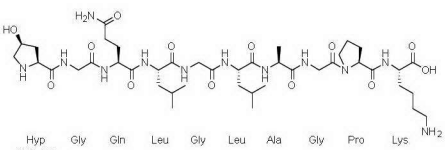
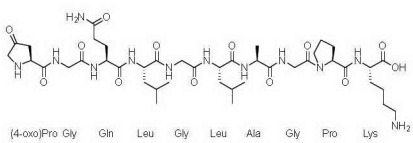
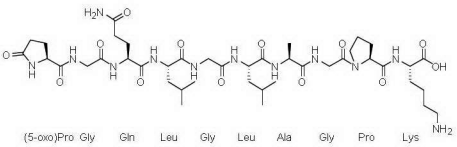
A protein analysis of the extracellular matrix derived from animal chondrocytes was performed in Baek's group of Center of Biomedical Mass Spectrometry (Diatech Korea Co., Ltd., Seoul, Korea). Proline-GQDGLAGPK (P-GQDGLAGPK), which is a part of the amino acid sequence of the collagen type II α1 protein, was obtained through the above protein analysis. YDE-001 to YDE-075 peptides were synthesized by ANYGEN (Gwangju, Korea) by substituting a part of the above peptide (Fig. 1 and Table 11).

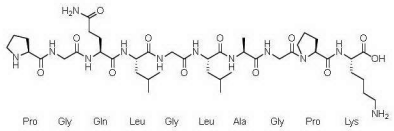
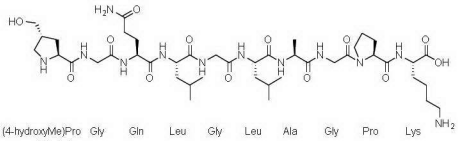
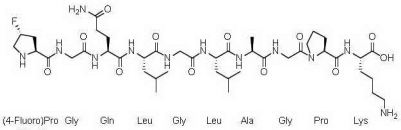
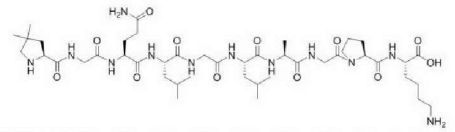
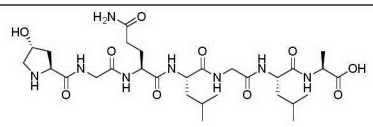
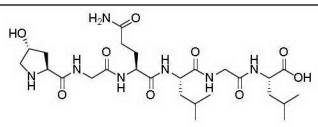
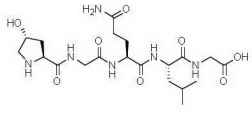
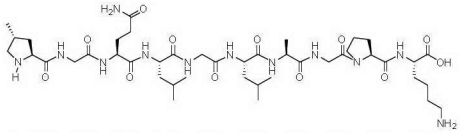
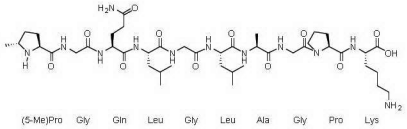
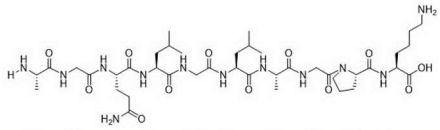
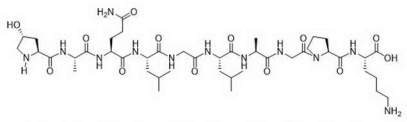
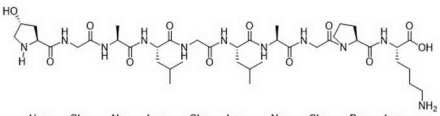
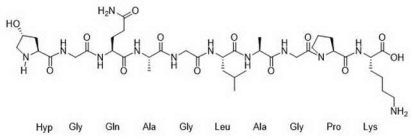
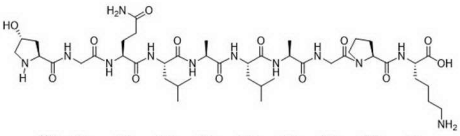
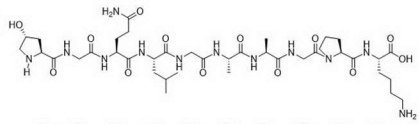
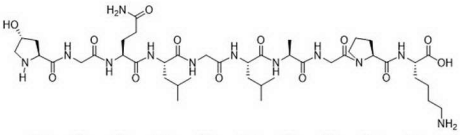
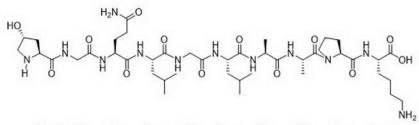
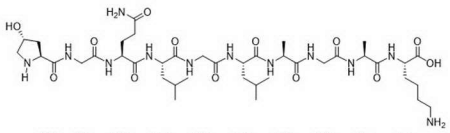
The process for synthesizing the YDE-001 to YDE-075 peptides and the purification procedure thereof conducted by ANYGEN were depicted in Figs. 2 and 3.

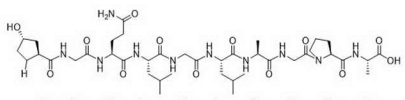
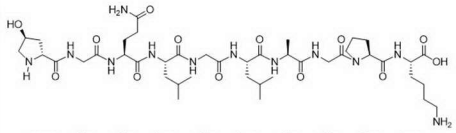
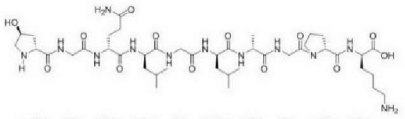
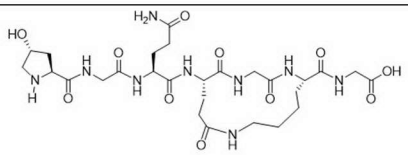
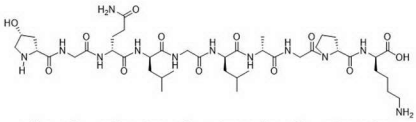
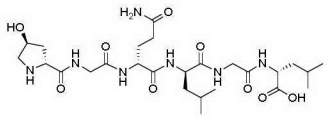
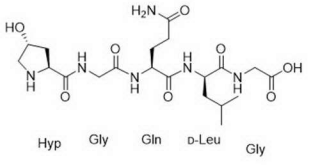
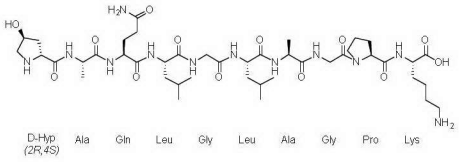
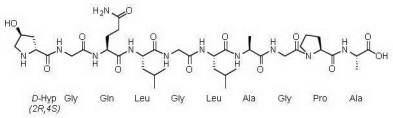
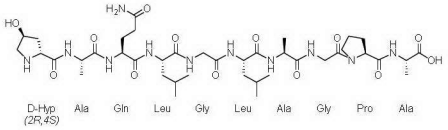
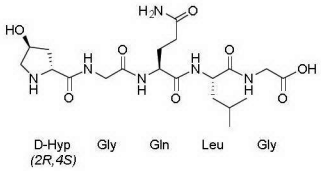
[Table 11]

No.	Structure of compound	No.	Structure of compound
YY-101		YY-102	

YDE-001		YDE-002	
YDE-003		YDE-004	
YDE-005		YDE-006	
YDE-007		YDE-008	
YDE-009		YDE-010	
YDE-011		YDE-012	
YDE-013		YDE-014	
YDE-015		YDE-016	
YDE-017		YDE-018	

YDE-019		YDE-020	
YDE-021		YDE-022	
YDE-023		YDE-024	
YDE-025		YDE-026	
YDE-027		YDE-028	
YDE-029		YDE-030	
YDE-031		YDE-032	
YDE-033		YDE-034	
YDE-035		YDE-036	

YDE -037		YDE -038	
YDE -039		YDE -040	
YDE -041		YDE -042	
YDE -043		YDE -044	
YDE -045		YDE -047	
YDE -048		YDE -049	
YDE -050		YDE -051	
YDE -052		YDE -053	
YDE -054		YDE -055	

YDE -056		YDE -057	
YDE -058		YDE -059	
YDE -060		YDE -064	
YDE -066		YDE -072	
YDE -073		YDE -074	
YDE -075			

Experimental Example 1: Analysis of YDE derivatives

The YDE derivatives prepared in Working Example 1 were analyzed by HPLC. As a result, it was confirmed that the purities of synthesized YDE-001, YDE-002, YDE-003, YDE-004, YDE-005, YDE-006, YDE-007, YDE-008, YDE-009, YDE-010, YDE-011, YDE-012, YDE-013, YDE-014, YDE-015, YDE-016, YDE-017, YDE-018, YDE-019, YDE-020, YDE-021, YDE-022, YDE-023, YDE-024, YDE-025, YDE-026, YDE-027, YDE-028, YDE-029, YDE-030, YDE-031, YDE-032, YDE-033, YDE-034, YDE-035, YDE-036, YDE-037, YDE-038, YDE-039, YDE-040, YDE-041, YDE-042, YDE-043, YDE-044, YDE-045, YDE-047, YDE-048, YDE-049, YDE-050, YDE-051, YDE-052, YDE-053, YDE-054, YDE-055, YDE-

056, YDE-057, YDE-058, YDE-059, YDE-060, YDE-064, YDE-066, YDE-072, YDE-073, YDE-074, and YDE-075 were 99.7%, 99.7%, 99.7%, 99.7%, 99.5%, 98.9%, 98.0%, 98.8%, 98.1%, 99.0%, 98.3%, 98.9%, 98.7%, 98.5%, 99.1%, 99.4%, 98.0%, 99.6%, 99.6%, 99.2%, 98.1%, 98.3%, 96.1%, 98.9%, 95.1%, 98.6%, 96.9%, 99.5%, 98.0%, 98.1%, 98.8%, 98.2%, 97.2%, 98.6%, 98.8%, 98.7%, 99.2%, 98.7%, 98.1%, 97.5%, 96.5%, 97.4%, 98.7%, 97.8%, 95.5%, 97.5%, 97.2%, 96.9%, 99.3%, 98.0%, 99.4%, 96.4%, 95.1%, 98.6%, 97.4%, 98.8%, 97.4%, 95.8%, 98.9%, 96.9%, 98.8%, 97.7%, 95.0%, 97.9%, and 96.3%, respectively (Figs. 4 to 68).

In addition, the YDE derivatives prepared in Working Example 1 were analyzed by Ion-Mass. As a result, it was confirmed that the molecular weights of synthesized YDE-001, YDE-002, YDE-003, YDE-004, YDE-005, YDE-006, YDE-007, YDE-008, YDE-009, YDE-010, YDE-011, YDE-012, YDE-013, YDE-014, YDE-015, YDE-016, YDE-017, YDE-018, YDE-019, YDE-020, YDE-021, YDE-022, YDE-023, YDE-024, YDE-025, YDE-026, YDE-027, YDE-028, YDE-029, YDE-030, YDE-031, YDE-032, YDE-033, YDE-034, YDE-035, YDE-036, YDE-037, YDE-038, YDE-039, YDE-040, YDE-041, YDE-042, YDE-043, YDE-044, YDE-045, YDE-047, YDE-048, YDE-049, YDE-050, YDE-051, YDE-052, YDE-053, YDE-054, YDE-055, YDE-056, YDE-057, YDE-058, YDE-059, YDE-060, YDE-064, YDE-066, YDE-072, YDE-073, YDE-074, and YDE-075 were 969.6, 954.8, 967.7, 977.1, 968.1, 926.9, 941.1, 910.7, 939.7, 953.0, 953.7, 987.8, 1003.8, 1025.9, 996.7, 1011.0, 1011.4, 968.7, 1044.4, 1061.4, 1084.5, 1035.0, 984.9, 999.1, 969.7, 942.0, 937.6, 967.3, 988.1, 960.6, 954.2, 991.1, 954.4, 990.7, 950.9, 937.6, 968.1, 955.4, 966.0, 709.3, 622.2, 486.8, 951.3, 951.3, 911.4, 967.5, 896.5, 911.0, 967.3, 911.2, 953.2, 967.2, 927.4, 896.4, 952.8, 953.4, 670.1, 953.3, 599.7, 486.5, 966.1, 895.8, 909.1, and 486.4, respectively (Figs. 69 to 133).

Experimental Example 2: Evaluation of the eye protection effect on dry eye syndrome by the YDE derivatives

Experimental Example 2.1: Preparation of rats with dry eye syndrome

In order to evaluate the eye protection effect on dry eye syndrome by YDE-001 to YDE-028 prepared in Working Example 1, a total of 320 Sprague-Dawley-

type male rats (OrientBio, Seungnam, Korea) were adapted for 7 days. Thereafter, dry eye syndrome was induced in 264 test rats through extraorbital lacrimal gland excision (hereinafter, ELGE). 8 test rats without the eye abnormality were subjected to a sham operation as a control group.

The rats weresystemically anesthetized by inhaling a mixed gas of 2% to 3% of isoflurane (Hana Pharm. Co., Hwasung, Korea), 70% of N_2O, and 28.6% of O_2 using a rodent anesthesia machine (Surgivet, Waukesha, Wis., USA) and a ventilator (Model 687, Harvard Apparatus, Cambridge, UK). Thereafter, the extraorbital lacrimal gland located in the subdermal area above the masseter muscle and under the optic nerve was excised through a transverse incision in a size of 10 mm on the anterior part of the left ear tragus. The skin was sutured by a general method. The ELGE operation time did not exceed 5 minutes for each rat. After 6 days following the ELGE operation, confirmation was performed through the Schirmer test by measuring the amount of tear secretion whether dry eye syndrome had been induced. Meanwhile, each rat of the control group with the sham operation was checked for the presence and location of the extraorbital lacrimal gland through a skin incision, and the skin was then sutured without the excision thereof (Fig. 134).

The average weight of the ELGE test group measured before the ELGE operation was 241.59 ± 13.56 g, and the average weight measured after 6 days from the ELGE operation was 297.38 ± 34.02 g. The average weight of the control group measured before the sham operation was 240.13±25.63 g, and the average weight measured after 6 days from the sham operation was 297.38±34.02 g (Fig. 135).

The average amount of tear secretion of the control group was 8.34 ± 0.73 mm^3, and the average amount of tear secretion of the ELGE test group was 3.55 ± 0.70 mm^3. 8 rats per group and a total of 32 groups were selected based on the average amount of tear secretion.

As a reference drug, 3% diquafosol sodium (Santen, Tokyo, Japan; hereinafter, DS), which is currently on the market, was used.

The present animal tests were conducted with a prior approval of the Animal Experimental Ethics Committee of Daegu Haany University (Approval No. DHU2017-003, January 12, 2017). All test animals were caused to fast for 18 hours

before the ELGE operation and final sacrifice except for feeding water.

The 32 groups were summarized in Table 12.

[Table 12]

Group classification	32 groups in total; 8 rats per group
Sham control group	Group administered with physiological saline after the sham operation
ELGE control group	Group administered with physiological saline after the ELGE operation
Reference	Group administered with DS after the ELGE operation
YY-102	Group administered with a 0.3% YY-102 solution after the ELGE operation
YDE series	Group administered with any of 0.3% YDE-01 to YDE-28 solutions (28 groups in total)

In addition, in order to evaluate the eye protection effect on dry eye syndrome by YDE-029 to YDE-043 prepared in Working Example 1, a total of 200 Sprague-Dawley-type male rats (OrientBio, Seungnam, Korea) were adapted for 7 days. Dry eye syndrome was induced in 165 test rats through the ELGE. 8 test rats without the eye abnormality were subjected to the sham operation as a control group. The ELGE was carried out as described above.

The average weight of the ELGE test group measured before the ELGE operation was 264.09±11.53 g, and the average weight measured after 6 days from the ELGE operation was 316.13±15.77 g. The average weight of the control group measured before the sham operation was 263.50±9.24 g, and the average weight measured after 6 days from the sham operation was 315.25±10.85 g (Fig. 136).

The average amount of tear secretion of the control group was 10.90±1.69 mm^3, and the average amount of tear secretion of the ELGE test group was 4.83±0.99 mm^3. 8 rats per group and a total of 20 groups were selected based on the average amount of tear secretion.

As a reference drug, 3% DS, which is currently on the market, was used.

The present animal tests were conducted with prior approval of the Animal Experimental Ethics Committee of Daegu Haany University (Approval No. DHU2017-050, June 08, 2017). All test animals were caused to fast for 18 hours

before the ELGE operation and final sacrifice except for feeding water.

The 20 groups were summarized in Table 13.

[Table 13]

Group classification	20 groups in total; 8 rats per group
Sham control group	Group administered with physiological saline after the sham operation
ELGE control group	Group administered with physiological saline after the ELGE operation
Reference	Group administered with DS after the ELGE operation
YY-101	Group administered with a 0.3% YY-101 solution after the ELGE operation
YY-102	Group administered with a 0.3% YY-102 solution after the ELGE operation
YDE series	Group administered with any of 0.3% YDE-01 to YDE-28 solutions (15 groups in total)

Experimental Example 2.2: Administration of the YDE derivatives

For YDE-001 to YDE-028, YY-102 and the 28 YDE-series were each dissolved in physiological saline at a concentration of 3 mg/ml and administered at a dose of 5 μl/eye at 9:30 am and 3:30 pm daily for 14 days after 7 days from the ELGE operation for a total of 28 times. The DS solution was dissolved in physiological saline at a concentration of 30 mg/ml and administered at a dose of 5 μl/eye twice a day for 14 days after 7 days from the ELGE operation for a total of 28 times. For the sham control and the ELGE control groups, the same stimulation as the administration was applied. In order to prevent excessive eye dryness, the same volume of physiological saline was applied in the same manner in place of the test substances.

Further, For YDE-029 to YDE-043, YY-102 and the 15 YDE-series were each dissolved in physiological saline at a concentration of 3 mg/ml and administered at a dose of 5 μl/eye at 9:30 am and 3:30 pm daily for 14 days after 7 days from the ELGE operation for a total of 28 times. The DS solution was dissolved in physiological saline at a concentration of 30 mg/ml and administered at a dose of 5 μl/eye twice a day for 14 days after 7 days from the ELGE operation for a total of 28 times. For the sham control and the ELGE control groups, the same stimulation

as the administration was applied. In order to prevent excessive eye dryness, the same volume of physiological saline was applied in the same manner in place of the test substances (Fig. 137).

Test Example 2.3: Confirmation of the changes in the amount of tear secretion by the YDE derivatives

After 6 days from the ELGE surgery, the changes in the amount of tear secretion were measured at day 7 and day 14 after the administration of YDE-001 to YDE-043. The amount of tear secretion was measured by the decrease in the travel distance of tears absorbed by cobalt chloride paper in a size of 1 x 15 mm (Toyo Roshi Kaisha, Japan).

The cobalt chloride paper was placed in the lateral canthus of a rat for 60 seconds to absorb tears (Fig. 139). The length of the area absorbed from the corner of the cobalt chloride paper was measured with an electronic digital caliper (Mytutoyo, Tokyo, Japan) (Fig. 138).

Fig. 139 shows the results of the test, wherein A is for the sham control group, B is for the ELGE control group, C is for the DS reference group, D is for the YY-102 administered group, and E to AF are for the YDE-001 to YDE-028 administered groups in order.

As a result, it was confirmed that the amount of tear secretion was decreased after 6 days from the ELGE operation at days 7 and 14 after the application of physiological saline in the ELGE control group as compared with the sham control group. In the groups treated with YDE derivatives and the DS reference group, the amount of tear secretion was increased as compared with the ELGE control group, except for the groups treated with a 0.3% solution of YDE-9, YDE-10, YDE-17, YDE-19, YDE-20, YDE-21, YDE-22, YDE-25, YDE-27, and YDE-28, which did not show any significant changes in the amount of tear secretion after the administration thereof for 14 days. Especially, the amount of tear secretion was increased by more than 20% in the groups treated with a 0.3% solution of YDE-15, YDE-11, YDE-08, YDE-26, YDE-16, YDE-01, YDE-23, and YY-102 as compared with the DS reference group.

The specific amounts of tear secretion are shown in Fig. 140 and Table 14.

[Table 14]

No.	Tear Volumes (mm^3)	
	Day 7	Day 14
YY-101	7.66±0.61	6.00±0.69
YY-102	4.59±1.43	5.77±1.99
YDE-001	4.88±1.62	5.92±2.19
YDE-002	3.84±1.16	5.01±1.67
YDE-003	4.13±1.76	4.88±1.57
YDE-004	3.42±1.06	5.19±1.84
YDE-005	3.85±0.93	5.08±1.91
YDE-006	3.44±1.69	5.35±1.68
YDE-007	3.91±1.28	5.45±1.26
YDE-008	4.57±1.25	6.10±2.36
YDE-009	3.76±1.21	4.54±1.11
YDE-010	3.42±1.31	4.35±1.36
YDE-011	4.22±1.45	6.16±2.16
YDE-012	3.68±0.99	5.67±1.86
YDE-013	5.27±1.50	5.49±1.92
YDE-014	3.81±1.21	5.62±1.85
YDE-015	4.03±2.19	6.65±2.13
YDE-016	4.59±1.13	5.98±2.27
YDE-017	4.00±1.22	4.89±1.50
YDE-018	3.75±1.54	4.99±1.60
YDE-019	4.84±1.39	4.52±1.07
YDE-020	3.41±1.47	4.20±1.35
YDE-021	4.08±1.33	4.90±1.13
YDE-022	3.19±0.67	4.10±0.95
YDE-023	5.32±2.30	5.78±2.23
YDE-024	3.85±1.30	5.72±1.36
YDE-025	3.21±0.72	4.72±2.19
YDE-026	4.32±1.47	6.01±1.83
YDE-027	2.82±0.86	3.95±1.52
YDE-028	4.04±0.99	4.73±1.18

Fig. 141 shows the results of the test, wherein A is for the sham control group, B is for the ELGE control group, C is for the DS reference group, D is for the YY-102 administered group, and E to S are for the YDE-029 to YDE-043 administered groups in order.

As a result, it was confirmed that the amount of tear secretion was decreased after 6 days from the ELGE operation at days 7 and 14 after the application of

physiological saline in the ELGE control group as compared with the sham control group. In the groups treated with YDE derivatives and the DS reference group, the amount of tear secretion was increased as compared with the ELGE control group, except for the groups treated with a 0.3% solution of YDE-029, YDE-030, YDE-032, YDE-033, YDE-034, YDE-036, and YDE-41, which did not show any significant changes in the amount of tear secretion after the administration thereof for 14 days. Especially, the amount of tear secretion increased by more than 20% in the groups treated with a 0.3% solution of YDE-040, YDE-043, and YDE-042 in order as compared with the DS reference group.

The specific amounts of tear secretion are shown in Fig. 142 and Table 15.

[Table 15]

No.	Tear Volumes (mm^3)	
	Day 7	Day 14
YY-101	5.36±0.68	6.25±0.68
YY-102	5.77±1.01	6.60±0.64
YDE-029	5.33±1.43	6.03±1.71
YDE-030	5.69±1.79	6.65±2.17
YDE-031	5.63±1.97	5.91±0.85
YDE-032	5.58±0.80	5.03±0.93
YDE-033	4.99±1.20	4.54±1.16
YDE-034	6.16±1.01	6.43±1.86
YDE-035	4.96±0.96	6.25±0.79
YDE-036	4.95±1.05	5.13±1.03
YDE-037	4.98±0.66	5.80±0.90
YDE-039	6.04±1.01	6.44±1.96
YDE-040	5.77±1.05	8.63±1.53
YDE-041	5.01±1.26	6.25±2.15
YDE-042	6.30±1.08	7.97±1.48
YDE-043	5.90±1.06	8.16±1.42

Experimental Example 2.4: Confirmation of the changes in the corneal damage by the YDE derivatives

After YDE-001 to YDE-028 were each administered to the eyes 14 times, the changes in the corneal permeability were checked.

In order to measure the corneal permeability, Zolethyl 50™ (Virbac Lab., Carros, France), an animal anesthetic, was intraperitoneally injected at a dose of 25

mg/kg. Thereafter, saline containing a 1% (v/v) fluorescent solution (fluorescein sodium salt, Tokyo Kasei Kogyo Co., Tokyo, Japan) was applied to the eyes at a dose of 5 μl/eye. The eyes thus treated were closed and fixed with a tape. After 1 hour, the remaining fluorescent solution was removed using a cotton swab (Fig. 142). After 12 hours to 24 hours, the corneal permeability was measured using a blue light tungsten lamp and an ophthalmic slit lamp table top model biomicroscope (Model SM-70N; Takaci Seiko Co., Nakano, Japan) (Fig. 143).

Fig. 144 shows the results of the test, wherein A is for the sham control group, B is for the ELGE control group, C is for the DS reference group, D is for the YY-102 administered group, and E to AF are for the YDE-001 to YDE-028 administered groups in order.

As a result, the permeability of the fluorescent dye was increased in the ELGE control group as compared with the sham control group. The permeability of the fluorescent dye was not decreased in the groups treated with a 0.3% solution of YDE-10, YDE-20, YDE-22, YDE-25, YDE-27, and YDE-28 as compared with the ELGE control group at day 14 after the administration. In the groups treated with YDE derivatives and the DS reference group, the corneal permeability of the fluorescent dye was decreased as compared with the ELGE control group, except for the groups treated with a 0.3% solution of YDE-10, YDE-20, YDE-22, YDE-25, YDE-27, and YDE-28. Especially, the permeability of the fluorescent dye was decreased by more than 20% in the groups treated with a 0.3% solution of YDE-15, YDE-11, YDE-08, YDE-26, YDE-16, YDE-01, YDE-23, and YY-102, as compared with the DS reference group.

The specific permeabilities of the fluorescent dye are shown in Fig. 145 and Table 16.

[Table 16]

No.	Permeability of fluorescent dye (%)
YY-101	27.53±5.62
YY-102	27.48±14.37
YDE-001	25.49±11.62
YDE-002	38.26±11.25
YDE-003	40.45±6.46
YDE-004	35.05±11.74

YDE-005	37.98±11.53
YDE-006	33.23±13.26
YDE-007	32.79±10.77
YDE-008	20.32±11.87
YDE-009	41.50±7.86
YDE-010	49.29±12.06
YDE-011	18.11±11.61
YDE-012	31.01±11.38
YDE-013	32.24±7.84
YDE-014	31.15±10.87
YDE-015	15.95±6.48
YDE-016	24.57±10.34
YDE-017	39.76±7.42
YDE-018	38.19±10.96
YDE-019	40.39±12.57
YDE-020	47.84±13.47
YDE-021	37.00±10.49
YDE-022	47.82±10.01
YDE-023	26.51±8.18
YDE-024	30.63±10.41
YDE-025	47.10±11.45
YDE-026	22.63±11.23
YDE-027	50.24±11.94
YDE-028	41.17±10.25

In addition, YDE-029 to YDE-043 were each administered to the eyes 14 times, and the changes in the corneal permeability were then checked. The measurement of the corneal permeability was carried out in the same manner as described above (Fig. 146).

As a result, the permeability of the fluorescent dye was increased in the ELGE control group as compared with the sham control group. The permeability of the fluorescent dye was not decreased in the groups treated with a 0.3% solution of YDE-29, YDE-32, YDE-33, YDE-36, and YDE-41 as compared with the ELGE control group at day 14 after the administration. In the groups treated with YDE derivatives and the DS reference group, the corneal permeability of the fluorescent dye was decreased as compared with the ELGE control group, except for the groups treated with a 0.3% solution of YDE-29, YDE-32, YDE-33, YDE-36, and YDE-41. Especially, the permeability of the fluorescent dye was decreased by more than 20% in the groups treated with a 0.3% solution of YDE-40, YDE-43, and YDE-42, as

compared with the DS reference group.

The specific permeabilities of the fluorescent dye are shown in Fig. 147 and Table 17.

[Table 17]

No.	Permeability of fluorescent dye (%)
YY-101	33.80±11.11
YY-102	27.89±7.10
YDE-029	63.45±11.57
YDE-030	30.60±13.61
YDE-031	33.35±11.01
YDE-032	58.90±19.81
YDE-033	60.55±21.22
YDE-034	32.17±12.94
YDE-035	27.62±6.51
YDE-036	57.87±22.91
YDE-037	36.30±9.75
YDE-039	29.94±11.40
YDE-040	18.33±9.41
YDE-041	46.38±26.65
YDE-042	20.72±11.37
YDE-043	19.04±7.36

Experimental Example 3: Evaluation of the stability of the YDE derivatives

In order to confirm the stability of each test substance in an aqueous solution, 10 mg of each sample was dissolved in 1 ml of water to a concentration of 1 mg/ml, which was then charged to a glass vial, plugged with a rubber cap, sealed with an aluminum cap, and stored under long-term storage conditions (25°C, 75% RH). The stability of the test substance was evaluated by measuring the amount of related substances at the time of one week, two weeks, four weeks, eight weeks, and twelve weeks under the long-term storage conditions.

As a result, 66.5% of related substances was generated in YY-101 after two weeks. In contrast, 1.1% to 30.6% of related substances was generated in YDE-001 to YDE-028 after 12 weeks. The specific amounts are shown in Table 18.

[Table 18]

No.	Amount of related substances (%; after 12 weeks)

YY-101	66.51 (after 2 weeks)
YDE-001	3.92
YDE-002	4.93
YDE-003	6.86
YDE-004	2.11
YDE-005	2.97
YDE-006	3.67
YDE-007	3.76
YDE-008	4.42
YDE-009	4.71
YDE-010	4.39
YDE-011	3.83
YDE-012	3.57
YDE-013	5.92
YDE-014	6.72
YDE-015	13.05
YDE-016	11.33
YDE-017	11.88
YDE-018	25.39
YDE-019	13.43
YDE-020	21.54
YDE-021	21.33
YDE-022	19.23
YDE-023	30.66
YDE-024	20.59
YDE-025	5.17
YDE-026	10.15
YDE-027	12.74
YDE-028	1.15

Test Example 4: Evaluation of recovery of corneal damage by the YDE derivatives

In order to confirm whether the YDE derivatives could recover corneal damage, the cellular growth rate of human primary corneal epithelial cells was checked.

Specifically, primary corneal epithelial cells (ATCC, ATCC PCS-700-010) were seeded on a 96-well culture plate (Perkin Elmer, 6005680) containing the Corneal Epithelial Cell Basal Medium (ATCC, ATCC PCS-700-030) in the Corneal Epithelial Cell Growth Kit (ATCC, ATCC PCS-700-040) in an amount of 5×10^3 cells per well, which was then cultured for 24 hours under the conditions of 37°C

and 5% CO_2.

YDE-001 to YDE-075 were each dissolved in 100% DMSO (Sigma, D2660) to a concentration of 10 mM, which was then diluted with 100% DMSO to a concentration of the compound of 6, 1.9, 0.6, 0.2, 0.06, 0.02, 0.006, and 0.002 mM. 20 μl of the diluted YDE derivative was added to a 96-well microplate (Greiner Bio-One, 651201) containing 380 μl of the Corneal Epithelial Cell Basal Medium such that the concentration of DMSO was diluted to 5%.

After 24 hours, 20 μl of each of the YDE derivatives diluted in the 96-well microplate was added to the 96-well culture plate containing the cells. As a control group, hEGF (Sigma, E9644) was treated at the same concentration as the YDE derivatives. The cells treated with the YDE-derivatives or hEGF were cultured for 48 hours and 72 hours under the conditions of 37°C and 5% CO_2 (Figs. 148 to 155).

The cultured cells were treated with the CellTiter-Glo luminescent reagent (Promega, G7573) according to the manufacturer's instructions and reacted for 30 minutes at room temperature. Thereafter, the fluorescent signal (or luminescence signal) was checked using an Envision 2014 Multi-label plate reader. The measured values were normalized using a vehicle control (100% proliferation cell).

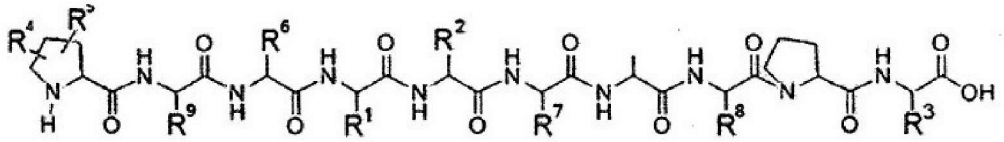
As a result, the cell proliferation was observed at concentrations of 0.3 μM or less in YY-101, YY-102, YDE-011, YDE-038, YDE-042, YDE-043, YDE-044, YDE-045, YDE-049, YDE-054, YDE-057, YDE-058, YDE-059, and YDE-060. Especially, a high cell proliferation rate was shown in YY-102, YDE-011, YDE-045, YDE-057, and YDE-060 (Figs. 156 to 173).

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What is claimed is:

1. A compound represented by Formula 1:

[Formula 1]



wherein R^1 to R^3 are each independently hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{1-10} alkoxy, substituted or unsubstituted C_{1-10} haloalkyl, substituted or unsubstituted C_{2-10} alkenyl, substituted or unsubstituted C_{2-10} alkynyl, substituted or unsubstituted C_{1-10} alkylene, substituted or unsubstituted C_{1-10} alkenylene, substituted or unsubstituted C_{1-10} alkynylene, substituted or unsubstituted C_{5-12} aryl, substituted or unsubstituted C_{7-12} arylalkyl, substituted or unsubstituted C_{5-14} arylalkynyl, substituted or unsubstituted C_{8-16} arylalkenyl, substituted or unsubstituted C_{3-10} heteroalkyl, substituted or unsubstituted C_{3-10} cycloalkyl, substituted or unsubstituted C_{3-10} heterocycloalkyl, or substituted or unsubstituted C_{5-12} heteroaryl, the heteroalkyl, heterocycloalkyl, or heteroaryl containing at least one of N, O, and S,

R^4 and R^5 are each independently hydrogen, substituted or unsubstituted C_{1-6} alkyl, $-X_2$, $-R_b$, $-O^-$, =O, $-CH_2OR_b$, or $-OR_b$;

provided that at least one of R^4 or R^5 is not H;

X_2 is F, Cl, Br, or I,

R_b is H, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{5-12} aryl, substituted or unsubstituted C_{7-12} arylalkyl, or substituted or unsubstituted heterocycle,

R^6 is hydrogen, unsubstituted C_{1-6} alkyl, or C_{1-6} alkyl substituted with $-C(=O)NH_2$,

R^7 is hydrogen or C_{1-6} alkyl, and

R^8 and R^9 are hydrogen or unsubstituted C_{1-6} alkyl;

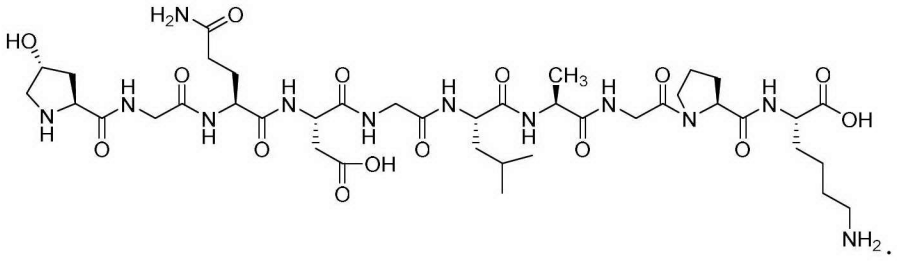
wherein when a group is substituted, unless otherwise indicated, the substituent is selected from X_1, $-R_a$, $-O^-$, =O, $-OR_a$, $-SR_a$, $-S^-$, $-N(R_a)_2$, $-N^+(R_a)_3$, $=NR_a$, $-C(X_1)_3$, -CN, -OCN, -SCN, -N=C=O, -NCS, -NO, $-NO_2$, =N-OH, $=N_2$, $-N_3$, $-NHC(=O)R_a$, $-C(=O)R_a$, $-C(=O)NR_aR_a$, $-S(=O)_2O^-$, $-S(=O)_2OH$, $-S(=O)_2R_a$, $-OS(=O)_2OR_a$, $-S(=O)_2NR_a$, -

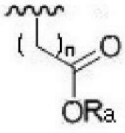
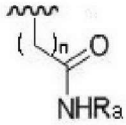
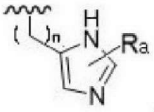
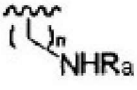
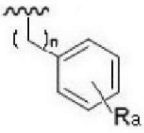
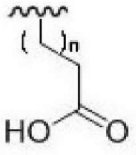
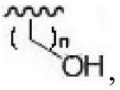
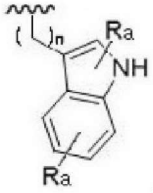
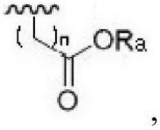
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$S(=O)R_a$, $-OP(=O)(OR_a)_2$, $-C(=O)R_a$, alkylene-$C(=O)R_a$, $-C(=S)R_a$, $-C(=O)OR_a$, alkylene-$C(=O)OR_a$, $-C(=O)O^-$, alkylene-$C(=O)O$-, $-C(=S)OR_a$, $-C(=O)SR_a$, $-C(=S)SR_a$, $-C(=O)NR_aR_a$, alkylene-$C(=O)NR_aR_a$, $-C(=S)NR_aR_a$, and $-C(-NR_a)NR_aR_a$; wherein X_1 is F, Cl, Br, or I, and

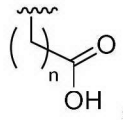
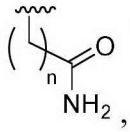
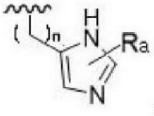
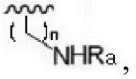
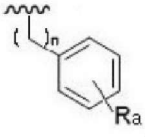
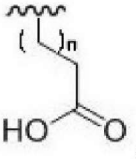
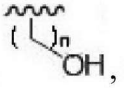
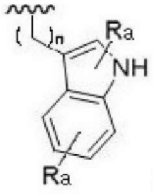
R_a is hydrogen, C_{1-6} alkyl, C_{5-12} aryl, C_{7-12} arylalkyl, or heterocycle,

further wherein the compound is not:



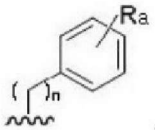
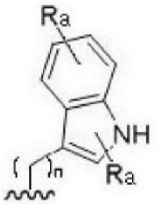
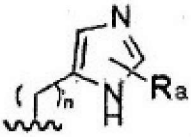
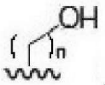
2. The compound of claim 1, wherein R^1 is selected from substituted or unsubstituted C_{1-6} alkyl,  ,  ,  ,  ,  ,  ,  ,  ,  , and ,

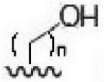
wherein R_a is hydrogen or C_{1-6} alkyl, and n is an integer from 1 to 10.

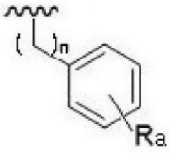
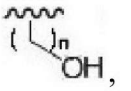
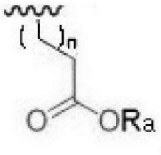
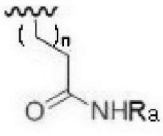
3. The compound of claim 1, wherein R^1 is selected from substituted or unsubstituted C_{1-6} alkyl,  ,  ,  ,  ,  ,  ,  , and  ; wherein R_a is hydrogen or C_{1-6} alkyl, and n is an integer from 1 to 10.

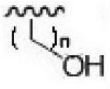
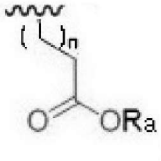
4. The compound of claim 1, wherein R^2 is selected from hydrogen, substituted or

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unsubstituted C_{1-6} alkyl,  ,  ,  , and  , wherein R_a is hydrogen or C_{1-6} alkyl, and n is an integer of 1 to 10.

5. The compound of claim 1, wherein R^2 is selected from hydrogen, substituted or unsubstituted C_{1-6} alkyl, and  , wherein n is an integer from 1 to 10.

6. The compound of claim 1, wherein R^3 is selected from substituted or unsubstituted C_{1-6} alkyl,  ,  ,  , and  , wherein R_a is hydrogen or C_{1-6} alkyl, and n is an integer of 1 to 10.

7. The compound of claim 1, wherein R^3 is selected from substituted or unsubstituted C_{1-6} alkyl,  , and  ; wherein R_a is hydrogen or C_{1-6} alkyl, and n is an integer of 1 to 10 .

8. The compound of claim 1, wherein

R^4 and R^5 are each independently selected from hydrogen, substituted or unsubstituted C_{1-6} alkyl, $-OR_b$, =O, $-CH_2OR_b$, and $-X_2$,

provided that at least one of R^4 or R^5 is not H; and

R_b is hydrogen or C_{1-6} alkyl.

9. The compound of claim 1, wherein

R^4 and R^5 are each independently selected from hydrogen, substituted or unsubstituted C_{1-6} alkyl, $-OR_b$, $-CH_2OR_b$, and -halogen,

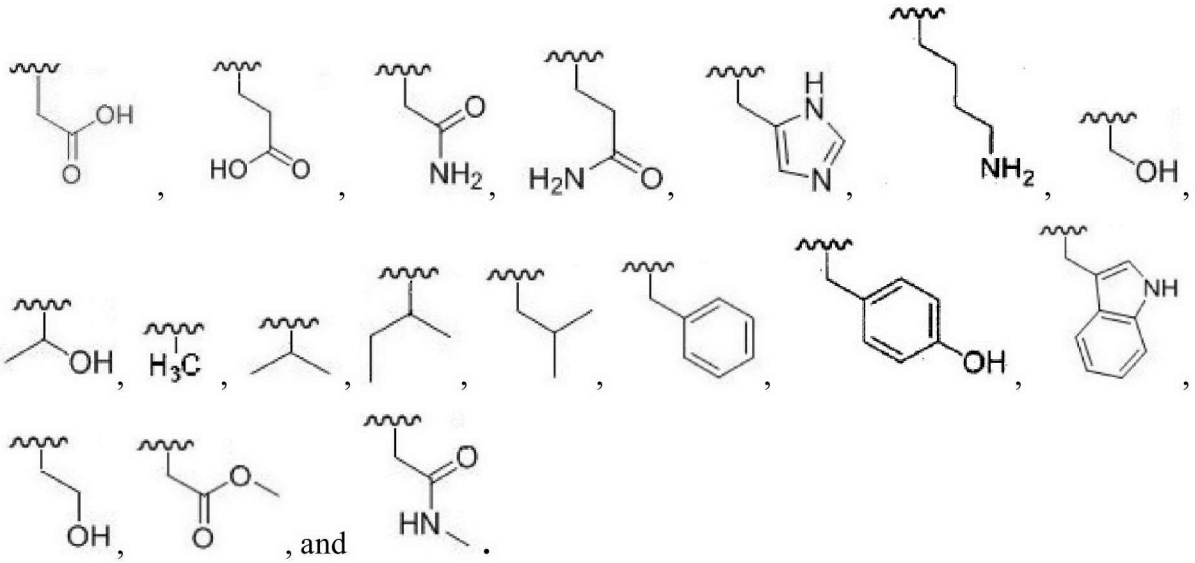
provided that at least one of R^4 or R^5 is not H; and

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R_b is hydrogen or C_{1-6} alkyl.

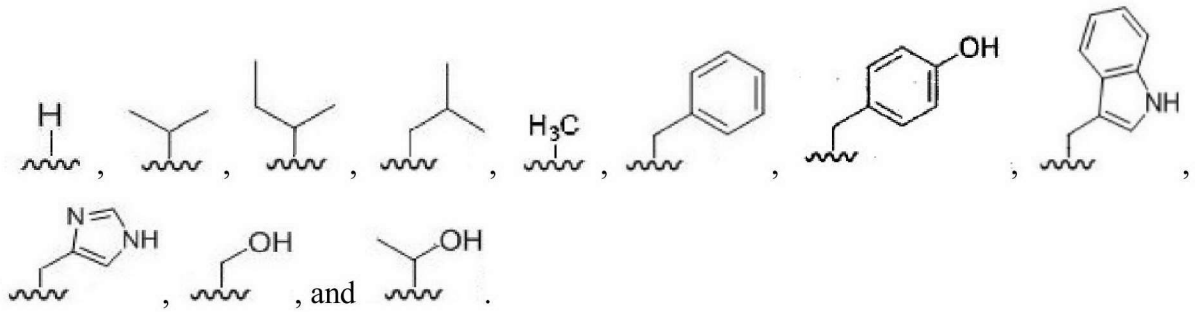
10. The compound of claim 1, wherein R^6 to R^9 are each independently hydrogen, unsubstituted C_{1-6} alkyl, or C_{1-6} alkyl, substituted with $-C(=O)NH_2$.

11. The compound of claim 2, wherein R^1 is selected from



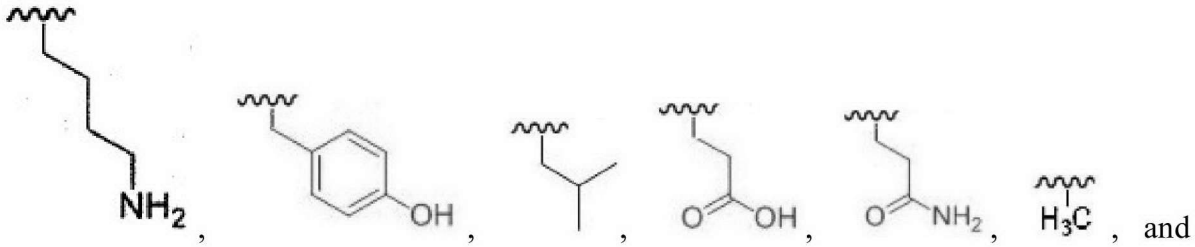
, and .

12. The compound of claim 4, wherein R^2 is selected from



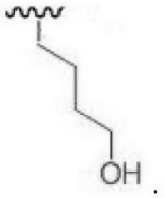
, and .

13. The compound of claim 6, wherein R^3 is selected from

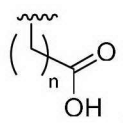
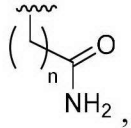
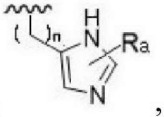
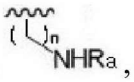
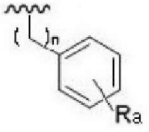
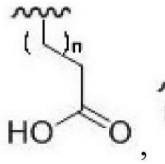
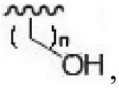
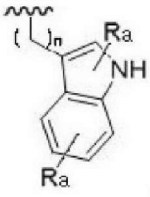


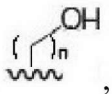
, and

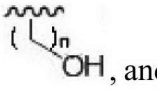
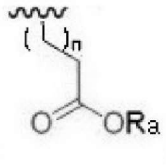
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14. The compound of claim 8, wherein R^4 is selected from H, -OH, =O, and $-CH_3$.

15. The compound of claim 1, wherein R^1 is selected from substituted or unsubstituted C_{1-6} alkyl,  ,  ,  ,  ,  ,  ,  ,  , and , wherein R_a is hydrogen or C_{1-6} alkyl, and n is an integer of 1 to 10,

wherein R^2 is selected from hydrogen, substituted or unsubstituted C_{1-6} alkyl, and  ,

R^3 is selected from substituted or unsubstituted C_{1-6} alkyl,  , and  ; wherein R_a is hydrogen or C_{1-6} alkyl, and n is an integer of 1 to 10;

R^4 and R^5 are each independently selected from hydrogen, substituted or unsubstituted C_{1-6} alkyl, $-OR_b$, $-CH_2OR_b$, and -halogen,

provided that at least one of R^4 or R^5 is not H;

R_b is hydrogen or C_{1-6} alkyl;

wherein when a group is substituted, unless otherwise indicated, the substituent is selected from $-X_1$, $-R_a$, $-O^-$, =O, $-OR_a$, $-SR_a$, $-S^-$, $-N(R_a)_2$, $-N^+(R_a)_3$, $=NR_a$, $-C(X_1)_3$, -CN, -OCN, -SCN, -N=C=O, -NCS, -NO, $-NO_2$, =N-OH, $=N_2$, $-N_3$, $-NHC(=O)R_a$, $-C(=O)R_a$, $-C(=O)NR_aR_a$, $-S(=O)_2O^-$, $-S(=O)_2OH$, $-S(=O)_2R_a$, $-OS(=O)_2OR_a$, $-S(=O)_2NR_a$, $-S(=O)R_a$, $-OP(=O)(OR_a)_2$, $-C(=O)R_a$, alkylene-$C(=O)R_a$, $-C(=S)R_a$, $-C(=O)OR_a$, alkylene-$C(=O)OR_a$, $-C(=O)O^-$, alkylene-C(=O)O-, $-C(=S)OR_a$, $-C(=O)SR_a$, -

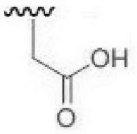
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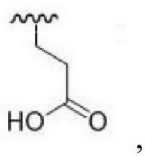
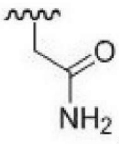
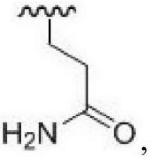
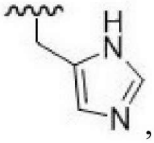
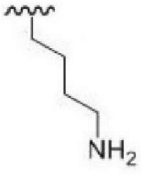
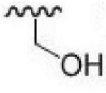
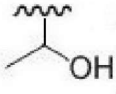
$C(=S)SR_a$, $-C(=O)NR_aR_a$, alkylene-$C(=O)NR_aR_a$, $-C(=S)NR_aR_a$, and $-C(-NR_a)NR_aR_a$, X_1 is F, Cl, Br, or I, R_a is hydrogen, C_{1-6} alkyl, C_{5-12} aryl, C_{7-12} arylalkyl, or heterocycle,

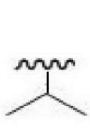
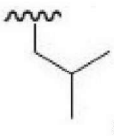
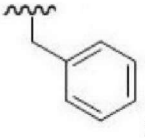
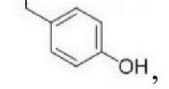
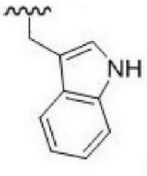
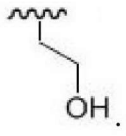
wherein R^6 to R^9 are each independently hydrogen, unsubstituted C_{1-6} alkyl, or C_{1-6} alkyl substituted with $-C(=O)NH_2$,

and further wherein the compound is not:

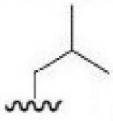
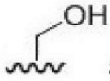
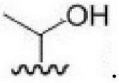
HyP-Gly-Gln-Asp-Gly-Leu-Ala-Gly-Pro-Lys.

16. The compound of claim 11 or 15, wherein R^1 is selected from  ,

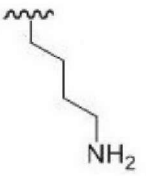
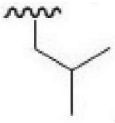
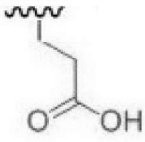
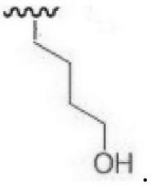
 ,  ,  ,  ,  ,  ,  ,  ,

 ,  ,  ,  ,  ,  , and  .

17. The compound of claim 12 or 15, wherein R^2 is one selected from  ,  ,

 ,  ,  ,  and  .

18. The compound of claim 13 or 15, wherein R^3 is one selected from

 ,  ,  ,  , and  .

19. The compound of claim 15 wherein R^4 is one selected from H, -OH, F and $-CH_3$.

20. The compound of claim 1, which is any one selected from HyP-Gly-Gln-Glu-Gly-Leu-

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Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asn-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Gln-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-His-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Lys-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Ser-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Thr-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Ala-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Val-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Ile-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Phe-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Tyr-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Trp-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Ser(Homo)-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp(Me)-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asn(Me)-Gly-Leu-Ala-Gly-Pro-Lys, D-HyP(2R, 4S)-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, D-Hyp(2R,4S)-Gly-D-Gln-D-Leu-Gly-D-Leu-D-Ala-Gly-D-Pro-D-Lys, D-Hyp(2R, 4R)-Gly-D-Gln-D-Leu-Gly-D-Leu-D-Ala-Gly-D-Pro-D-Lys, HyP-Gly-Gln-Asp-Val-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Ile-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Leu-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Ala-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Phe-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Tyr-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Trp-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-His-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Ser-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Thr-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Leu-Ala-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Tyr, HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Leu, HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Glu, HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Gln, HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Nle(6-OH), HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Ala, D-HyP(2R, 4S)-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Ala, Hyp(2S, 4S)-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, (4-oxo)Pro-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, (5-oxo)Pro-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, (4-hydroxyMe)Pro-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, (4-Fluoro)Pro-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, (4-Dimethyl)Pro-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, (4-Me)Pro-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, (5-Me)Pro-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, Hyp-Gly-Ala-Leu-Gly-Leu-Ala-Gly-Pro-Lys, Hyp-Gly-Gln-Leu-Gly-Ala-Ala-Gly-Pro-Lys, Hyp-Gly-Gln-Leu-Gly-Leu-Ala-Ala-Pro-Lys, Hyp-Ala-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, D-Hyp(2R, 4S)-Ala-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, and D-Hyp(2R, 4S)-Ala-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Ala.

21. A peptide having an amino acid sequence represented by HyP-Gly-Gln-Xaa^1-Gly-Leu-Ala-Gly-Pro-Lys, wherein Xaa^1 is selected from Glu, Asn, Gln,

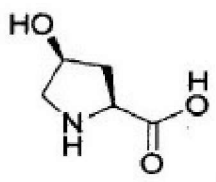
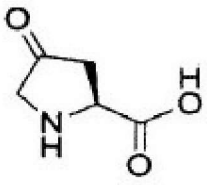
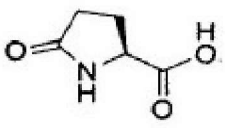
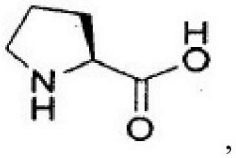
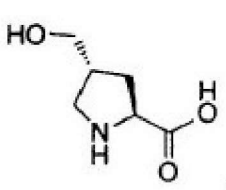
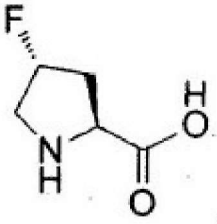
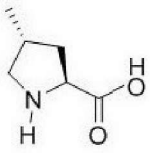
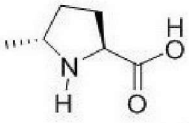
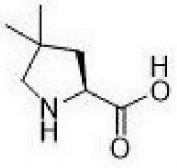
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His, Lys, Ser, Thr, Ala, Val, Ile, Leu, Phe, Tyr, Trp, homo-Ser, Asp(Me), and Asn(Me), preferably wherein Xaa^1 is selected from Glu, Asn, Gln, Asn, Gln, His, Lys, Ser, Thr, Ala, Val, Leu, Phe, Tyr, Trp, and homo-Ser.

22. A peptide having an amino acid sequence represented by HyP-Gly-Gln-Asp-Xaa^2-Leu-Ala-Gly-Pro-Lys, wherein Xaa^2 is selected from Val, Ile, Leu, Ala, Phe, Tyr, Trp, Ser, Thr, and (N-Me)Gly.

23. A peptide having an amino acid sequence represented by HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Xaa^3, wherein Xaa^3 is selected from Tyr, Leu, Glu, Gln, Ala, and Nle(6-OH).

24. A peptide having an amino acid sequence represented by PD-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, wherein PD is any one selected from the following formulae:

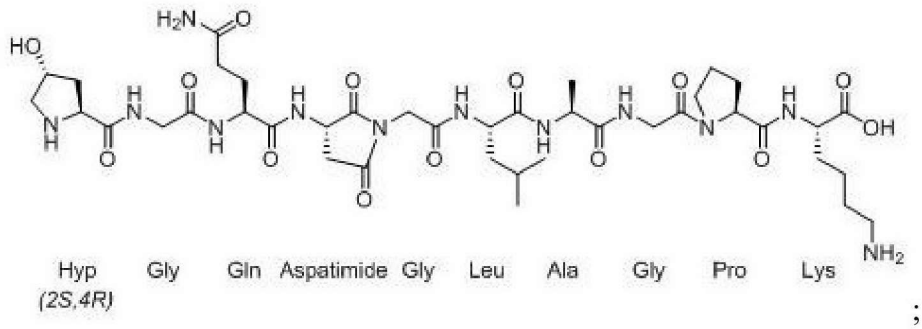

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25. A peptide having any one amino acid sequence selected from the group consisting of Ala-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, Hyp-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Ala-Lys, HyP-Gly-Gln-Leu-Gly-Leu-Ala, HyP-Gly-Gln-Glu-Gly-Lys-Gly, HyP-Gly-Gln-Leu-Gly-Leu, $_{D}$-HyP(2R, 4S)-Gly-$_{D}$-Gln-$_{D}$-Leu-Gly-$_{D}$-Leu, HyP-Gly-Gln-Leu-Gly, HyP-Gly-Gln-$_{D}$-Leu-Gly, and $_{D}$-HyP(2R, 4S)-Gly-Gln-Leu-Gly.

26. A compound represented by Formula 8 or Formula 10:

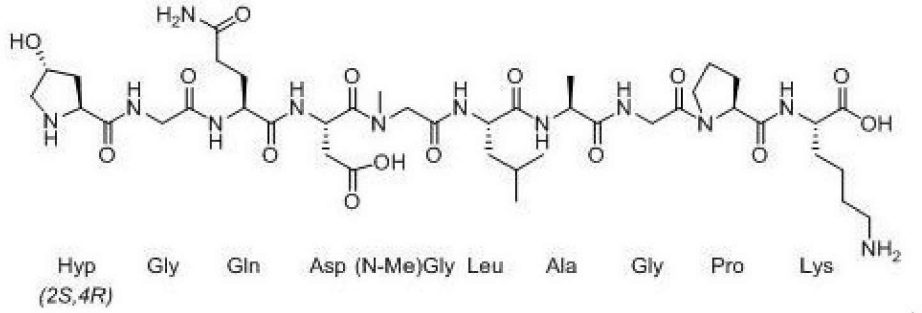
2018281617 31 May 2022

[Formula 8]



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[Formula 10]



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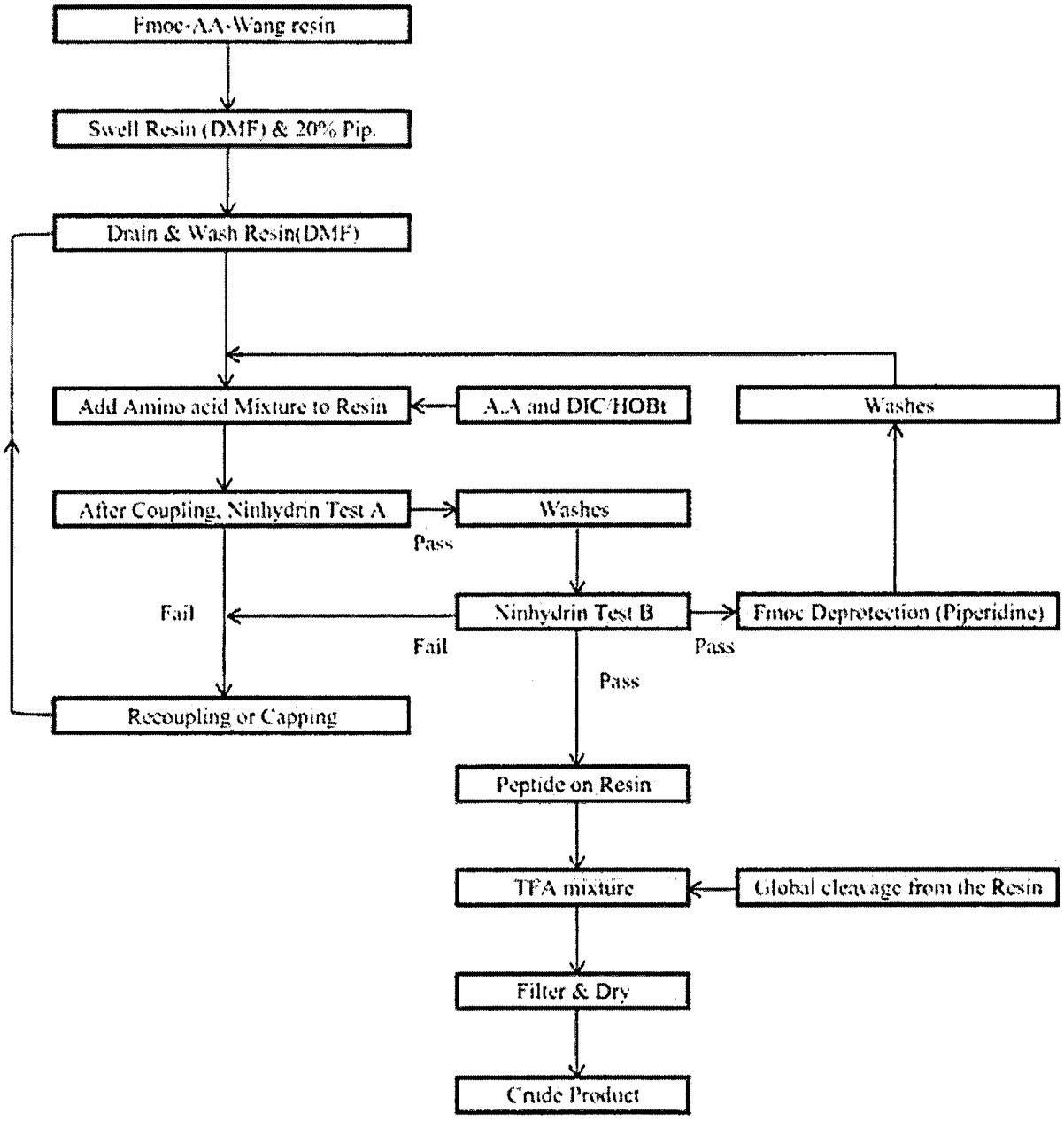
27. Use of a compound according to any one of claims 1 to 20 and 26, or the peptide according to any one of claims 21 to 25, in the manufacture of a medicament for treating an eye disease, wherein the eye disease is selected from retinopathy, keratitis, dry-macular degeneration, wet-macular degeneration, dry eye syndrome, keratoconjunctivitis sicca and keratoconjunctival epithelium disorder.

28. A method for treating an eye disease in a subject comprising administering a compound according to any one of claims 1 to 20 and 26, or the peptide according to any one of claims 21 to 25, to the subject, wherein the eye disease is selected from retinopathy, keratitis, dry-macular degeneration, wet-macular degeneration, dry eye syndrome, keratoconjunctivitis sicca and keratoconjunctival epithelium disorder.

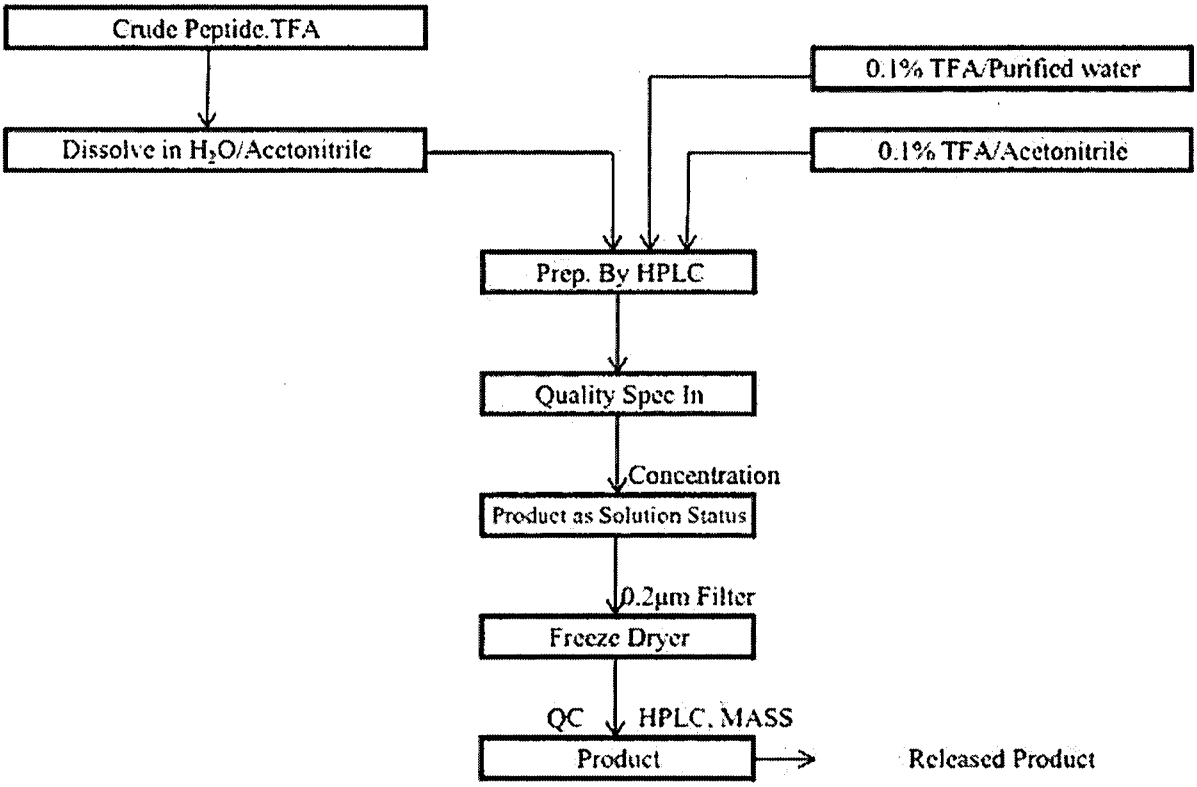
도 1

No.	Lot Number	Peptide Name	Sequence	M.W.	Purity (%)	Amount (mg)	Solubility (0.5mg/ml)
1	K161389	YDE-001	OGQEGLAGPK (O : Hydroxyproline)	969.1	>99.7%	5.0mg 10.0mg	Water
2	K161390	YDE-002	OGQNGLAGPK (O : Hydroxyproline)	954.0	>99.7%	5.0mg 10.0mg	Water
3	K161391	YDE-003	OGQQGLAGPK (O : Hydroxyproline)	968.1	>99.7%	5.0mg 10.0mg	Water
4	K161392	YDE-004	OGQHGLAGPK (O : Hydroxyproline)	977.1	>99.7%	5.0mg 10.0mg	Water
5	K161393	YDE-005	OGQKGLAGPK (O : Hydroxyproline)	968.1	>99.5%	5.0mg 10.0mg	Water
6	K161394	YDE-006	OGQSGLAGPK (O : Hydroxyproline)	927.0	>98.9%	5.0mg 10.0mg	Water
7	K161395	YDE-007	OGQTGLAGPK (O : Hydroxyproline)	941.0	>98.6%	5.0mg 10.0mg	Water
8	K161396	YDE-008	OGQAGLAGPK (O : Hydroxyproline)	911.0	>98.8%	5.0mg 10.0mg	Water
9	K161397	YDE-009	OGQVGLAGPK (O : Hydroxyproline)	939.1	>98.1%	5.0mg 10.0mg	Water
10	K161398	YDE-010	OGQIGLAGPK (O : Hydroxyproline)	953.1	>99.0%	5.0mg 10.0mg	Water
11	K161399	YDE-011	OGQLGLAGPK (O : Hydroxyproline)	953.1	>98.3%	5.0mg 10.0mg	Water
12	K161400	YDE-012	OGQFGLAGPK (O : Hydroxyproline)	987.1	>98.9%	5.0mg 10.0mg	Water
13	K161401	YDE-013	OGQYGLAGPK (O : Hydroxyproline)	1003.1	>98.7%	5.0mg 10.0mg	Water
14	K161402	YDE-014	OGQWGLAGPK (O : Hydroxyproline)	1026.2	>98.5%	5.0mg 10.0mg	Water
15	K161403	YDE-015	OGQDVLAGPK (O : Hydroxyproline)	997.1	>99.1%	5.0mg 10.0mg	Water
16	K161404	YDE-016	OGQDILAGPK (O : Hydroxyproline)	1011.1	>99.4%	5.0mg 10.0mg	Water
17	K161405	YDE-017	OGQDLLAGPK (O : Hydroxyproline)	1011.1	>98.0%	5.0mg 10.0mg	Water
18	K161406	YDE-018	OGQDALAGPK (O : Hydroxyproline)	969.1	>99.6%	5.0mg 10.0mg	Water
19	K161407	YDE-019	OGQDFLAGPK (O : Hydroxyproline)	1045.2	>99.6%	5.0mg 10.0mg	Water
20	K161408	YDE-020	OGQDYLAGPK (O : Hydroxyproline)	1061.2	>99.2%	5.0mg 10.0mg	Water
21	K161409	YDE-021	OGQDWLAGPK (O : Hydroxyproline)	1084.2	>98.1%	5.0mg 10.0mg	Water
22	K161410	YDE-022	OGQDHLAGPK (O : Hydroxyproline)	1035.1	>98.3%	5.0mg 10.0mg	Water
23	K161411	YDE-023	OGQDSLAGPK (O : Hydroxyproline)	985.1	>96.1%	5.0mg 10.0mg	Water
24	K161412	YDE-024	OGQDTLAGPK (O : Hydroxyproline)	999.1	>98.9%	5.0mg 10.0mg	Water
25	K161413	YDE-025	OGQD-Sar-LAGPK (Sar : me-Gly) (O : Hydroxyproline)	969.1	>95%	5.0mg 10.0mg	Water
26	K161414	YDE-026	OGQS*GLAGPK (S* : homo-Ser) (O : Hydroxyproline)	941.1	>95%	5.0mg 10.0mg	Water
27	K161415	YDE-027	OGQD*GLAGPK (D* : D(OMe)) (O : Hydroxyproline)	969.1	>95%	5.0mg 10.0mg	water
28	K161416	YDE-028	OGQN*GLAGPK (N* : N(NMe) (O : Hydroxyproline)	968.1	>95%	5.0mg 10.0mg	Water

도 2


Fmoc-AA-Wang resin
Swell Resin (DMF) & 20% Pip.
Drain & Wash Resin(DMF)
Add Amino acid Mixture to Resin
A.A and DIC/HOBt
Washes
After Coupling, Ninhydrin Test A
Washes
Pass
Fail
Ninhydrin Test B
Fmoc Deprotection (Piperidine)
Fail
Pass
Pass
Recoupling or Capping
Peptide on Resin
TFA mixture
Global cleavage from the Resin
Filter & Dry
Crude Product

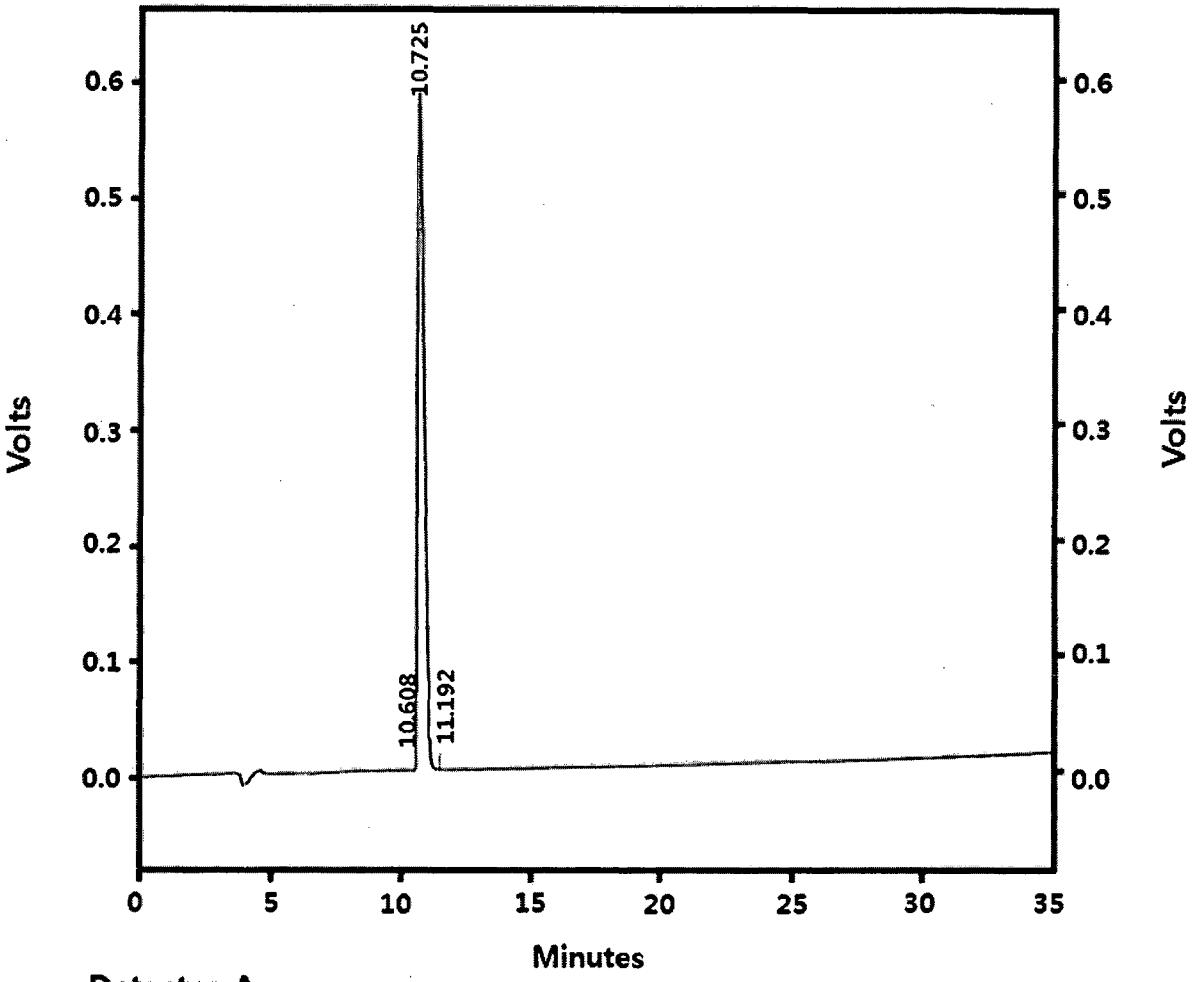
도 3


Crude Peptide.TFA
Dissolve in H_2O/Acetonitrile
0.1% TFA/Purified water
0.1% TFA/Acetonitrile
Prep. By HPLC
Quality Spec In
Concentration
Product as Solution Status
0.2μm Filter
Freeze Dryer
QC
HPLC, MASS
Product
Released Product

도 4

Shimadzu CLASS-VP V6.14 SP1 manual *Area % Report*

Sample ID : K161389 (YDE-001)

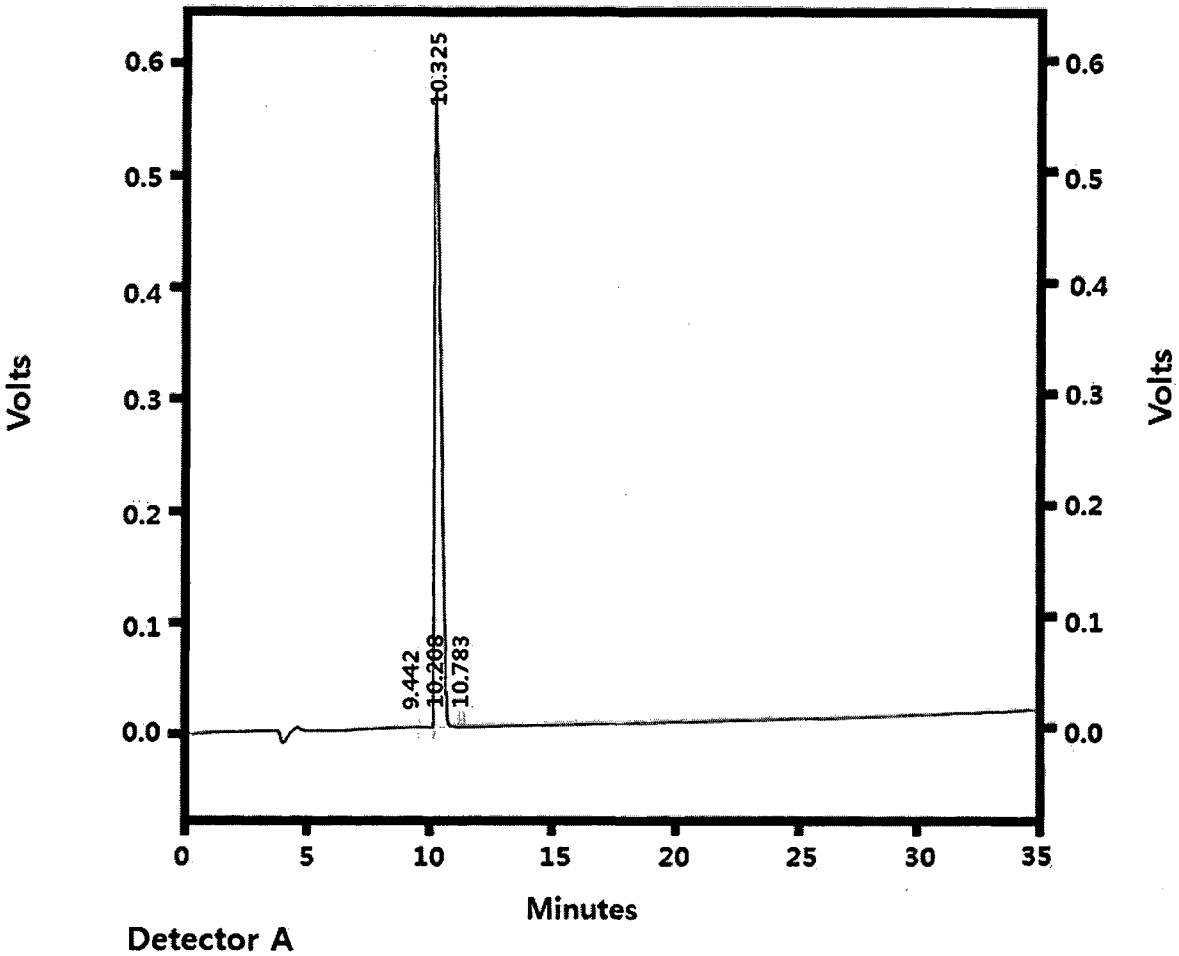


Detector A (230nm)	Pk #	Retention Time	Area	Area %
	1	10.608	783	0.008
	2	10.725	10120624	99.730
	3	11.192	26596	0.262
Totals			10148003	100.000

도 5

Shimadzu CLASS-VP V6.14 SP1 manual *Area % Report*

Sample ID : K161390 (YDE-002)



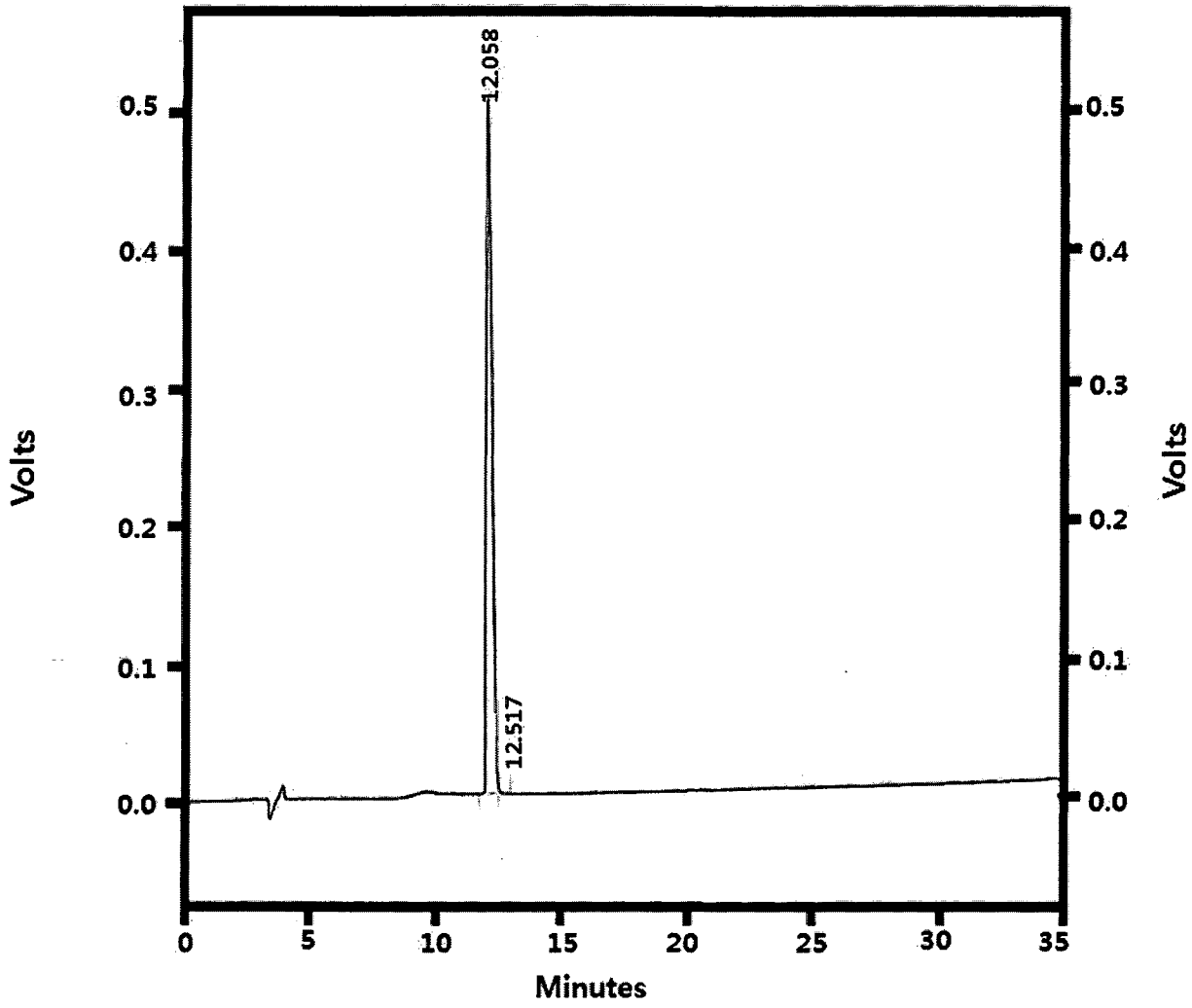
Detector A

(230nm) Pk #	Retention Time	Area	Area %
1	9.442	290	0.003
2	10.208	456	0.005
3	10.325	9921099	99.715
4	10.783	27655	0.278
Totals		9949500	100.000

도 6

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K161391 (YDE-003)



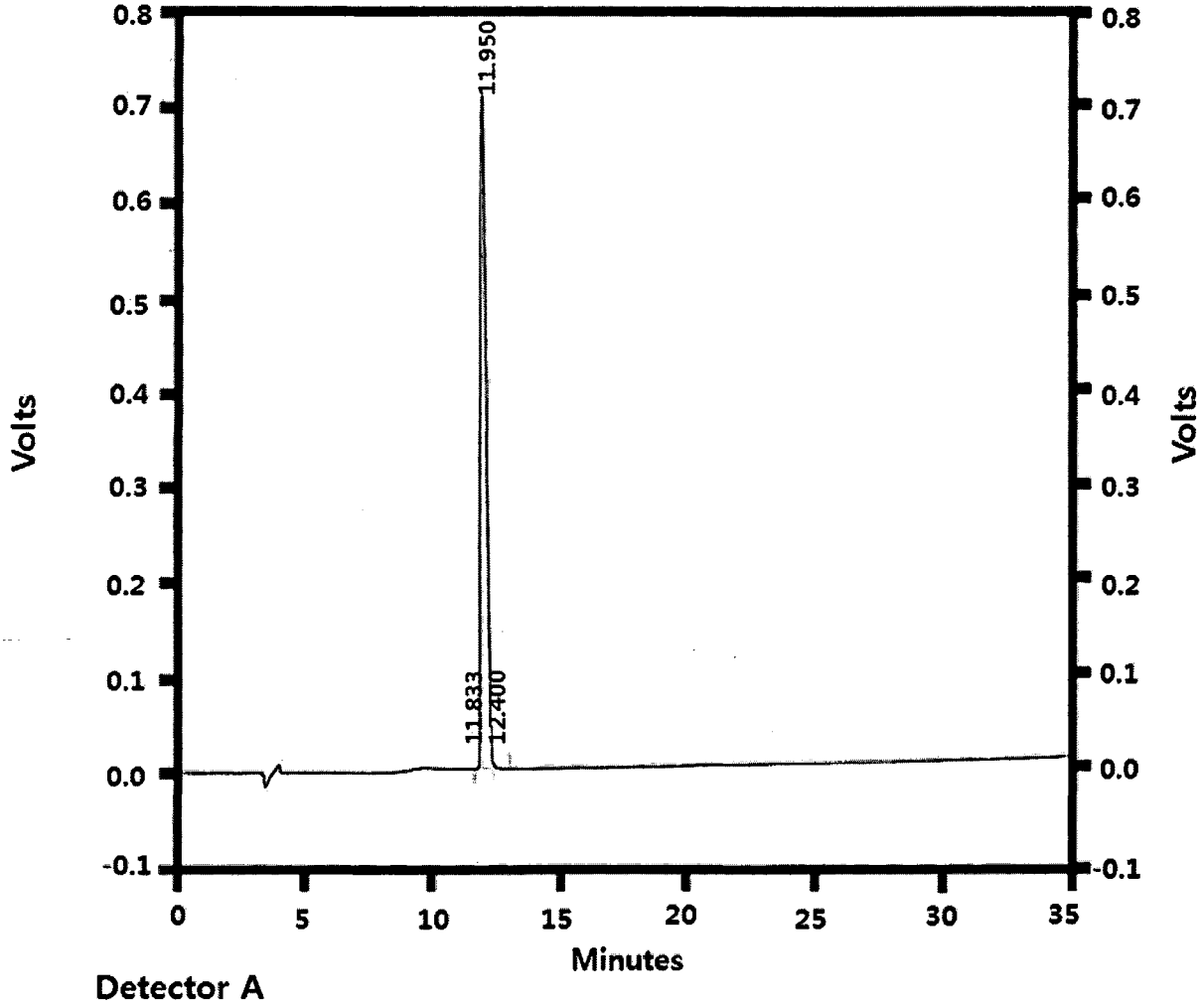
Detector A
(230nm)

Pk #	Retention Time	Area	Area %
1	12.058	7863599	99.774
2	12.517	17816	0.226
Totals		7881415	100.000

도 7

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K161392 (YDE-004)



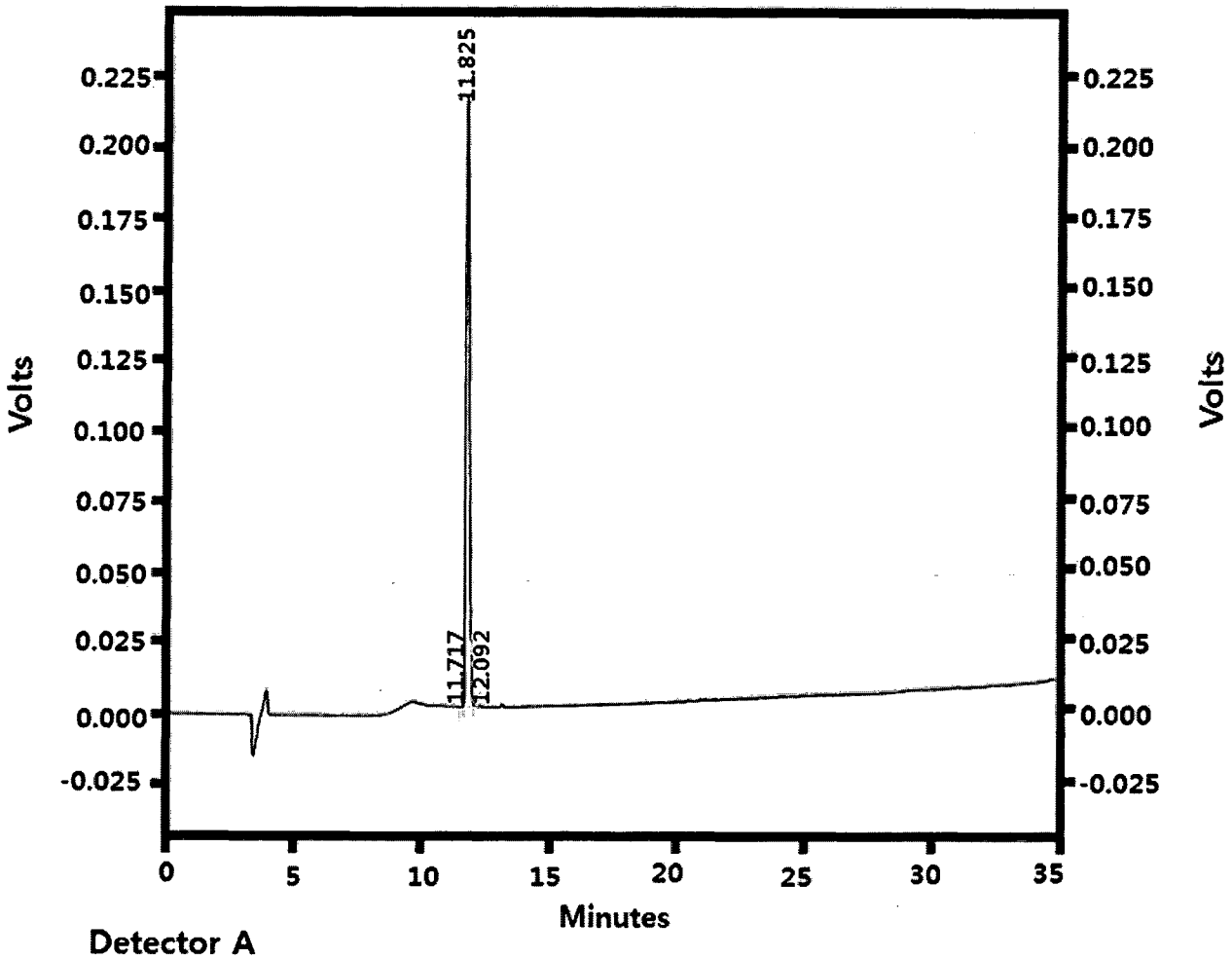
Detector A
(230nm)

Pk #	Retention Time	Area	Area %
1	11.833	4175	0.038
2	11.950	10864330	99.735
3	12.400	24696	0.227
Totals		10893201	100.000

도 8

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K161393 (YDE-005)



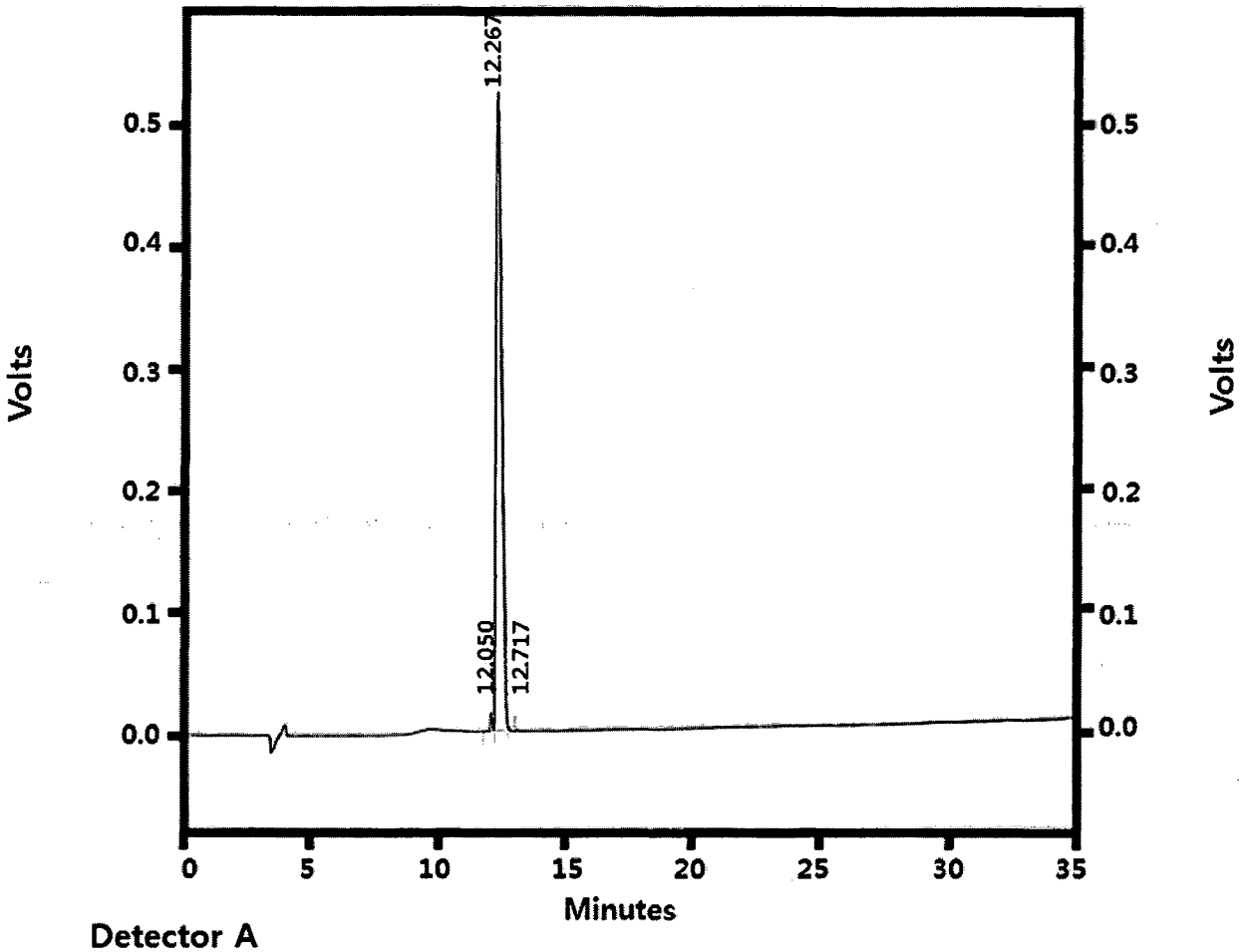
Detector A
(230nm)

Pk #	Retention Time	Area	Area %
1	11.717	2003	0.102
2	11.825	1950157	99.552
3	12.092	6778	0.346
Totals		1958938	100.000

도 9

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K161394 (YDE-006)



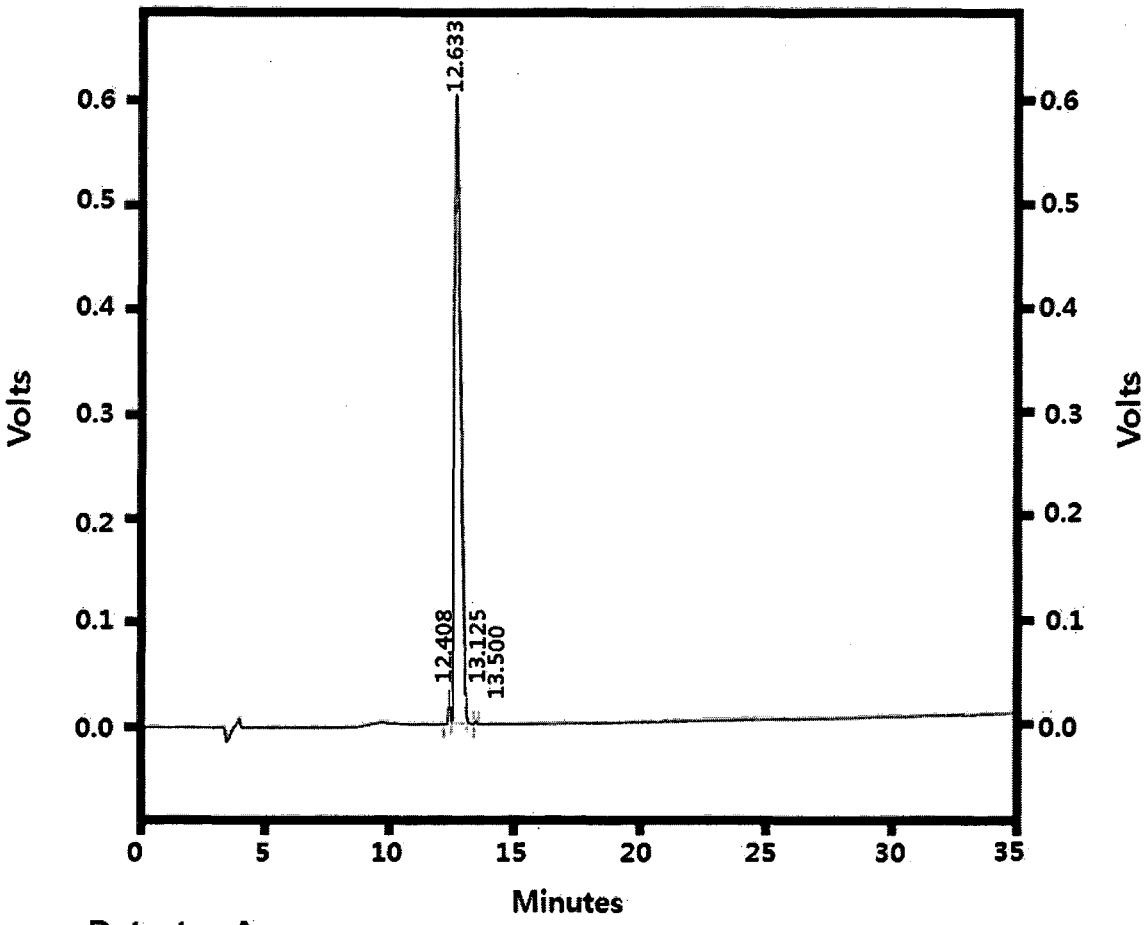
Detector A
(230nm)

Pk #	Retention Time	Area	Area %
1	12.050	78741	0.961
2	12.267	8100790	98.903
3	12.717	11116	0.136
Totals		8190647	100.000

표 10

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K161395 (YDE-007)

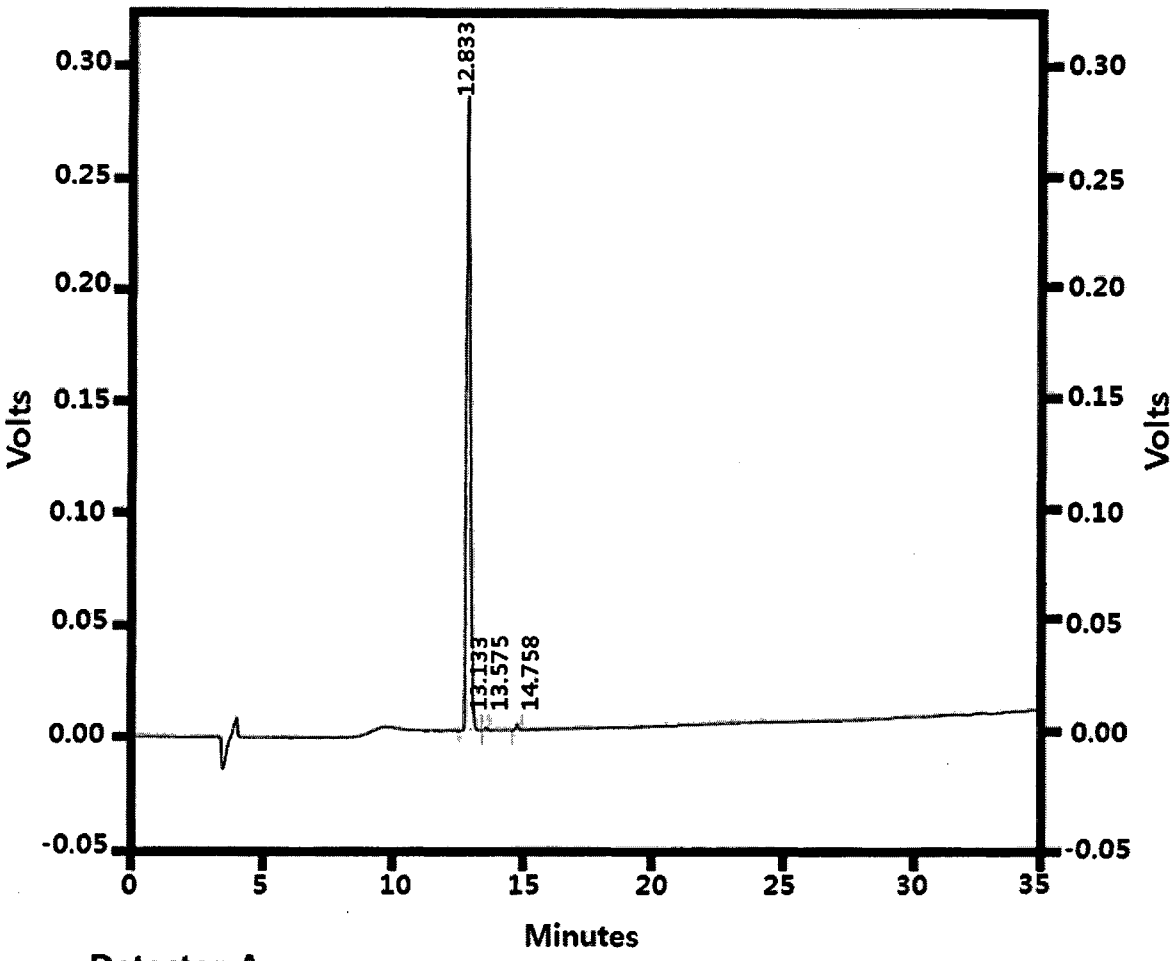


Detector A (230nm) Pk #	Retention Time	Area	Area %
1	12.408	171422	1.618
2	12.633	10390868	98.067
3	13.125	18102	0.171
4	13.500	15280	0.144
Totals		10595672	100.000

도 11

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K161396 (YDE-008)



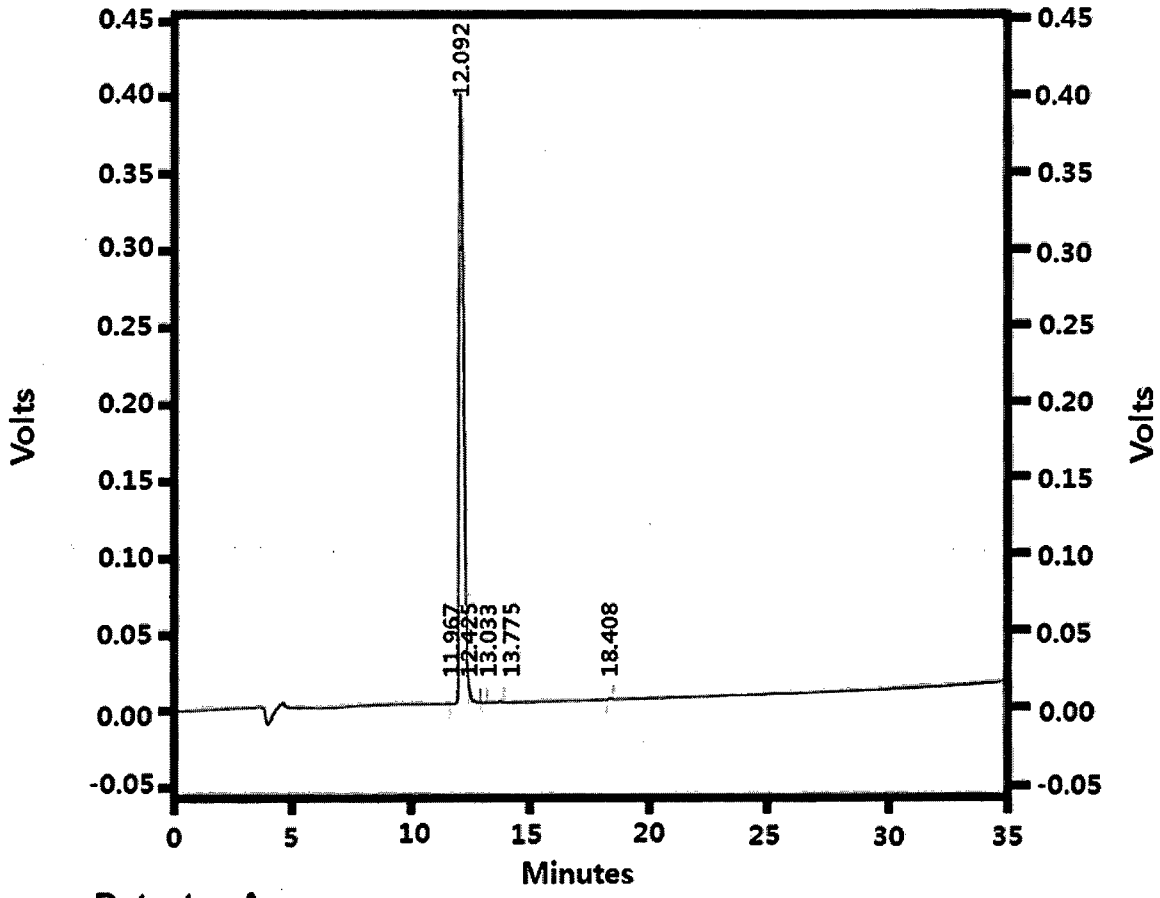
Detector A
(230nm)

Pk #	Retention Time	Area	Area %
1	12.833	2920911	98.891
2	13.133	11156	0.378
3	13.575	6889	0.233
4	14.758	14724	0.498
Totals		2953680	100.000

도 12

Shimadzu CLASS-VP V6.14 SP1 manual *Area % Report*

Sample ID : K161397 (YDE-009)



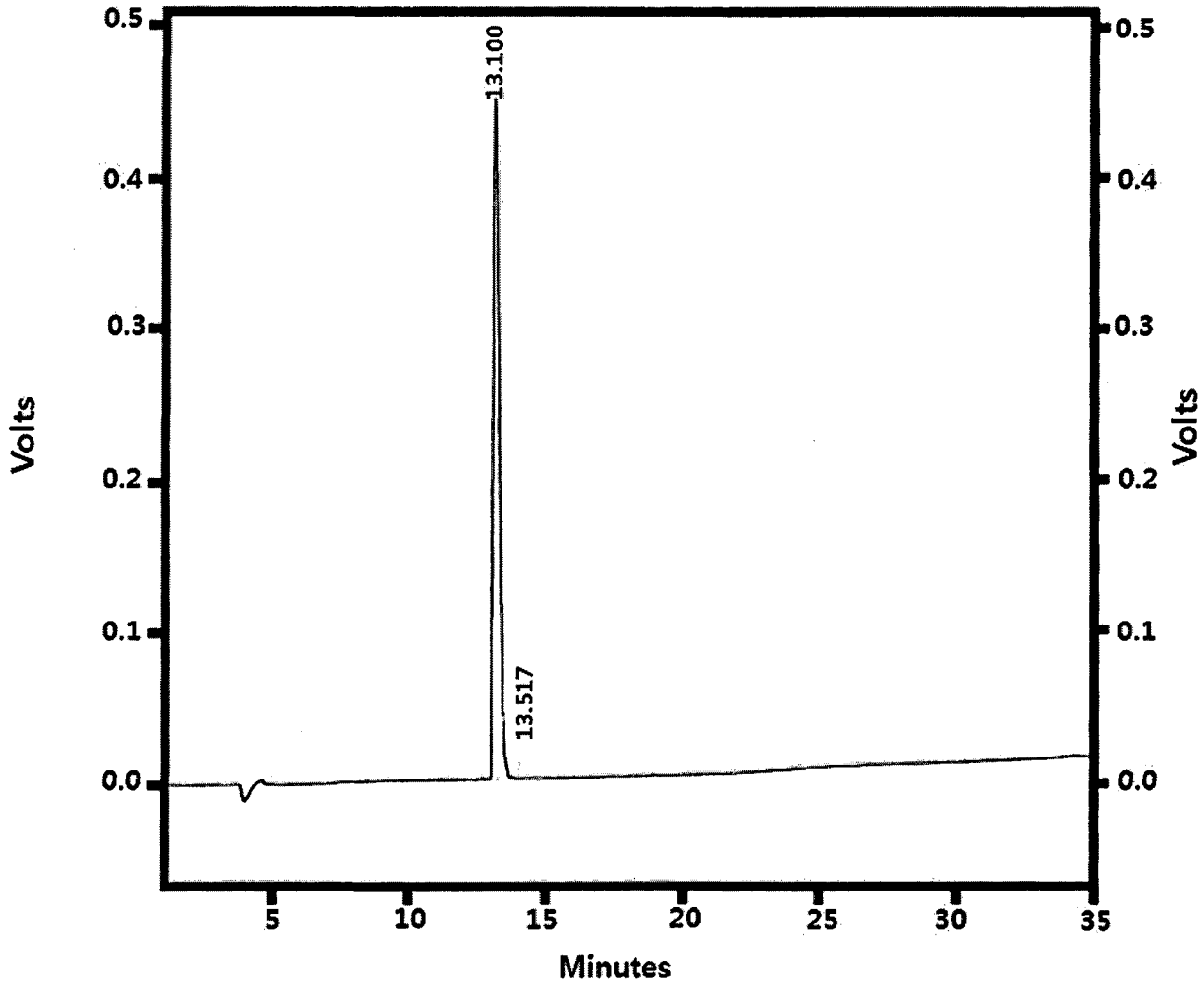
Detector A (230nm)

Pk #	Retention Time	Area	Area %
1	11.967	1118	0.020
2	12.092	5394758	98.184
3	12.425	87049	1.584
4	13.033	706	0.013
5	13.775	5416	0.099
6	18.408	5476	0.100
Totals		5494523	100.000

도 13

Shimadzu CLASS-VP V6.14 SP1 MANUAL *Area % Report*

Sample ID : K161398 (YDE-010)

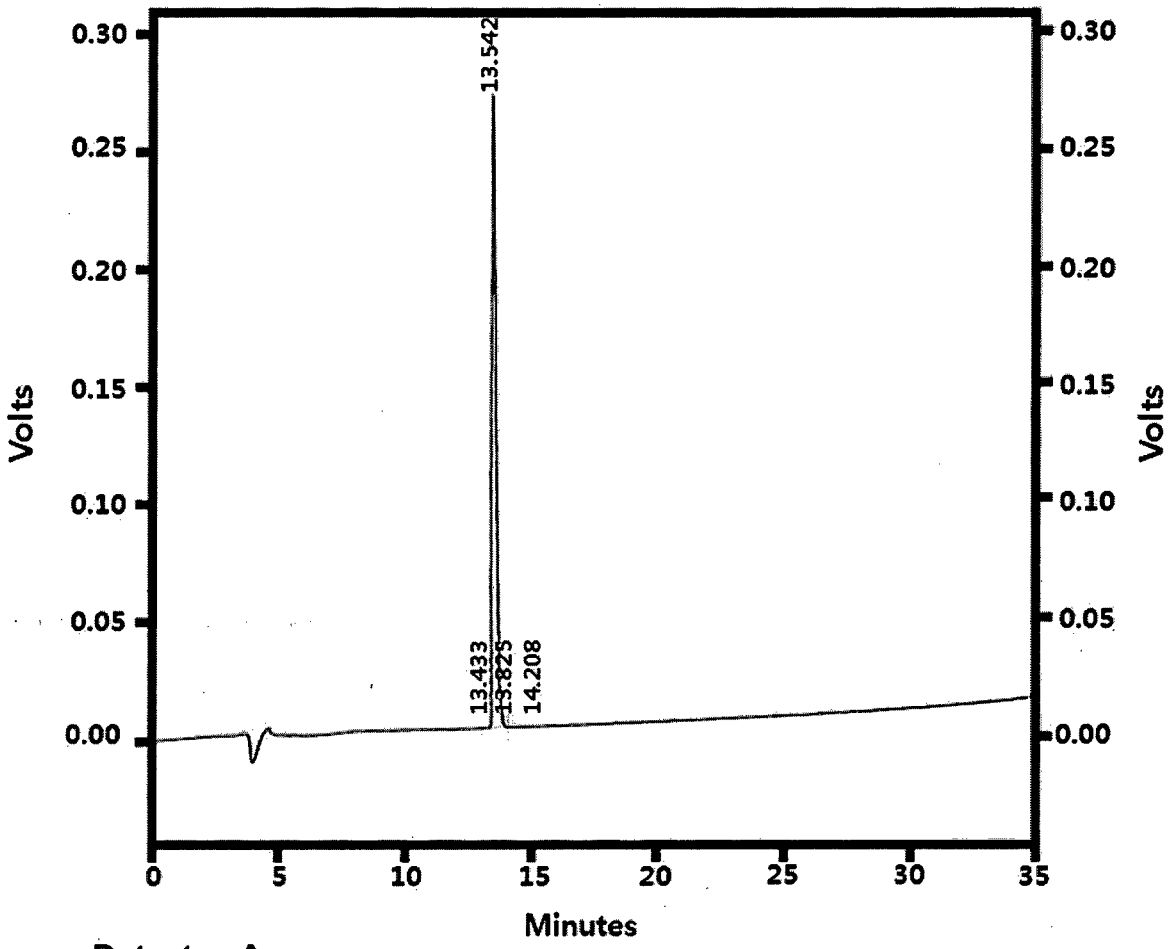


Detector A (230nm)	Pk #	Retention Time	Area	Area %
	1	13.100	6966383	99.047
	2	13.517	67028	0.953
	Totals		7033411	100.000

도 14

Shimadzu CLASS-VP V6.14 SP1 manual *Area % Report*

Sample ID : K161399 (YDE-011)



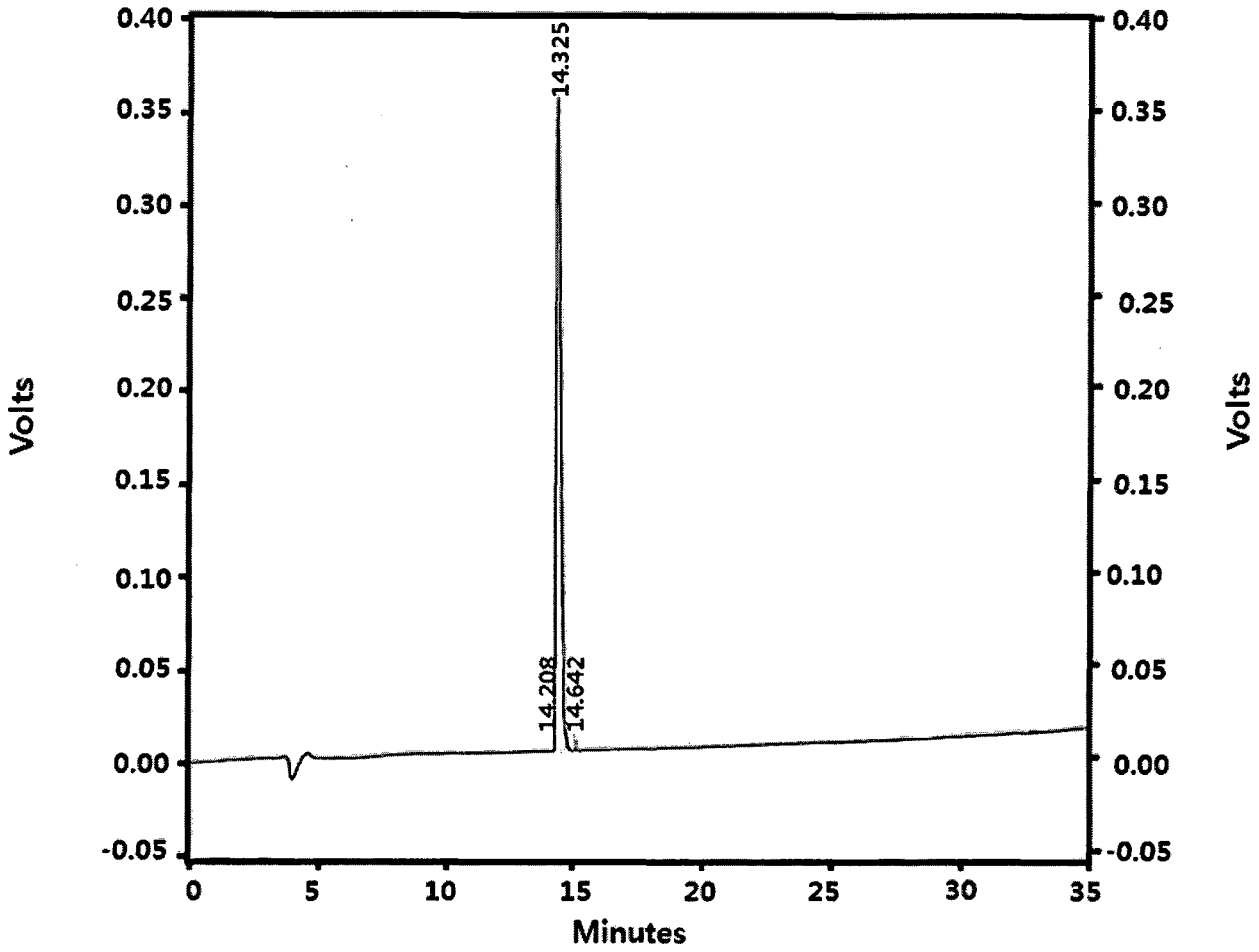
Detector A
(230nm)

Pk #	Retention Time	Area	Area %
1	13.433	857	0.027
2	13.542	3082773	98.389
3	13.825	48609	1.551
4	14.208	1010	0.032
Totals		3133249	100.000

도 15

Shimadzu CLASS-VP V6.14 SP1 manual *Area % Report*

Sample ID : K161400 (YDE-012)



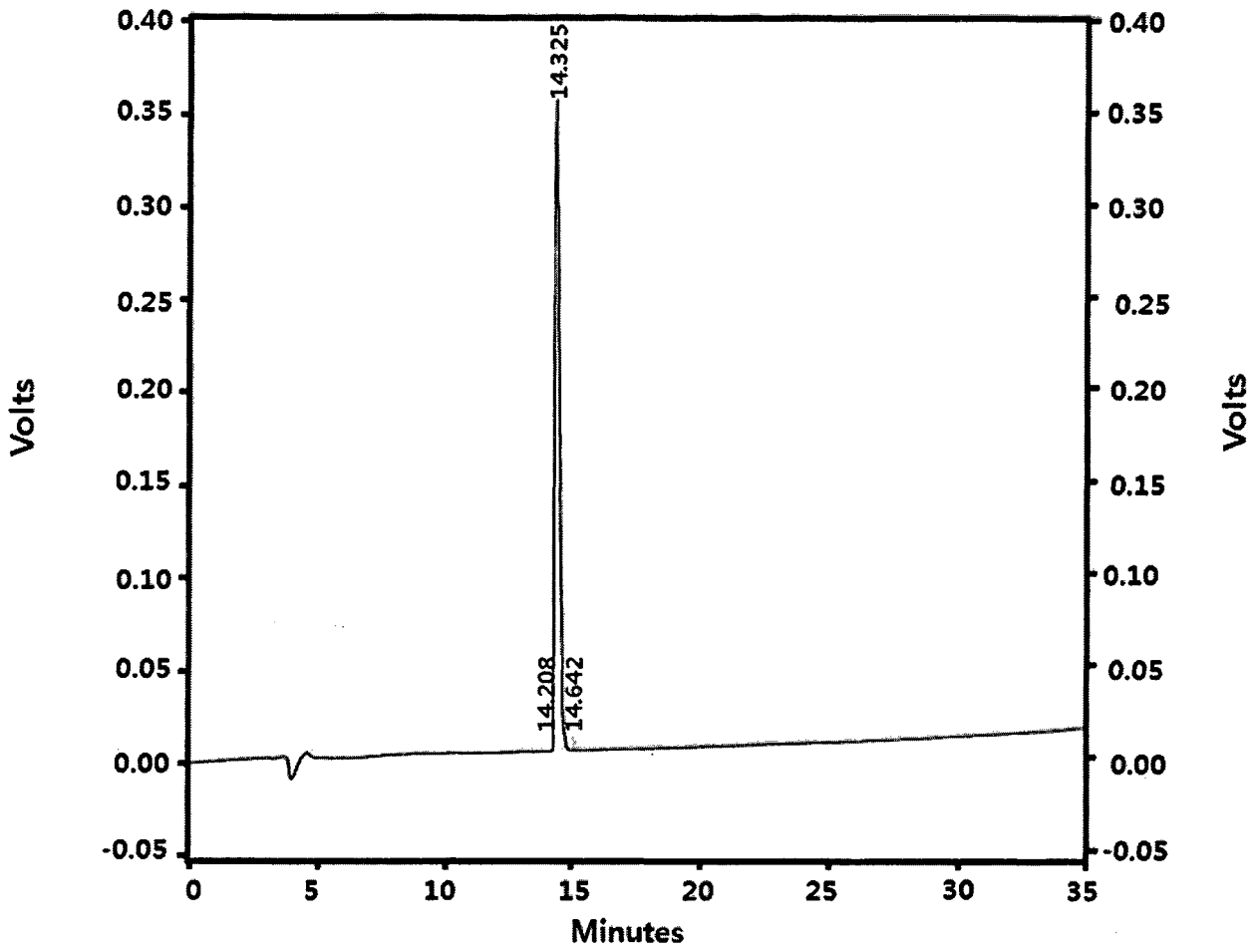
Detector A
(230nm)

Pk #	Retention Time	Area	Area %
1	14.208	534	0.012
2	14.325	4465205	98.962
3	14.642	46297	1.026
Totals		4512036	100.000

도 16

Shimadzu CLASS-VP V6.14 SP1 manual *Area % Report*

Sample ID : K161400 (YDE-012)

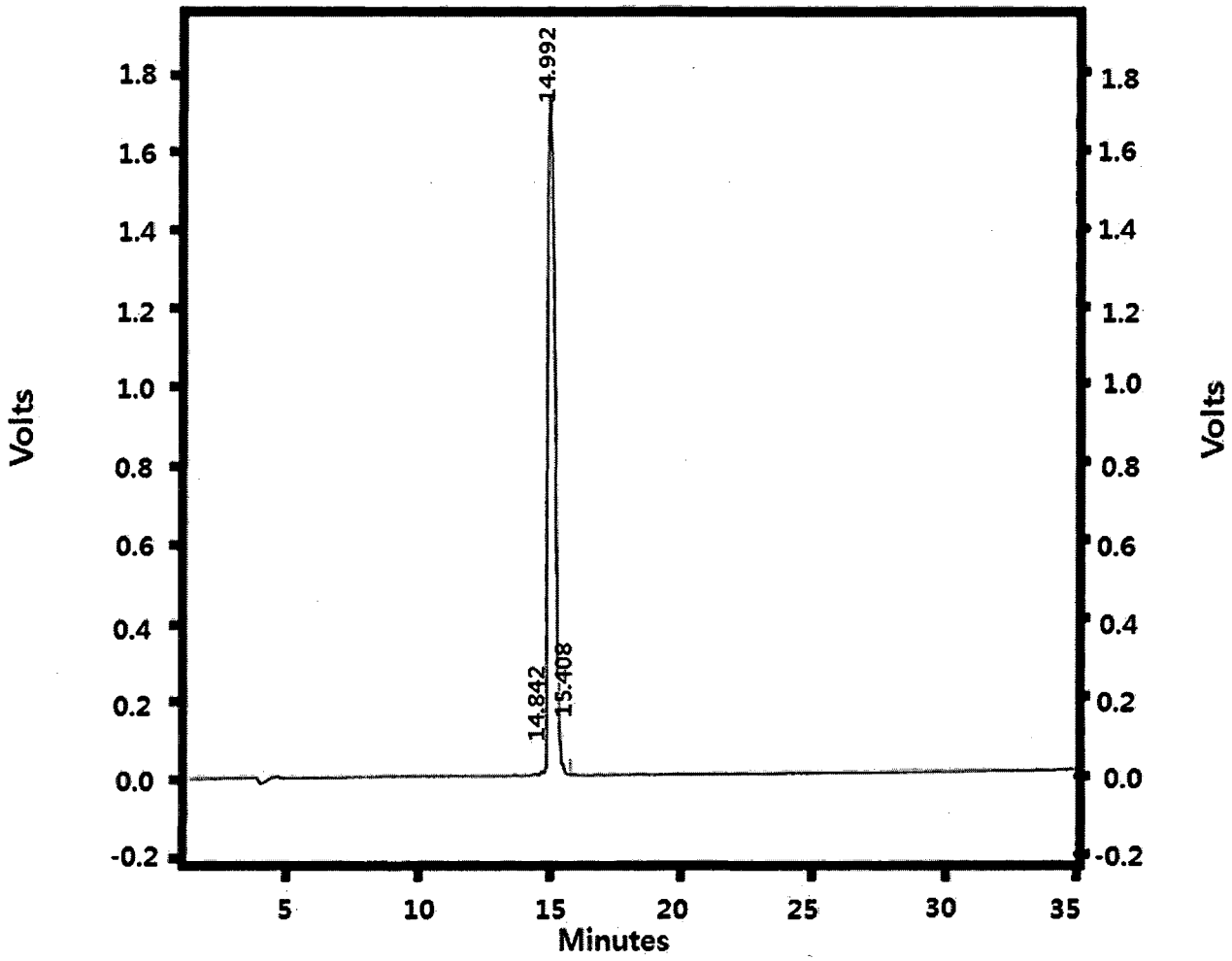


Detector A
(230nm)

Pk #	Retention Time	Area	Area %
1	14.208	534	0.012
2	14.325	4465205	98.962
3	14.642	46297	1.026
Totals		4512036	100.000

도 17

Sample ID : K161402 (YDE-014)



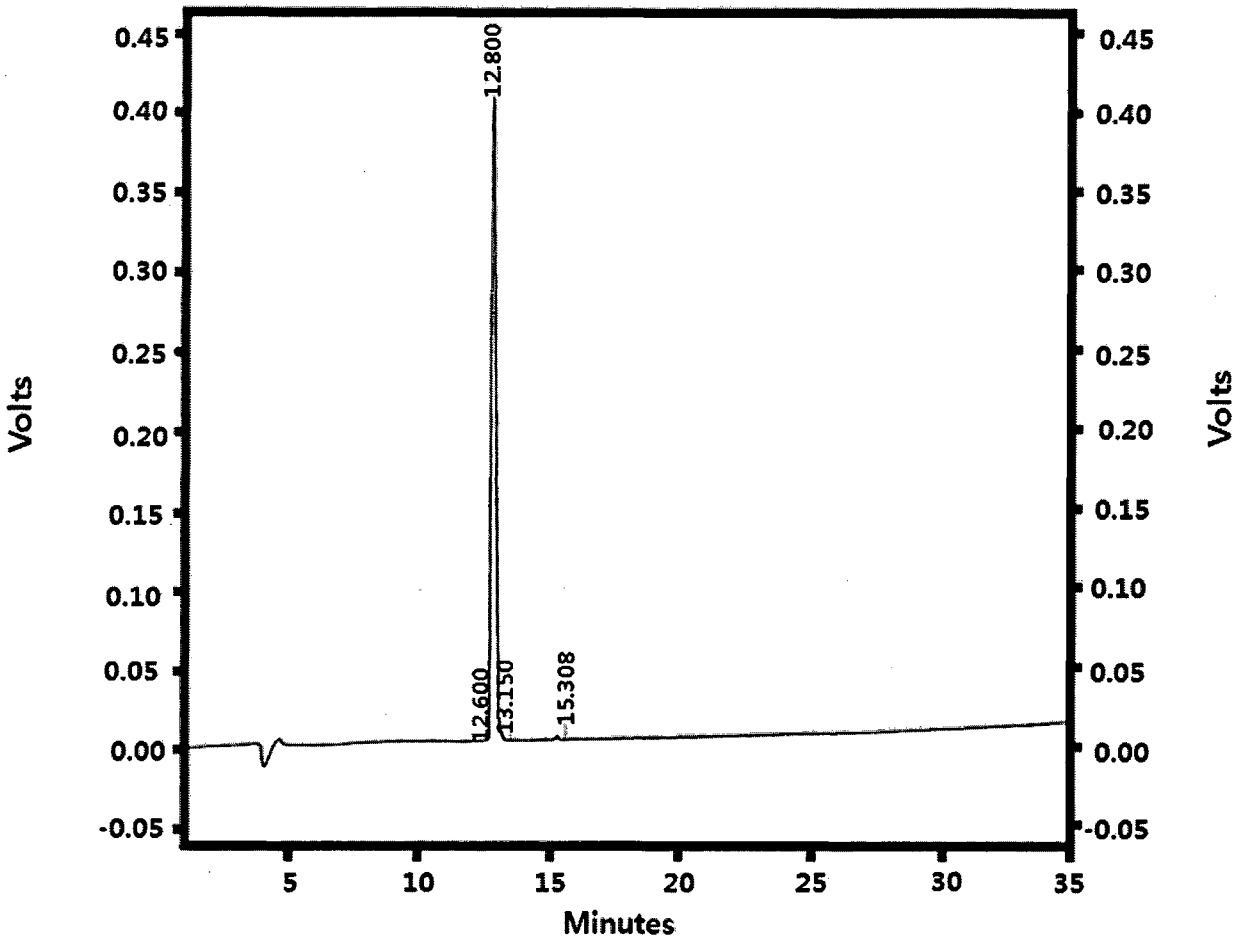
Detector A
(230nm)

Pk #	Retention Time	Area	Area %
1	14.842	78055	0.241
2	14.992	31942847	98.537
3	15.408	396165	1.222
Totals		32417067	100.000

도 18

Shimadzu CLASS-VP V6.14 SP1 MANUAL *Area % Report*

Sample ID : K161403 (YDE-015)



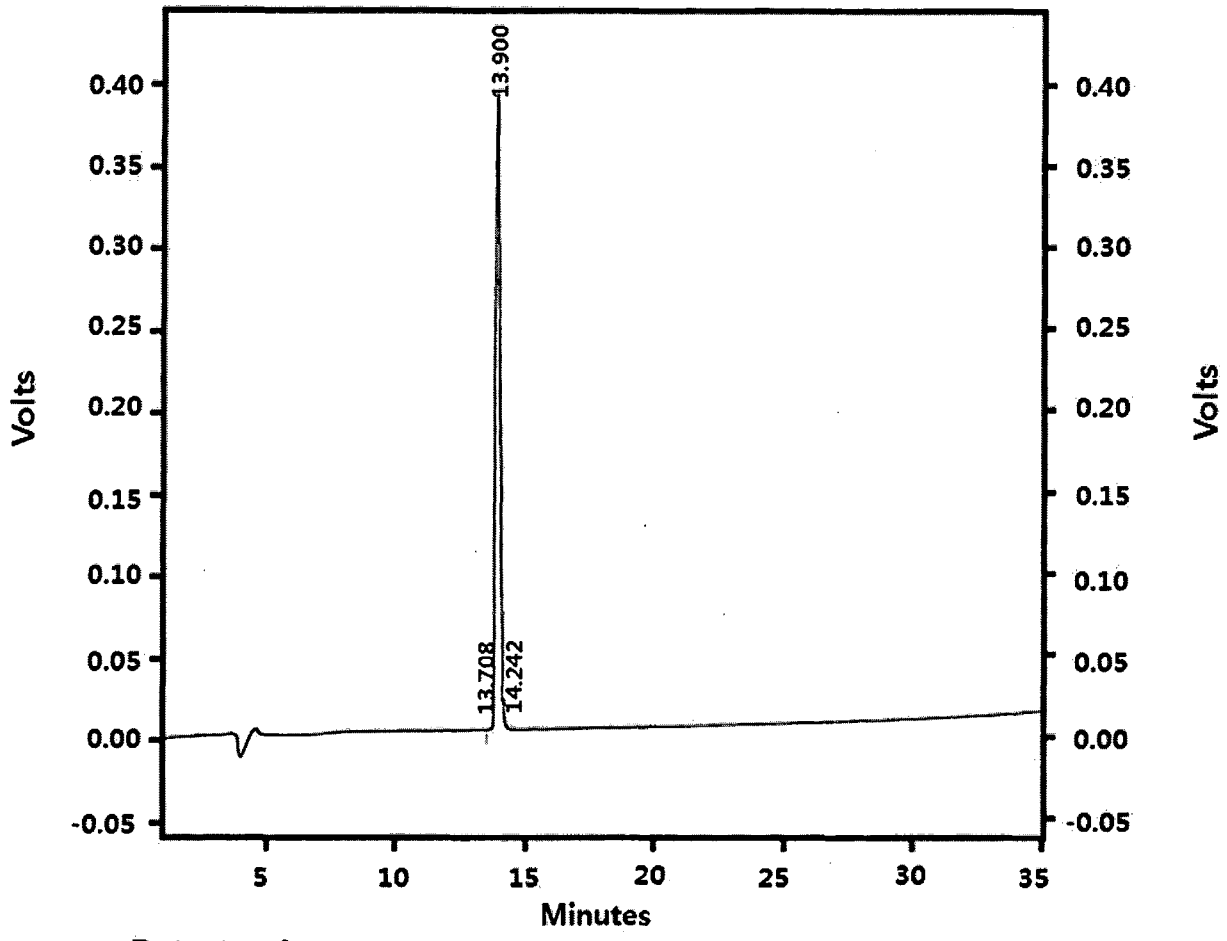
Detector A
(230nm)

Pk #	Retention Time	Area	Area %
1	12.600	3628	0.074
2	12.800	4859852	99.167
3	13.150	23016	0.470
4	15.308	14170	0.289
Totals		4900666	100.000

도 19

Shimadzu CLASS-VP V6.14 SP1 MANUAL *Area % Report*

Sample ID : K161404 (YDE-016)

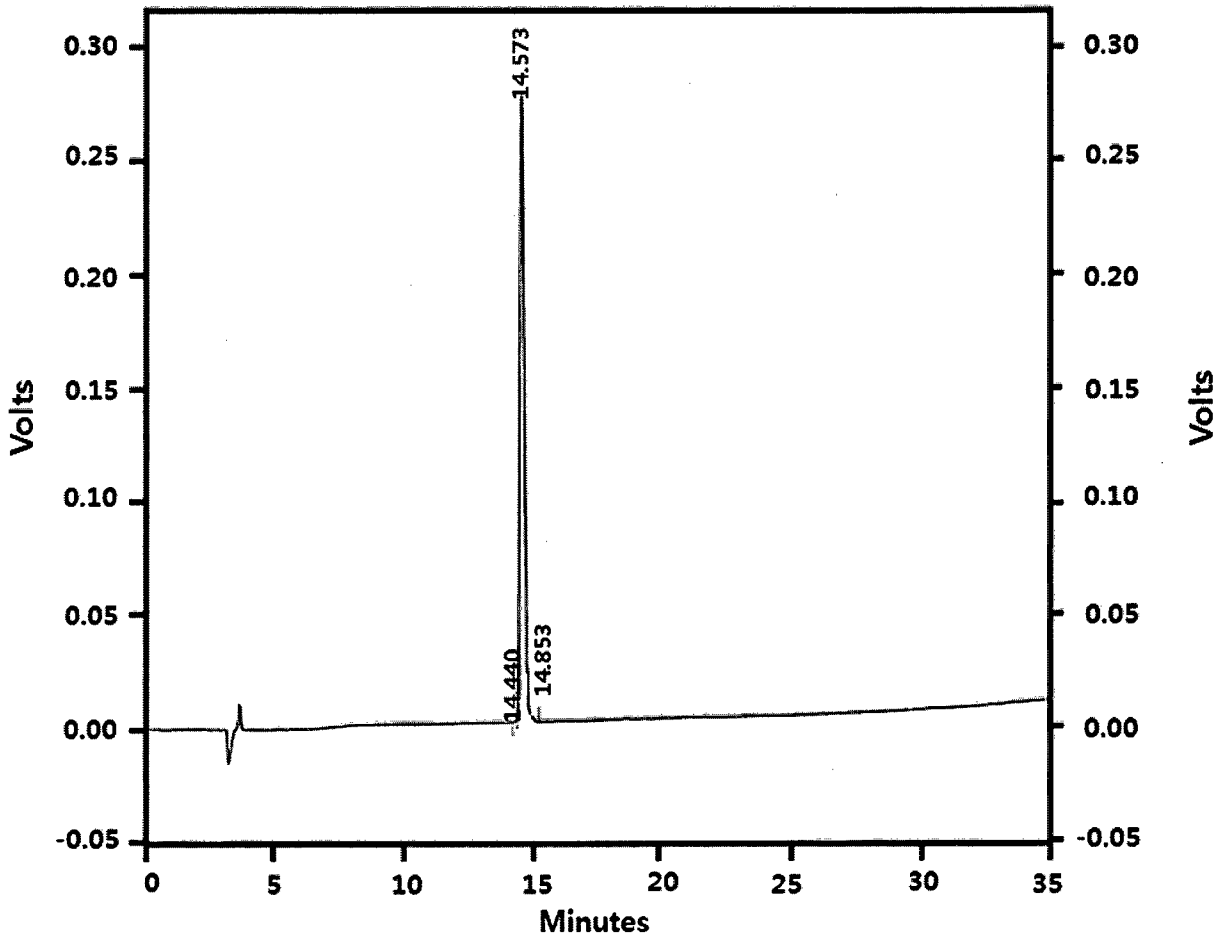


Detector A (230nm) Pk #	Retention Time	Area	Area %
1	13.708	6002	0.126
2	13.900	4752700	99.407
3	14.242	22362	0.468
Totals		4781064	100.000

도 20

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K161405 (YDE-017)

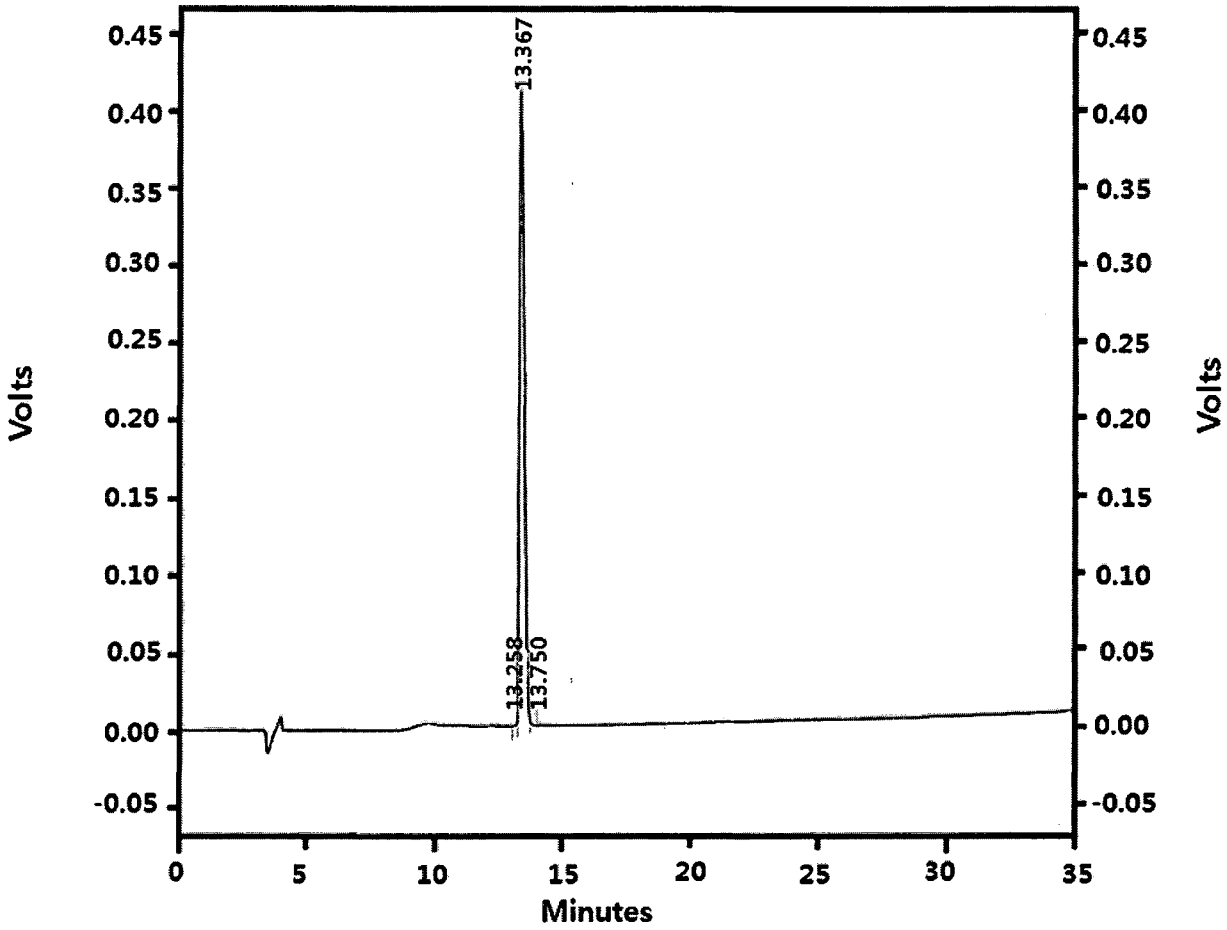


Detector A (230nm) Pk #	Retention Time	Area	Area %
1	14.440	5413	0.163
2	14.573	3259531	98.058
3	14.853	59145	1.779
Totals		3324089	100.000

도 21

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K161406 (YDE-018)



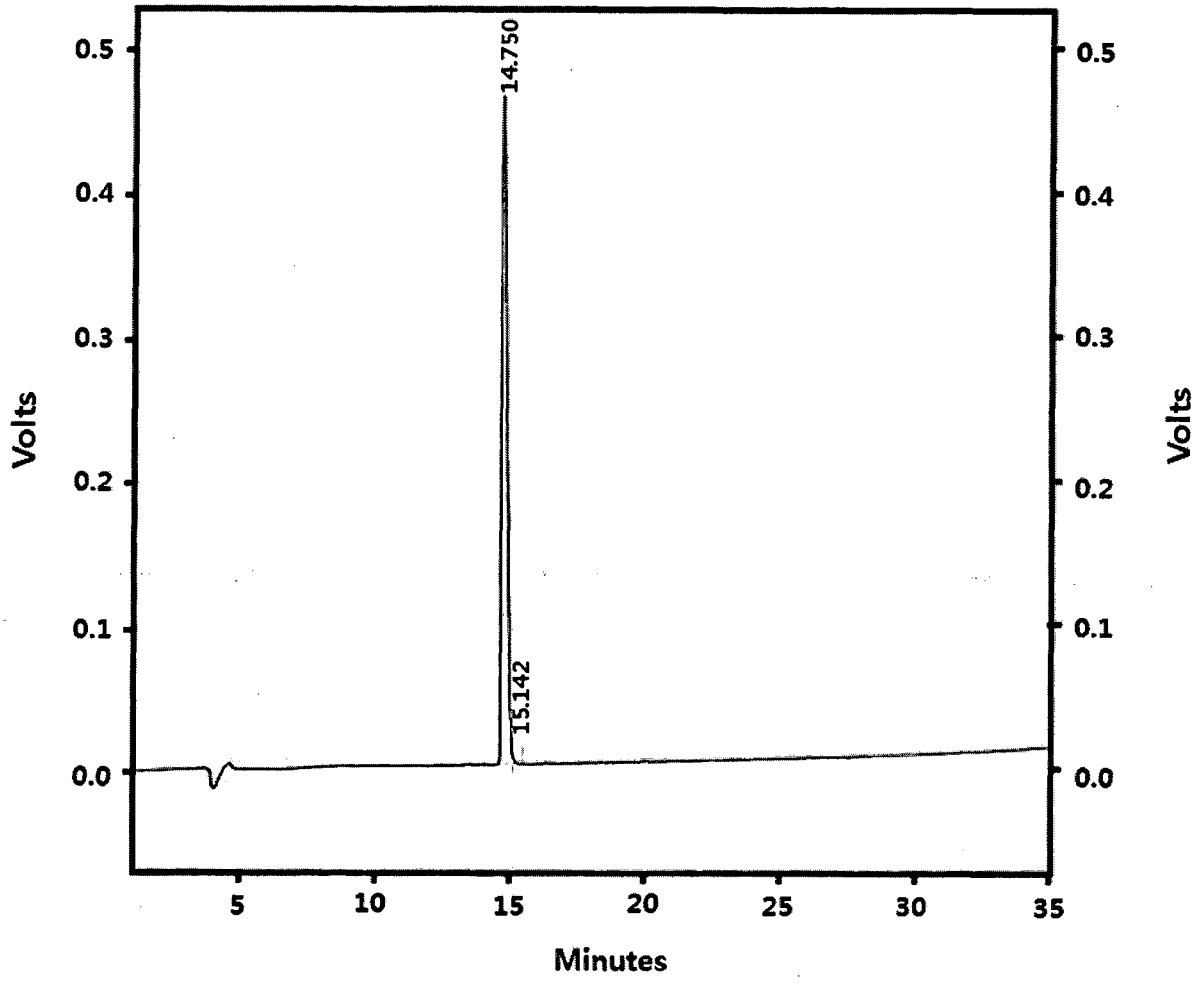
Detector A
(230nm)

Pk #	Retention Time	Area	Area %
1	13.258	4690	0.089
2	13.367	5263105	99.679
3	13.750	12277	0.233
Totals		5280072	100.000

도 22

Shimadzu CLASS-VP V6.14 SP1 MANUAL *Area % Report*

Sample ID : KI61407 (YDE-019)

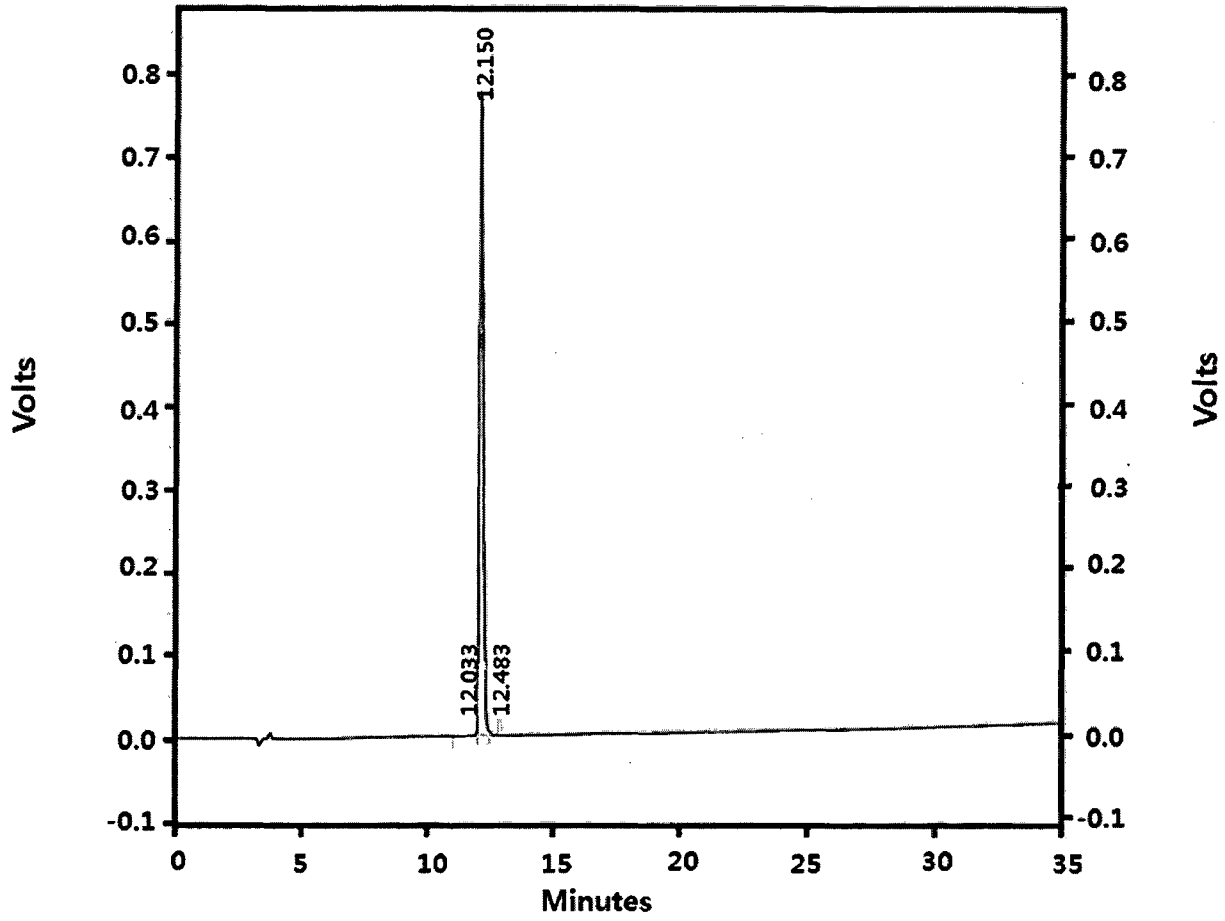


Detector A (230nm) Pk #	Retention Time	Area	Area %
1	14.750	6335299	99.670
2	15.142	20958	0.330
Totals		6356257	100.000

도 23

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K161408 (YDE-020)



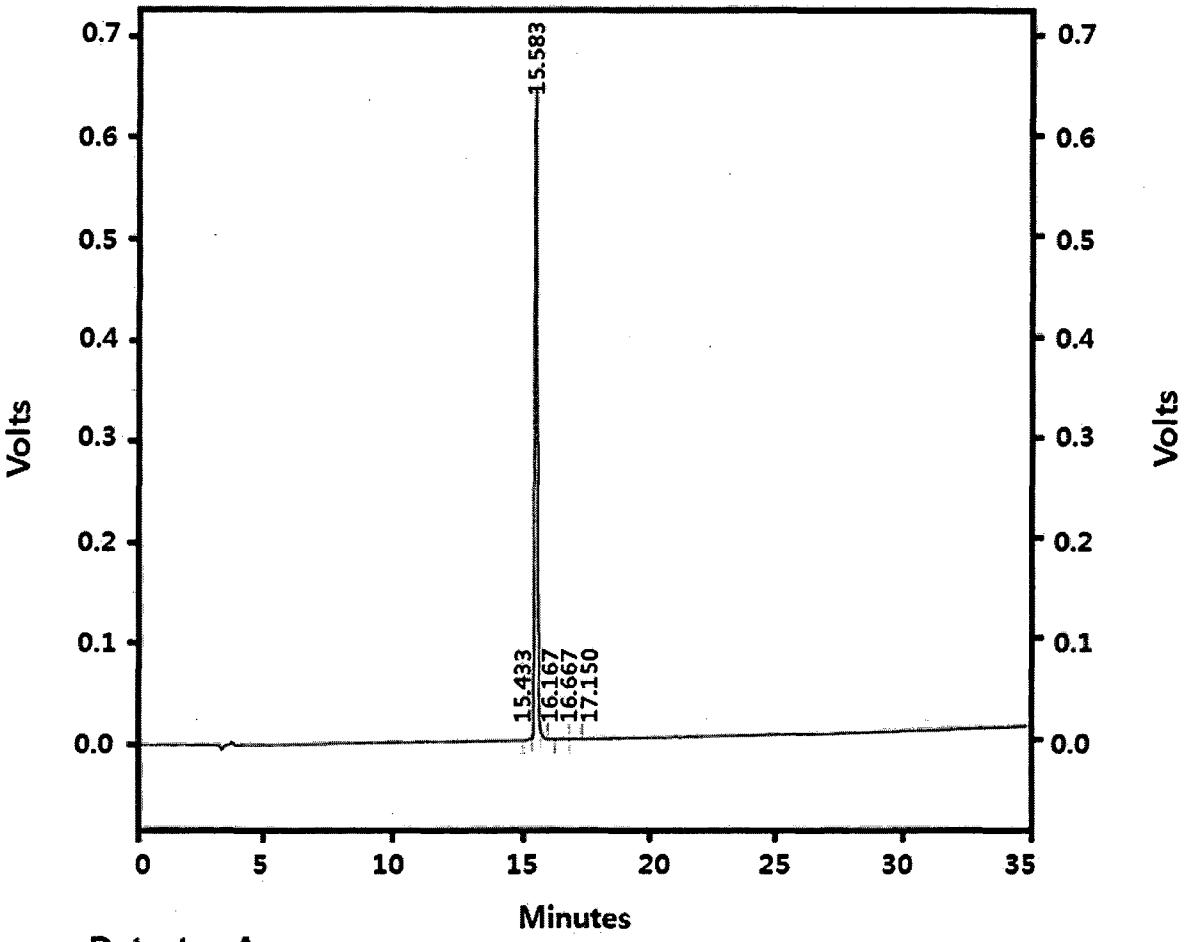
Detector A (230nm)

Pk #	Retention Time	Area	Area %
1	12.033	23465	0.300
2	12.150	7757581	99.214
3	12.483	38002	0.486
Totals		7819048	100.000

도 24

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K161409 (YDE-021)



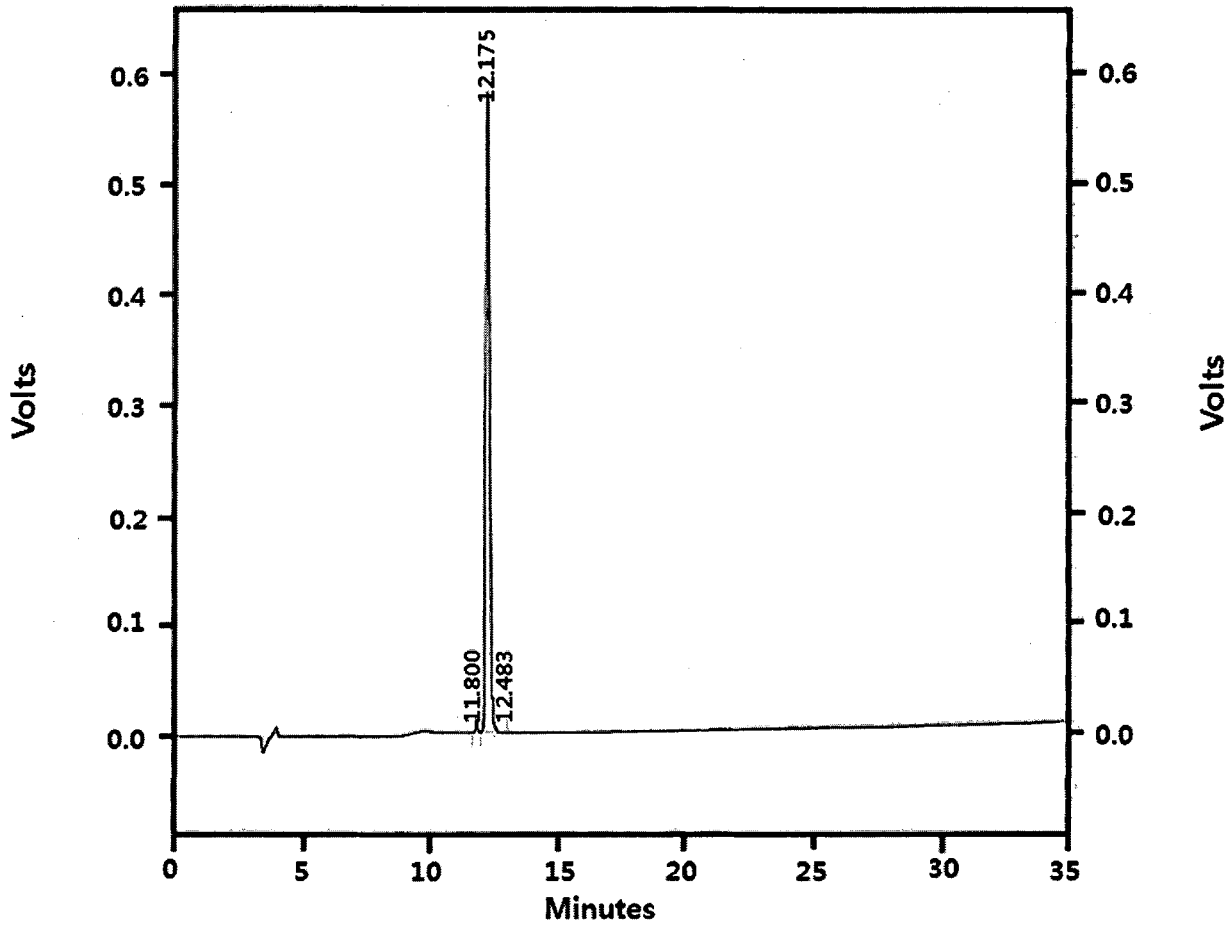
Detector A (230nm)

Pk #	Retention Time	Area	Area %
1	15.433	12207	0.250
2	15.583	4793036	98.162
3	16.167	61475	1.259
4	16.667	8052	0.165
5	17.150	8010	0.164
Totals		4882780	100.000

도 25

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K161410 (YDE-022)

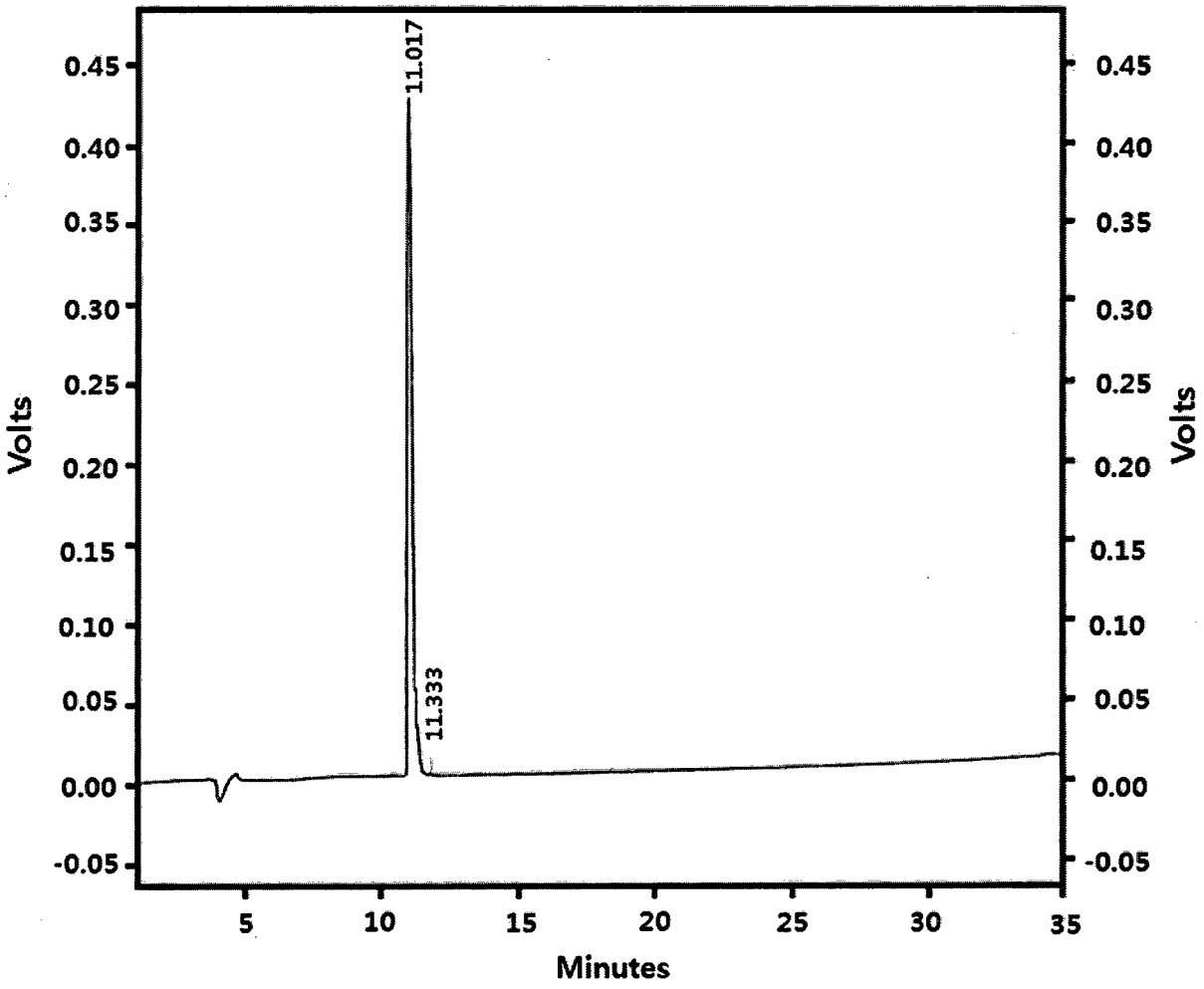


Detector A (230nm)	Pk #	Retention Time	Area	Area %
	1	11.800	67819	1.041
	2	12.175	6405639	98.306
	3	12.483	42551	0.653
Totals			6516009	100.000

도 26

Shimadzu CLASS-VP V6.14 SP1 MANUAL *Area % Report*

Sample ID : K161411 (YDE-023)

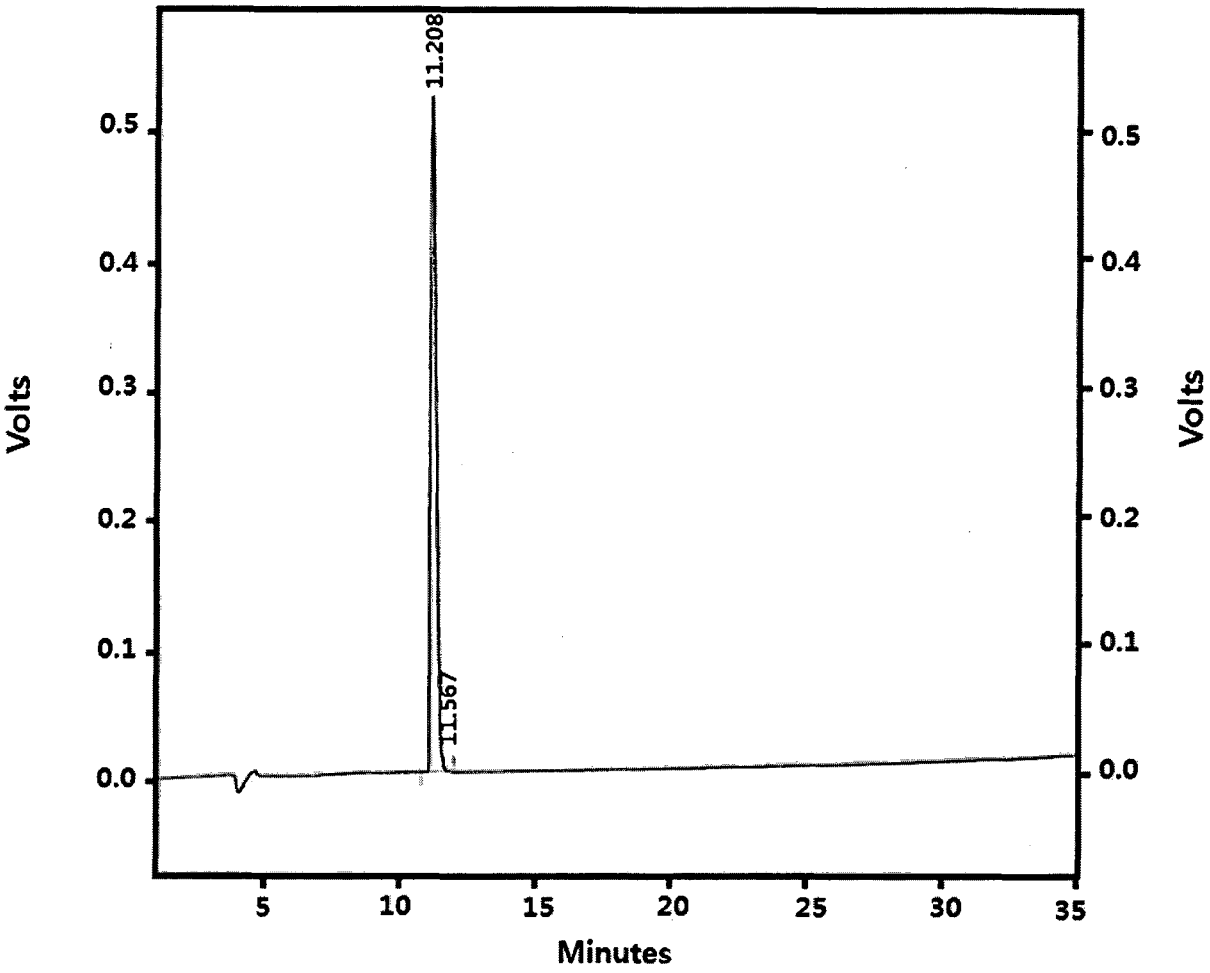


Detector A (230nm)	Pk #	Retention Time	Area	Area %
	1	11.017	5051126	96.145
	2	11.333	202520	3.855
	Totals		5253646	100.000

도 27

Shimadzu CLASS-VP V6.14 SP1 MANUAL *Area % Report*

Sample ID : K161412 (YDE-024)

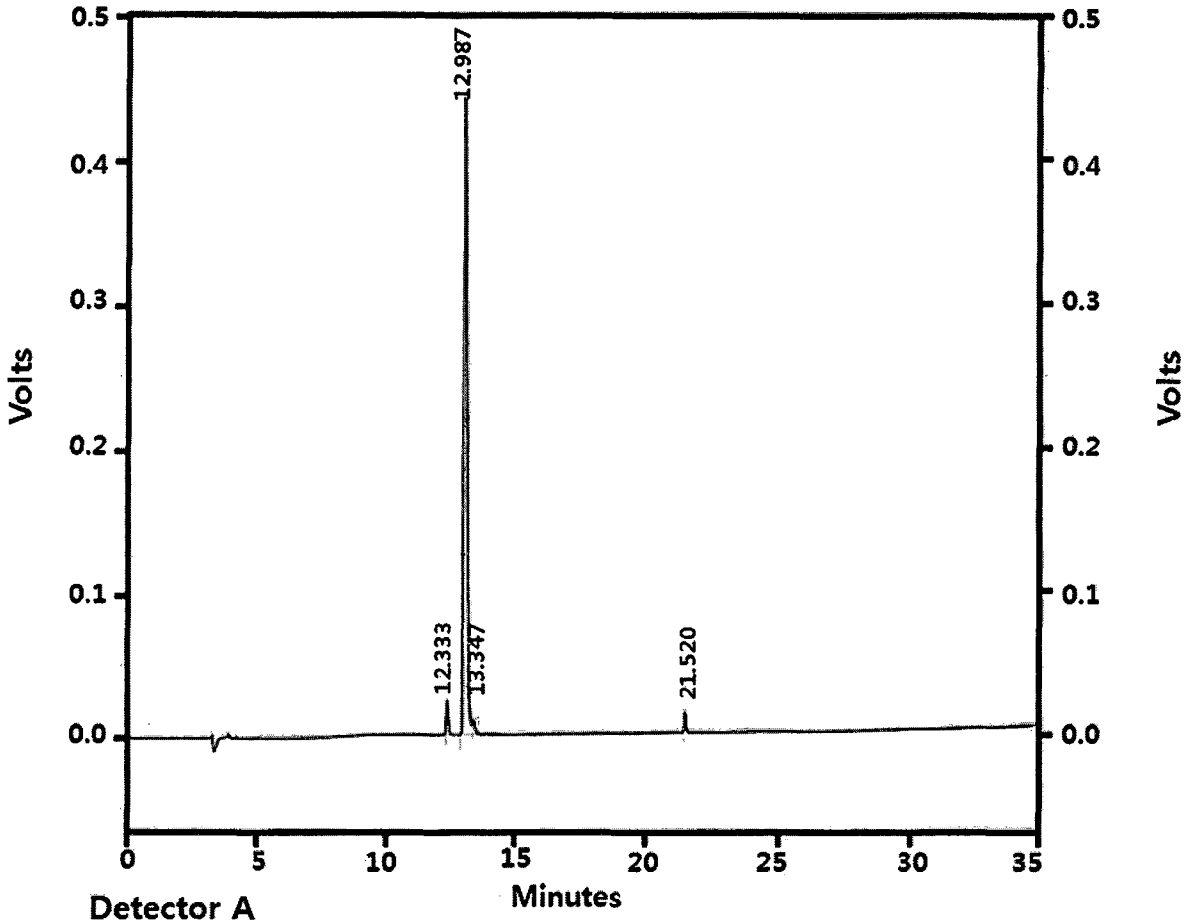


Detector A (230nm)	Pk #	Retention Time	Area	Area %
	1	11.208	7214585	98.998
	2	11.567	73036	1.002
	Totals		7287621	100.000

도 28

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K161413 (YDE-025)

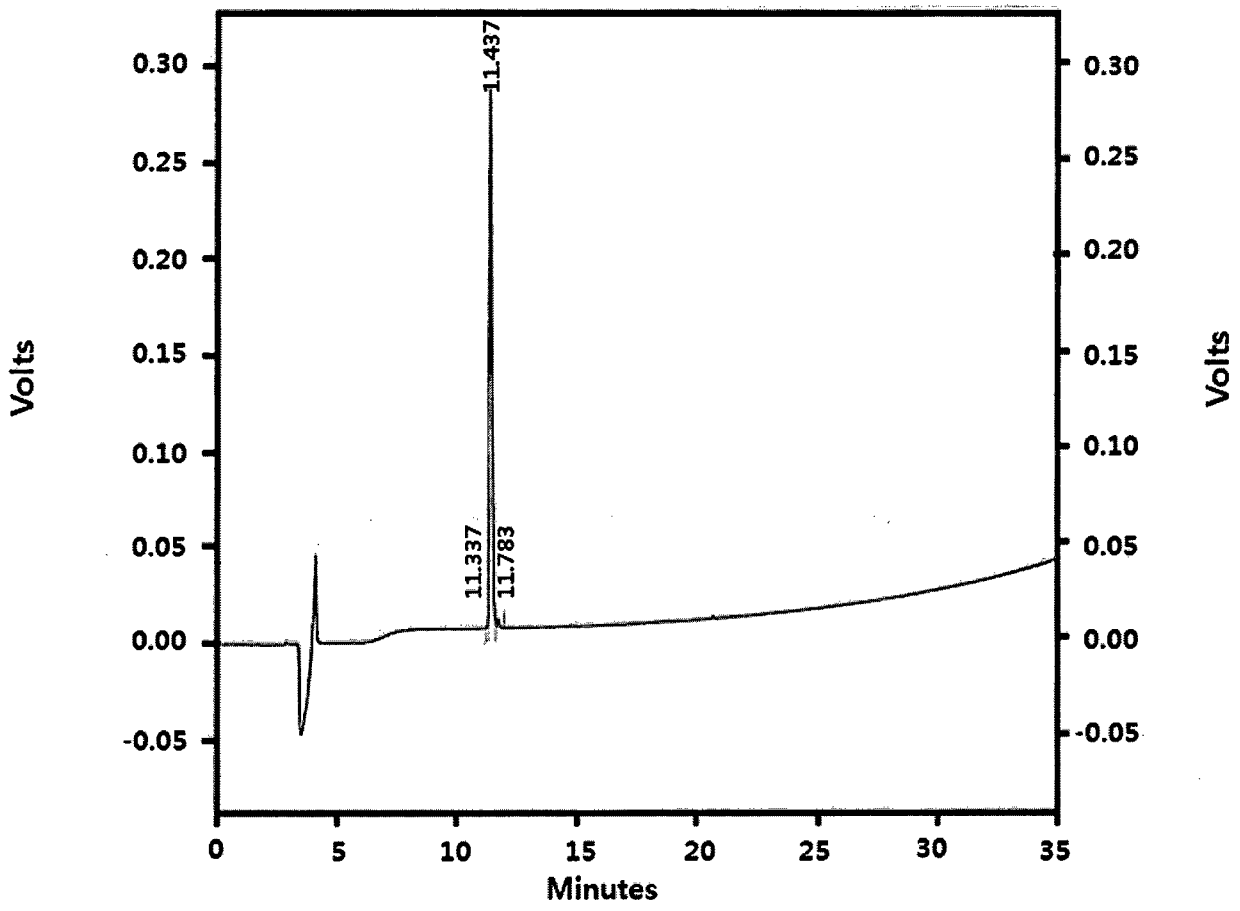


Detector A (230nm) Pk #	Retention Time	Area	Area %
1	12.333	89208	2.157
2	12.987	3936279	95.167
3	13.347	61019	1.475
4	21.520	49664	1.201
Totals		4136170	100.000

도 29

Shimadzu CLASS-VP V6.14 SP1 new 10AVP *Area % Report* *Page of 1*

Sample ID : K161414 (YDE-026)



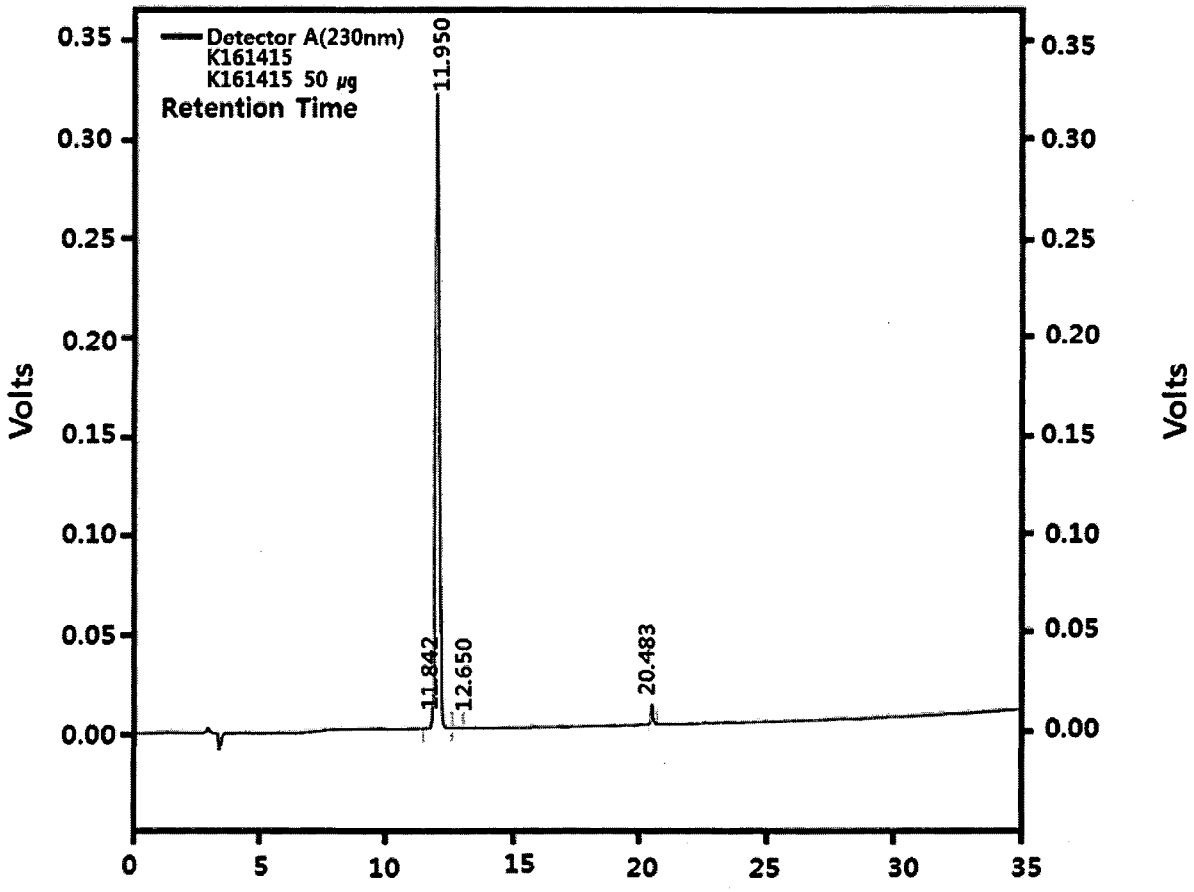
Detector A
(230nm)

Pk #	Retention Time	Area	Area %
1	11.337	1455	0.068
2	11.437	2109578	98.675
3	11.783	26862	1.256
Totals		2137895	100.000

도 30

Shimadzu CLASS-VP V6.14 SP1 Manual(AUTO Sampler) *Area % Report*

Sample ID : K161415 (YDE-027)

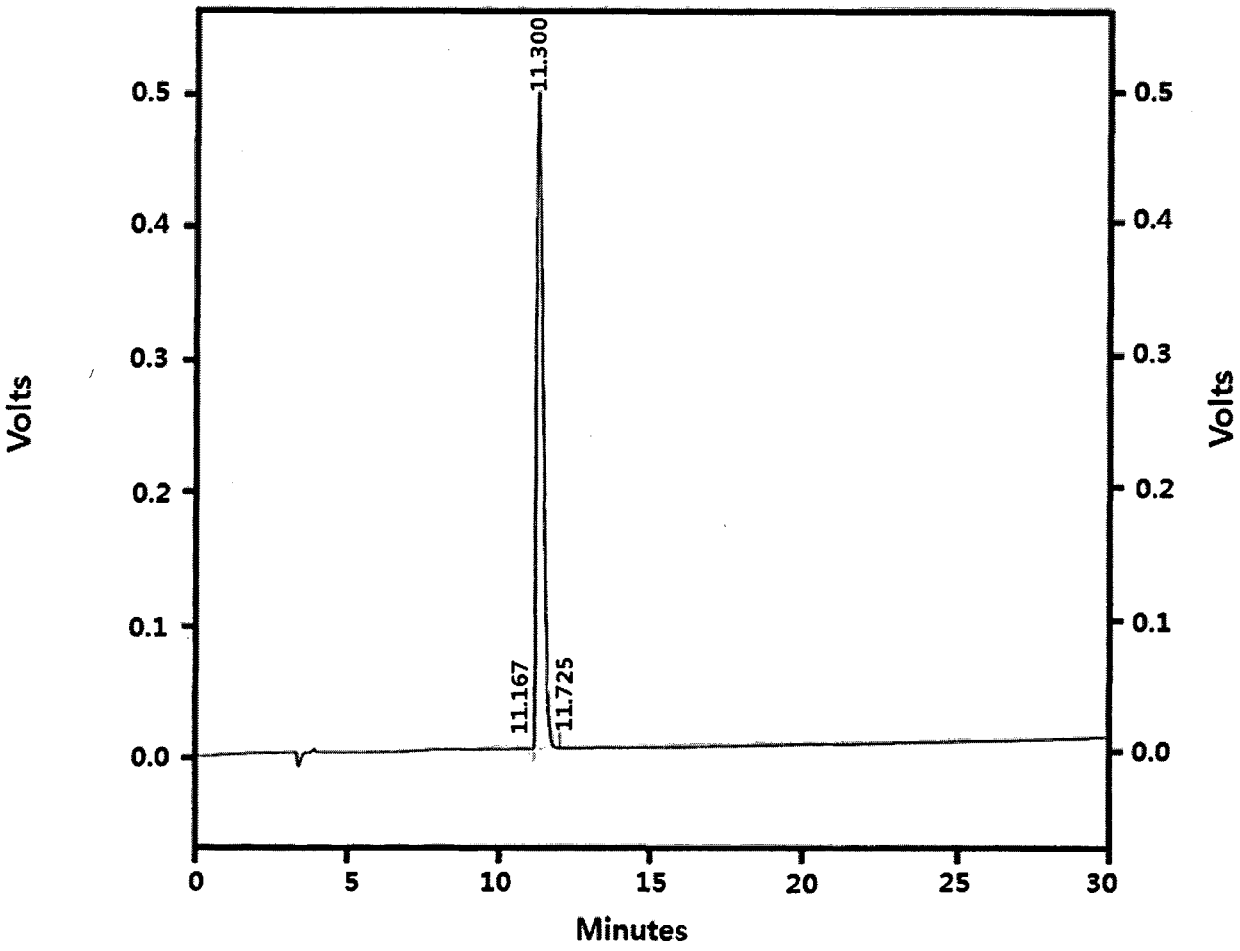


Detector A (230nm) Pk #	Retention Time	Area	Area %
1	11.842	41052	1.200
2	11.950	3316998	96.933
3	12.650	4962	0.145
4	20.483	58920	1.722
Totals		3421932	100.000

도 31

Shimadzu CLASS-VP V6.14 SP1 MANUAL *Area % Report*

Sample ID : K161416 (YDE-028)



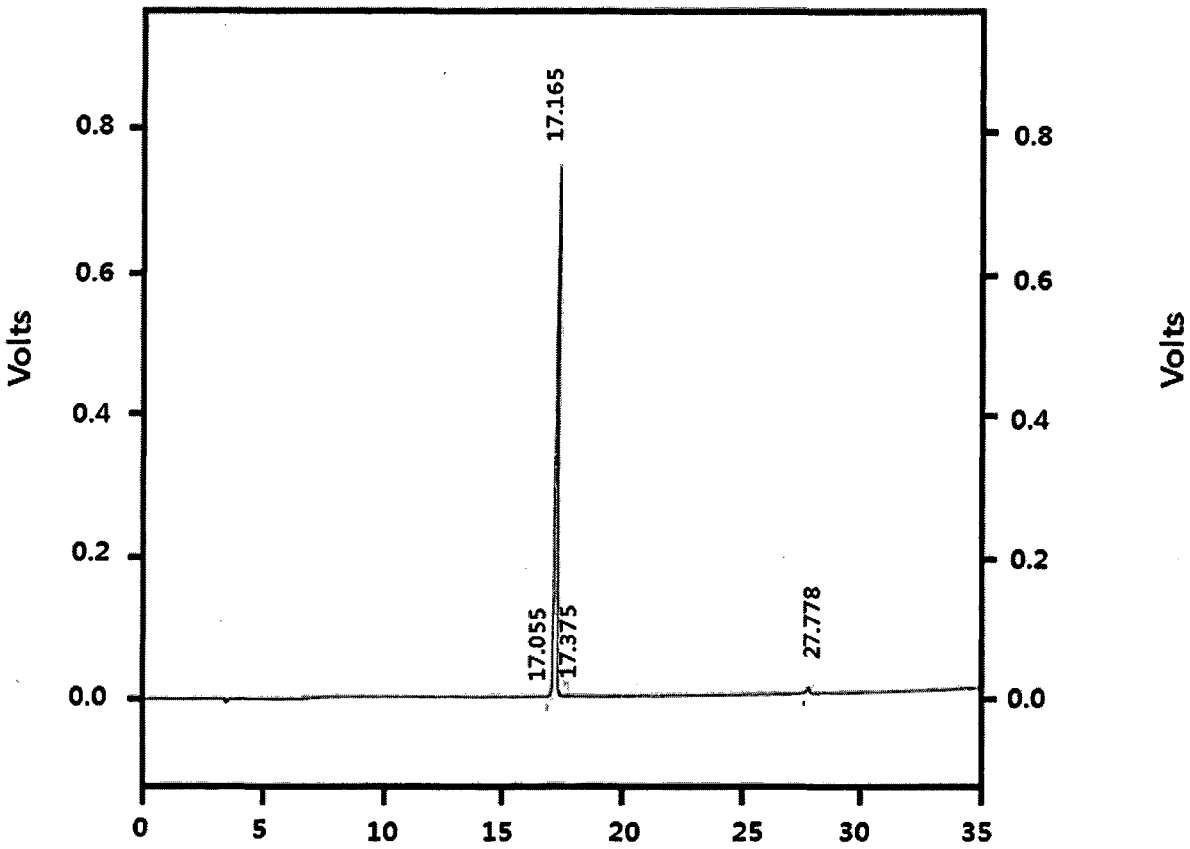
Detector A
(230nm)

Pk #	Retention Time	Area	Area %
1	11.167	150	0.002
2	11.300	7430217	99.528
3	11.725	35093	0.470
Totals		7465460	100.000

도 32

Shimadzu CLASS-VP V6.14 SP1 new 10AVP *Area % Report* *Page of 1*

Sample ID : K170461 (YDE-029)

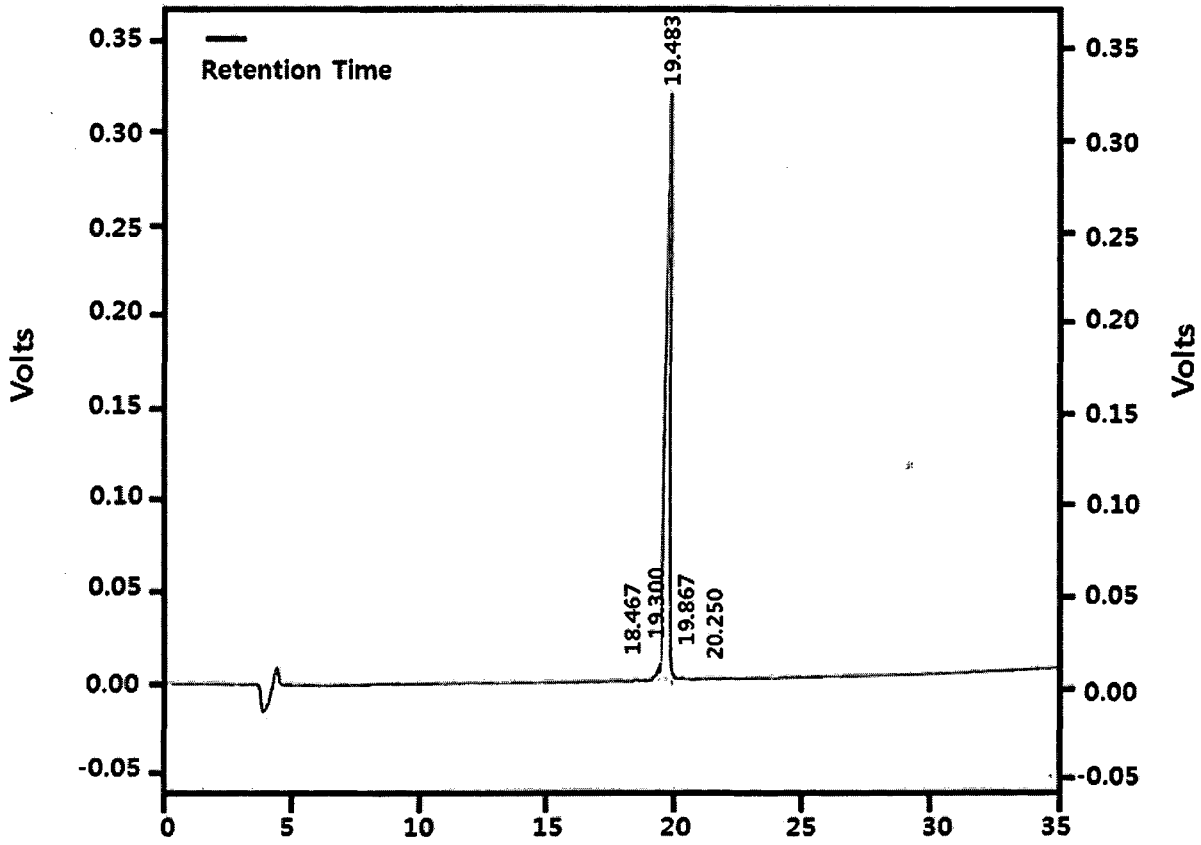


Detector A (230nm) Pk #	Retention Time	Area	Area %
1	17.055	22757	0.455
2	17.165	4899267	98.005
3	17.375	14310	0.286
4	27.778	62641	1.253
Totals		4998975	100.000

도 33

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K170462 (YDE-030)

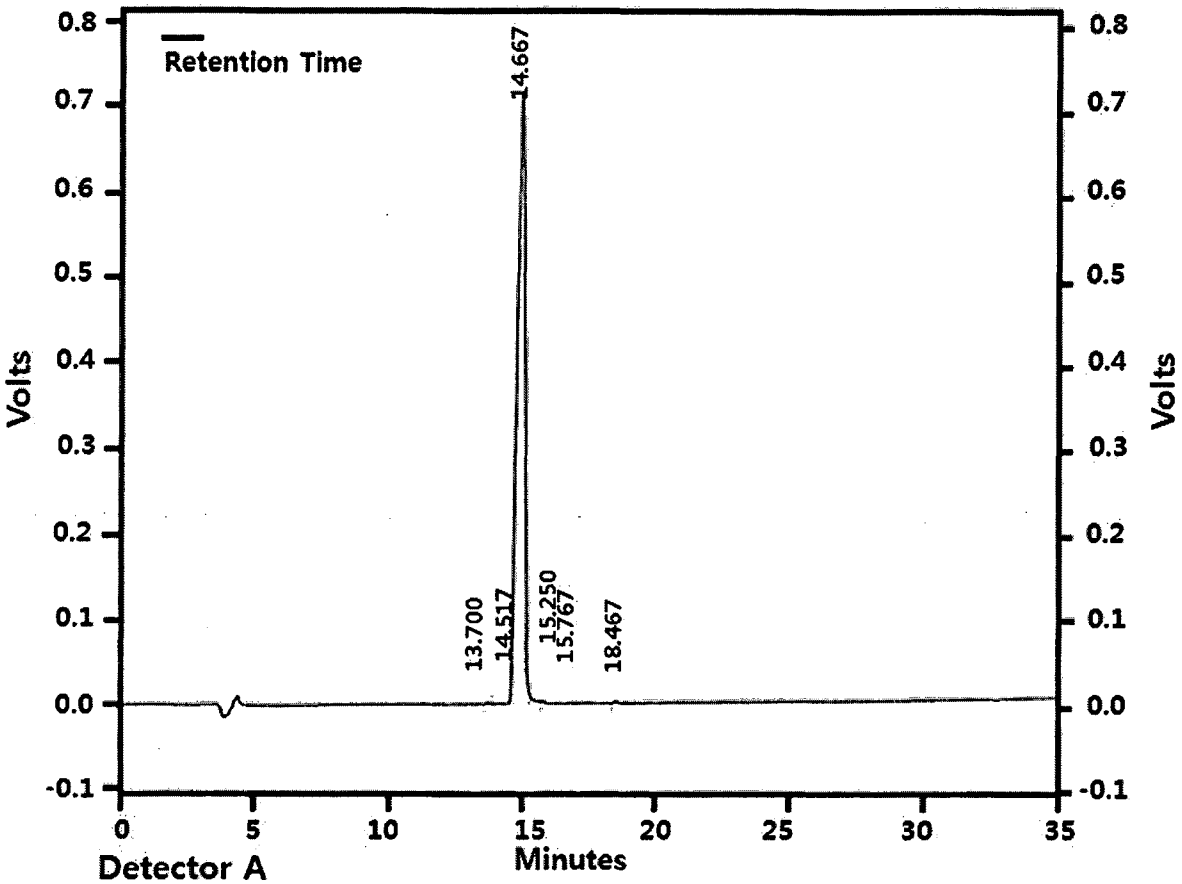


Detector A (230nm) Pk #	Retention Time	Area	Area %
1	18.467	4767	0.118
2	19.300	50062	1.243
3	19.483	3953901	98.180
4	19.867	16280	0.404
5	20.250	2175	0.054
Totals		4027185	100.000

도 34

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K170463 (YDE-031)



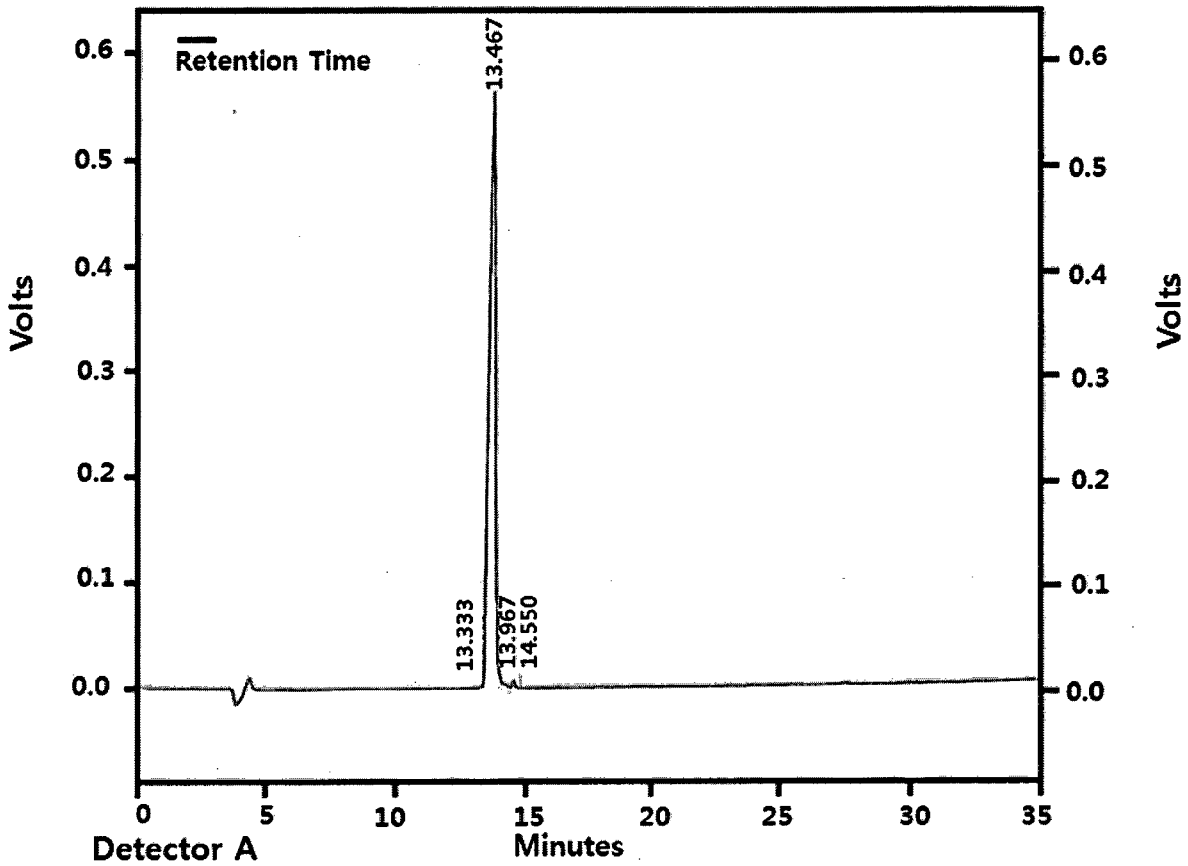
Detector A (230nm)

Pk #	Retention Time	Area	Area %
1	13.700	9470	0.066
2	14.517	5967	0.041
3	14.667	14223947	98.895
4	15.250	102756	0.714
5	15.767	25707	0.179
6	18.467	15003	0.104
Totals		14382850	100.000

도 35

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K170464 (YDE-032)



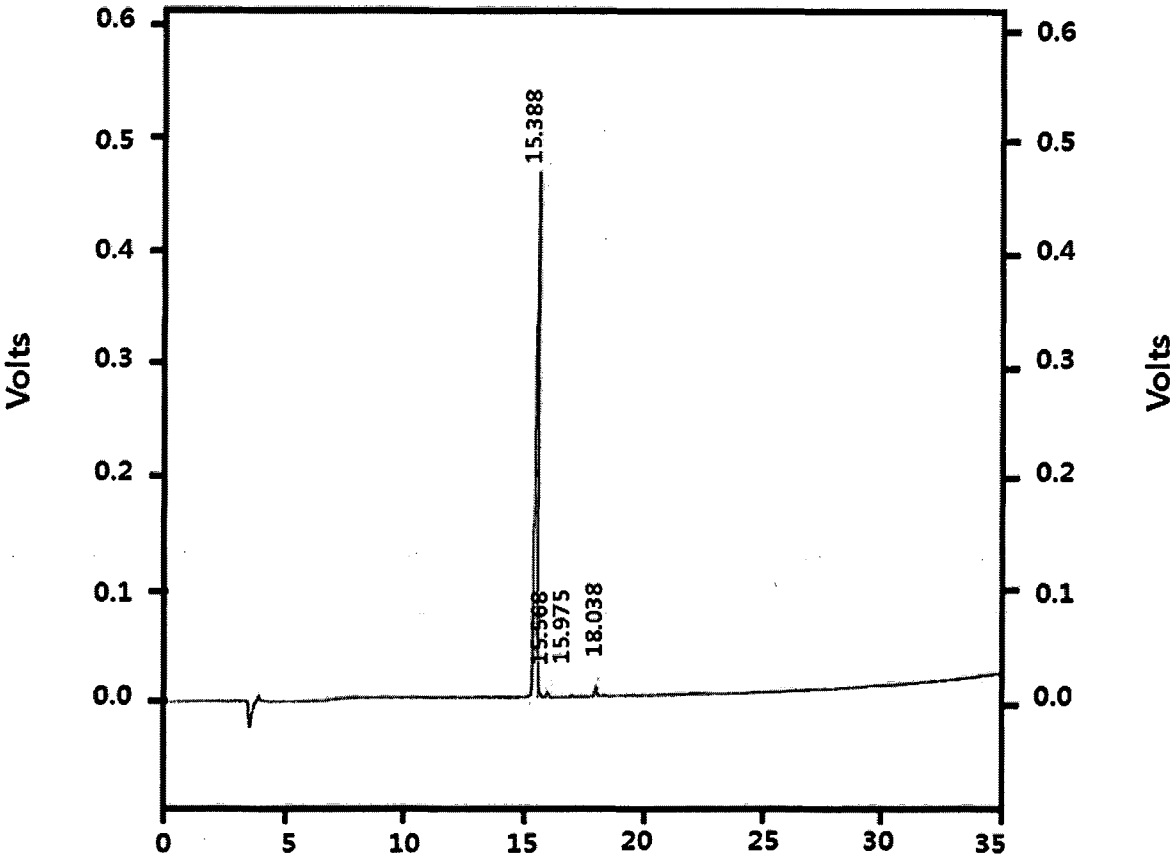
Detector A (230nm)

Pk #	Retention Time	Area	Area %
1	13.333	9786	0.099
2	13.467	9733951	98.224
3	13.967	118058	1.191
4	14.550	48177	0.486
Totals		9909972	100.000

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Shimadzu CLASS-VP V6.14 SP1 new 10AVP *Area % Report* *Page of 1*

Sample ID : K170465 (YDE-033)



Detector A (230nm) Pk #	Retention Time	Area	Area %
1	15.388	3503595	97.229
2	15.568	36015	0.999
3	15.975	25007	0.694
4	18.038	38811	1.077
Totals		3603428	100.000

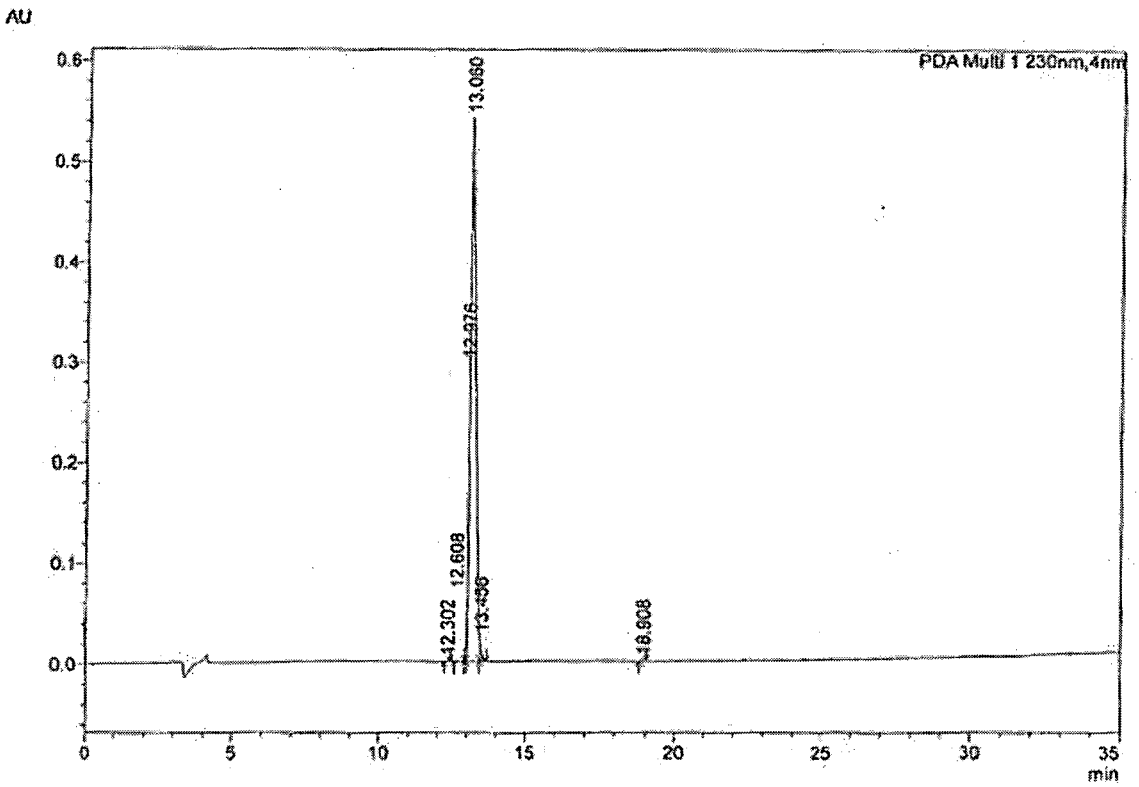
도 37

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name :K170467 (YDE-034)

<Chromatogram>



<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	12.302	3679	0.049
2	12.608	6351	0.084
3	12.976	21634	0.287
4	13.060	7431450	98.685
5	13.456	62871	0.835
6	18.908	4490	0.060
Total		7530474	100.000

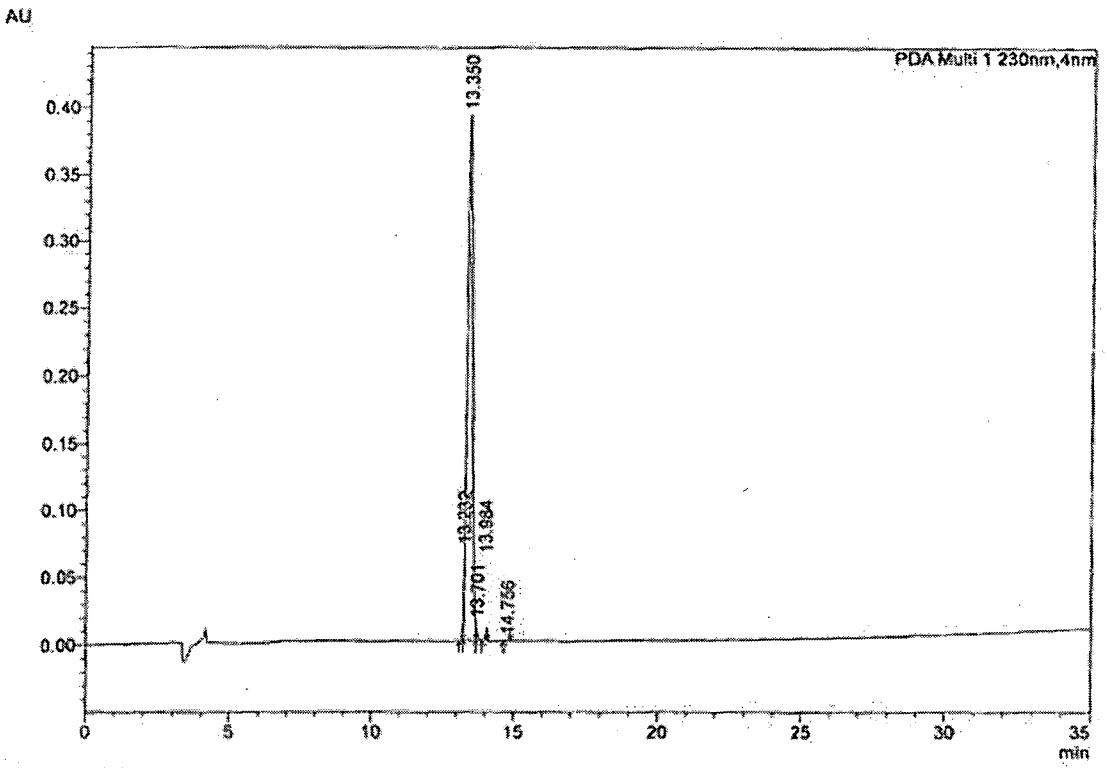
도 38

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name :K170468 (YDE-035)

<Chromatogram>



<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	13.232	12349	0.252
2	13.350	4845696	98.818
3	13.701	38529	0.786
4	13.984	2572	0.052
5	14.756	4526	0.092
Total		4903673	100.000

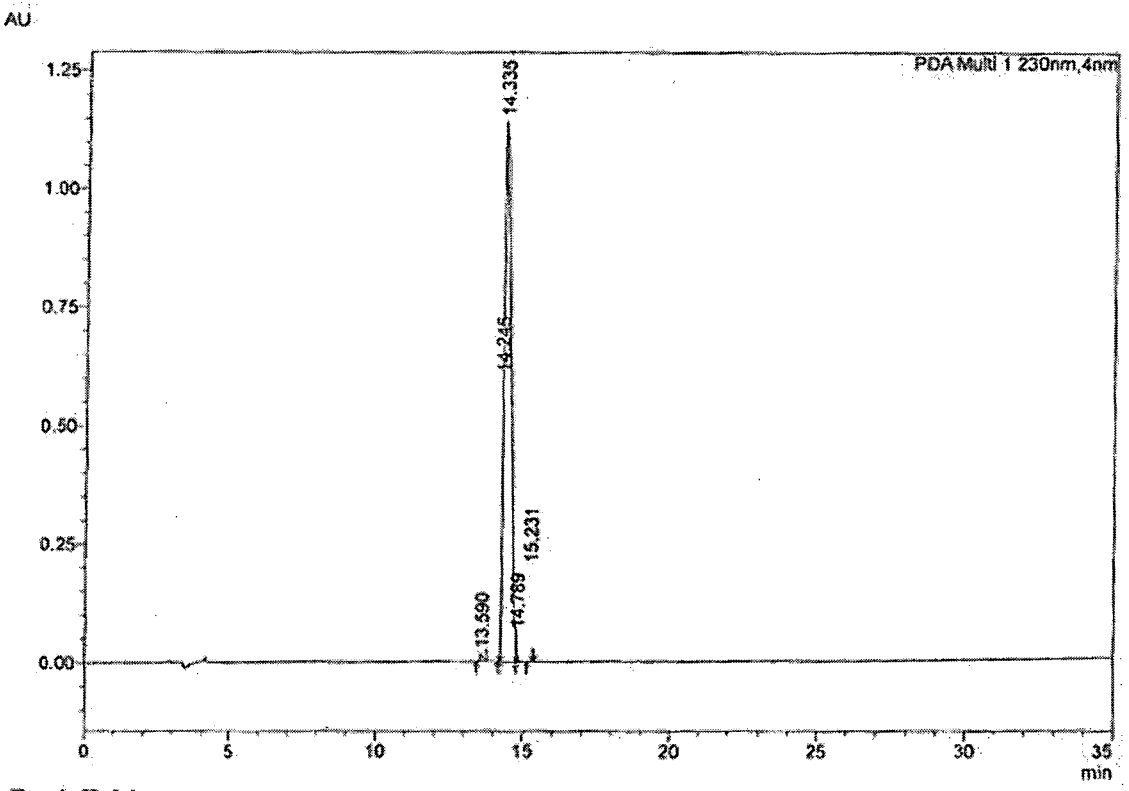
표 39

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name :K170469 (YDE-036)

<Chromatogram>



<Peak Table>

PDA Ch1 230nm

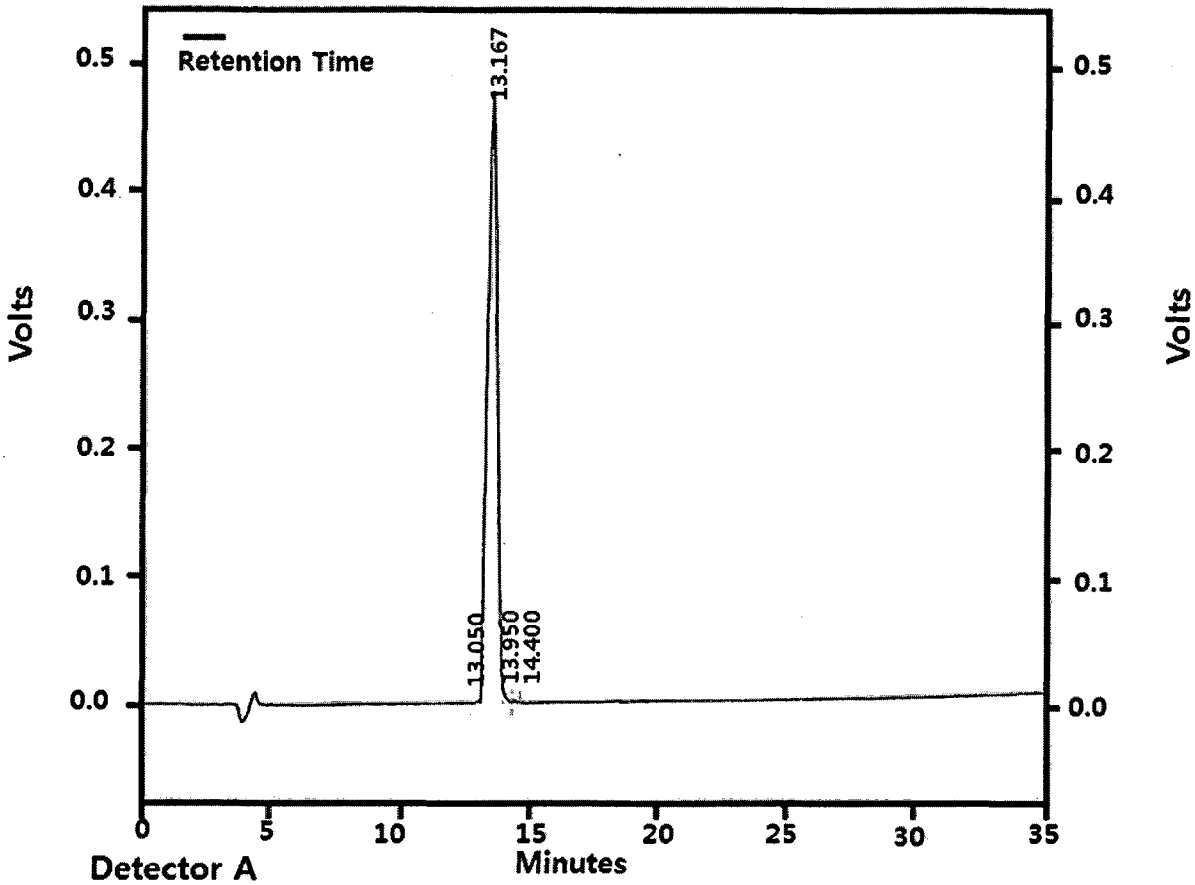
Peak#	Ret. Time	Area	Area%
1	13.590	95741	0.502
2	14.245	21037	0.110
3	14.335	18844050	98.765
4	14.789	113179	0.593
5	15.231	5631	0.030
Total		19079638	100.000

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Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K170470 (YDE-037)



Detector A (230nm)

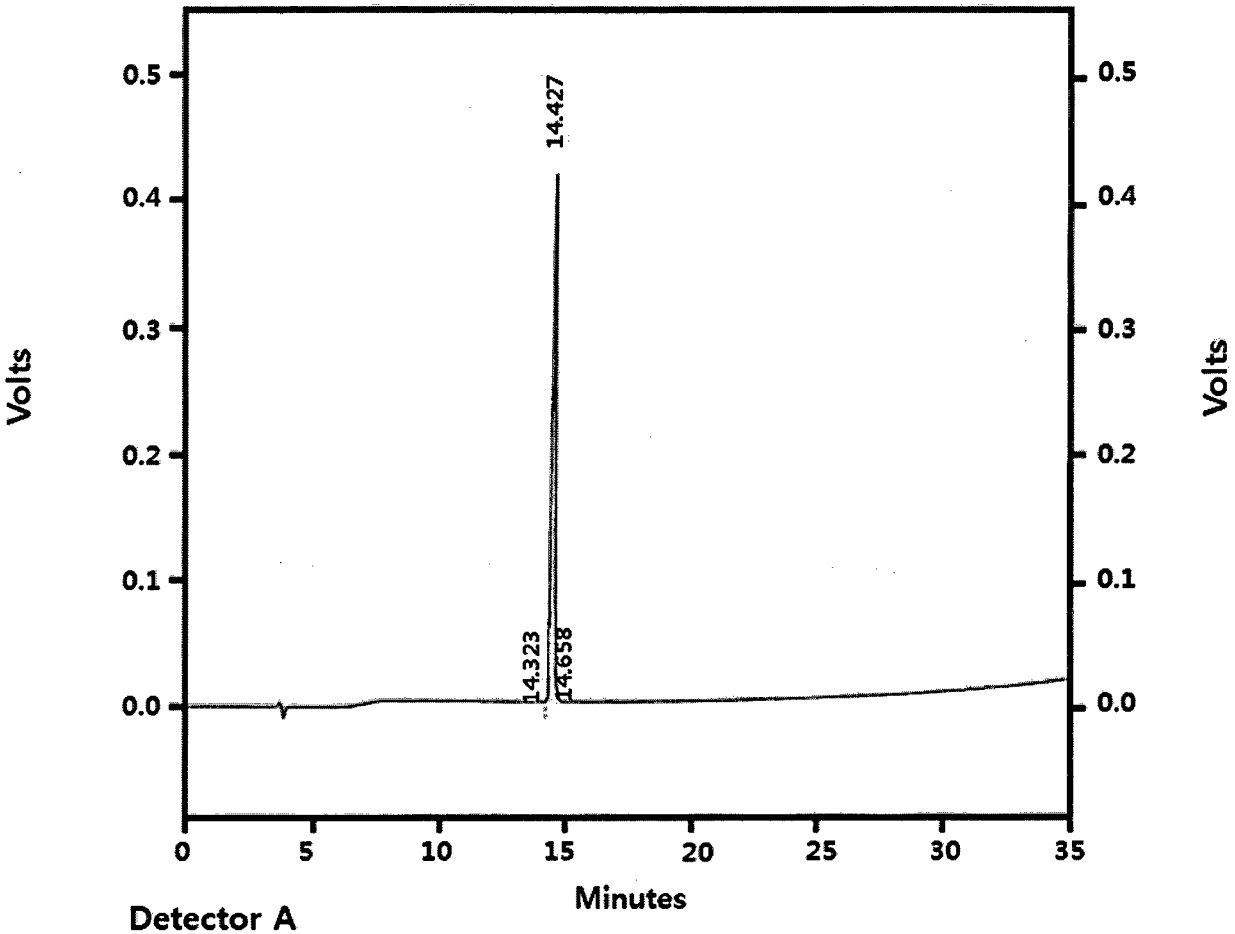
Pk #	Retention Time	Area	Area %
1	13.050	18320	0.148
2	13.167	12318048	99.237
3	13.950	60854	0.490
4	14.400	15548	0.125
Totals		12412770	100.000

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Shimadzu CLASS-VP V6.14 SP1 new 10AVP *Area % Report* *Page of 1*

Sample ID : K170471 (YDE-038)



Detector A (230nm)	Pk #	Retention Time	Area	Area %
	1	14.323	7412	0.197
	2	14.427	3716173	98.767
	3	14.658	38987	1.036
Totals			3762572	100.000

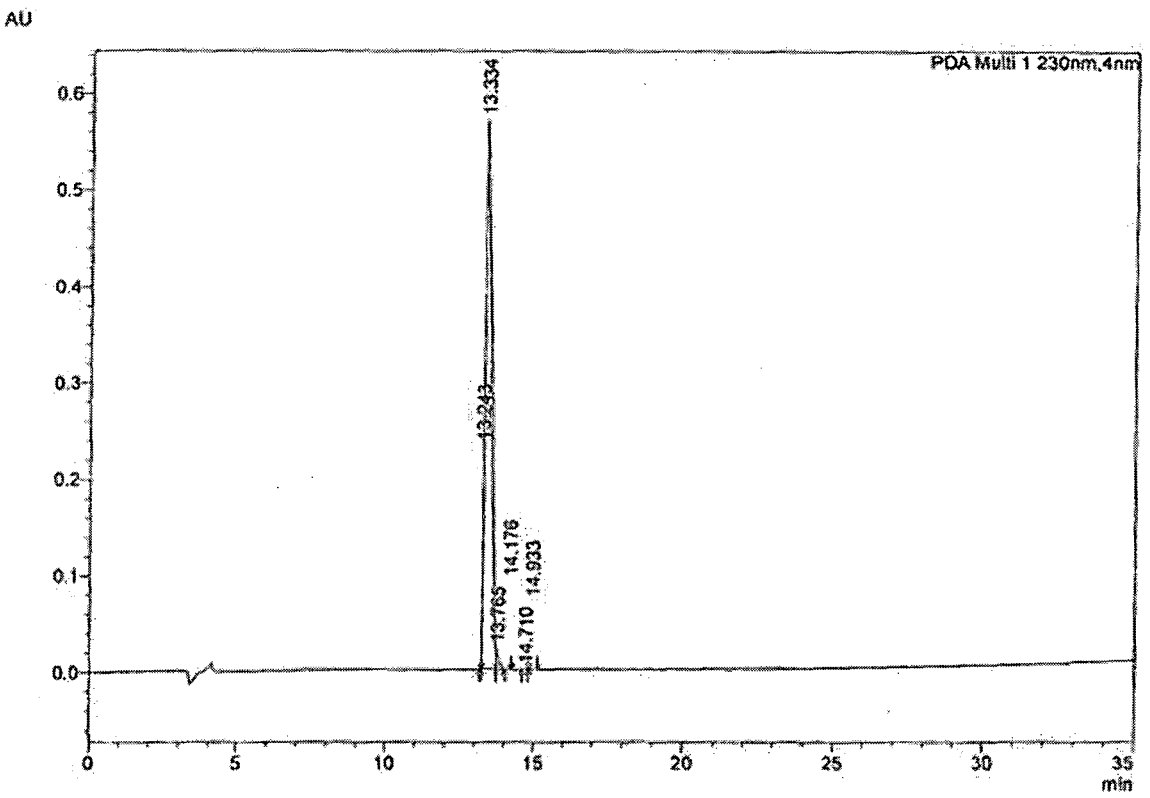
도 42

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name :K170484 (YDE-039)

<Chromatogram>



<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	13.243	10337	0.120
2	13.334	8471164	98.101
3	13.765	141934	1.644
4	14.176	1883	0.022
5	14.710	3097	0.036
6	14.933	6746	0.078
Total		8635161	100.000

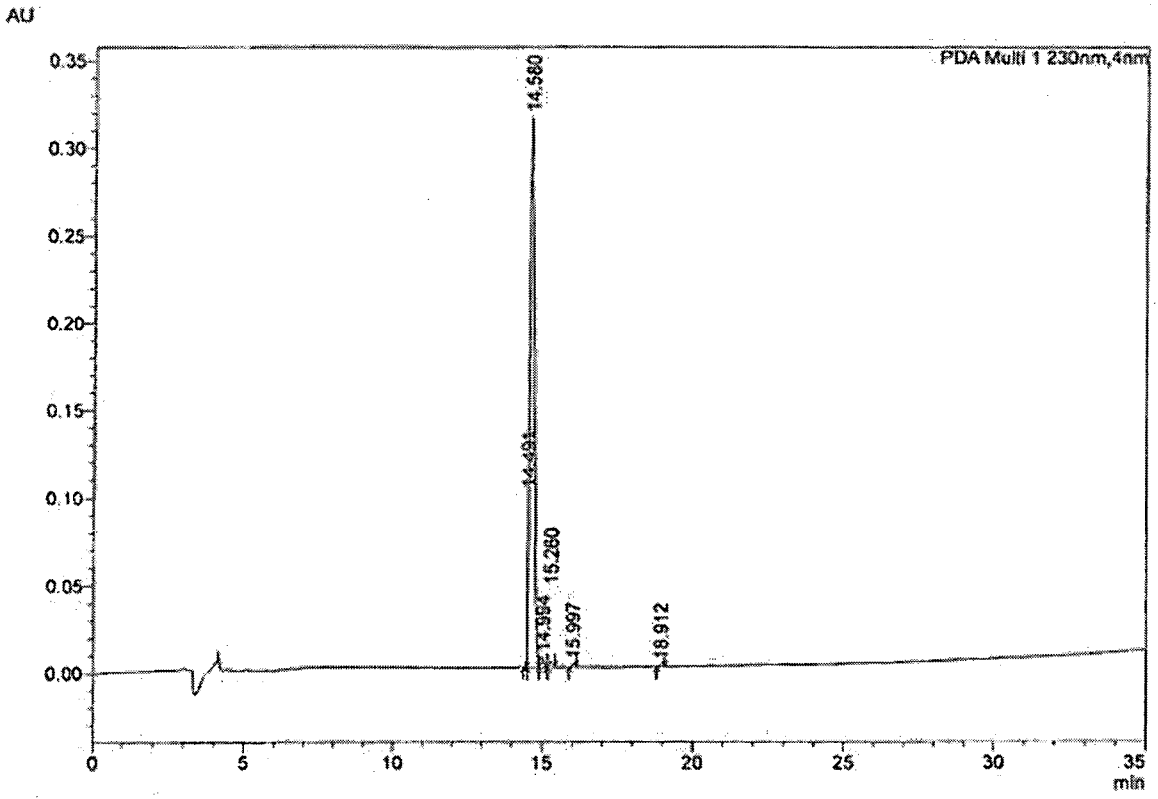
도 43

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name :K170485 (YDE-040)

<Chromatogram>



<Peak Table>

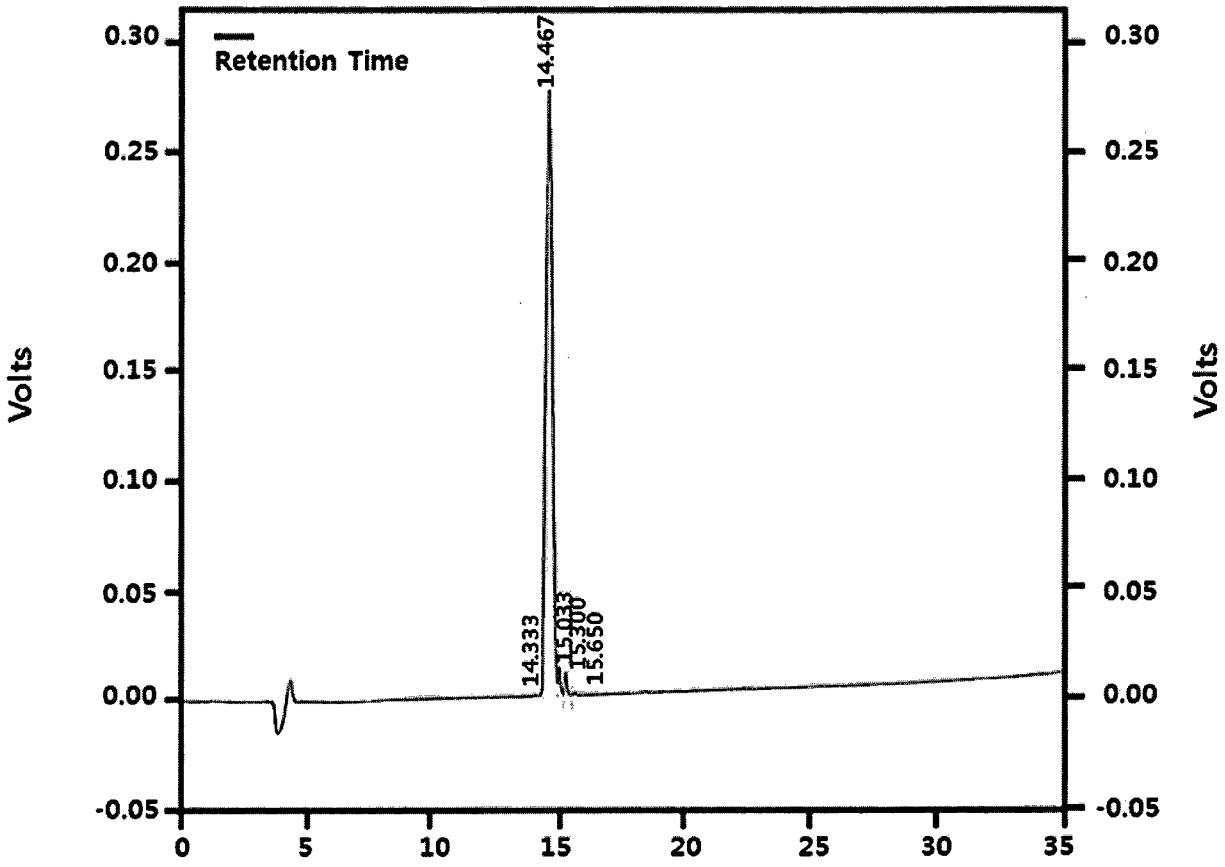
PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	14.491	8575	0.266
2	14.580	3145995	97.580
3	14.994	43744	1.357
4	15.260	10665	0.331
5	15.997	9068	0.281
6	18.912	5968	0.185
Total		3224014	100.000

도 44

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K170466 (YDE-041)



Detector A (230nm) Pk #	Retention Time	Area	Area %
1	14.333	8213	0.167
2	14.467	4742455	96.577
3	15.033	84778	1.726
4	15.300	67385	1.372
5	15.650	7689	0.157
Totals		4910520	100.000

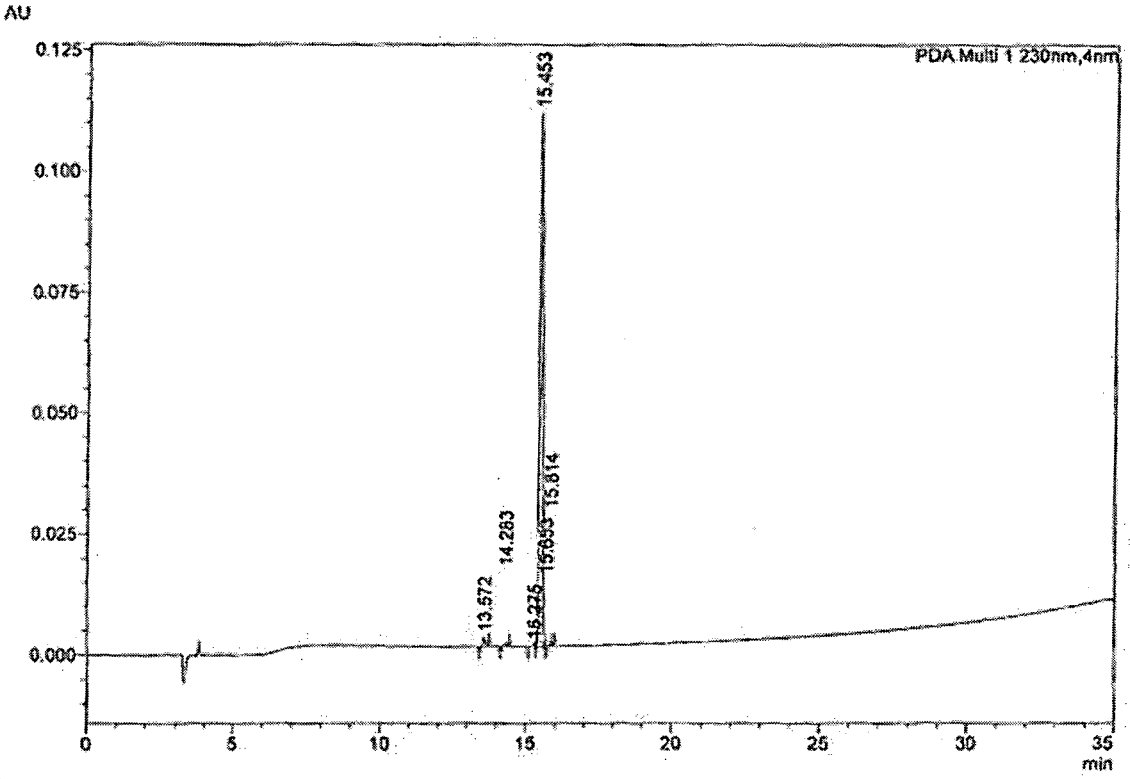
표 45

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name :K170696 (YDE-042)

<Chromatogram>



<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	13.572	10672	1.287
2	14.283	3251	0.392
3	15.275	1984	0.239
4	15.453	808105	97.476
5	15.653	3981	0.480
6	15.814	1036	0.125
Total		829028	100.000

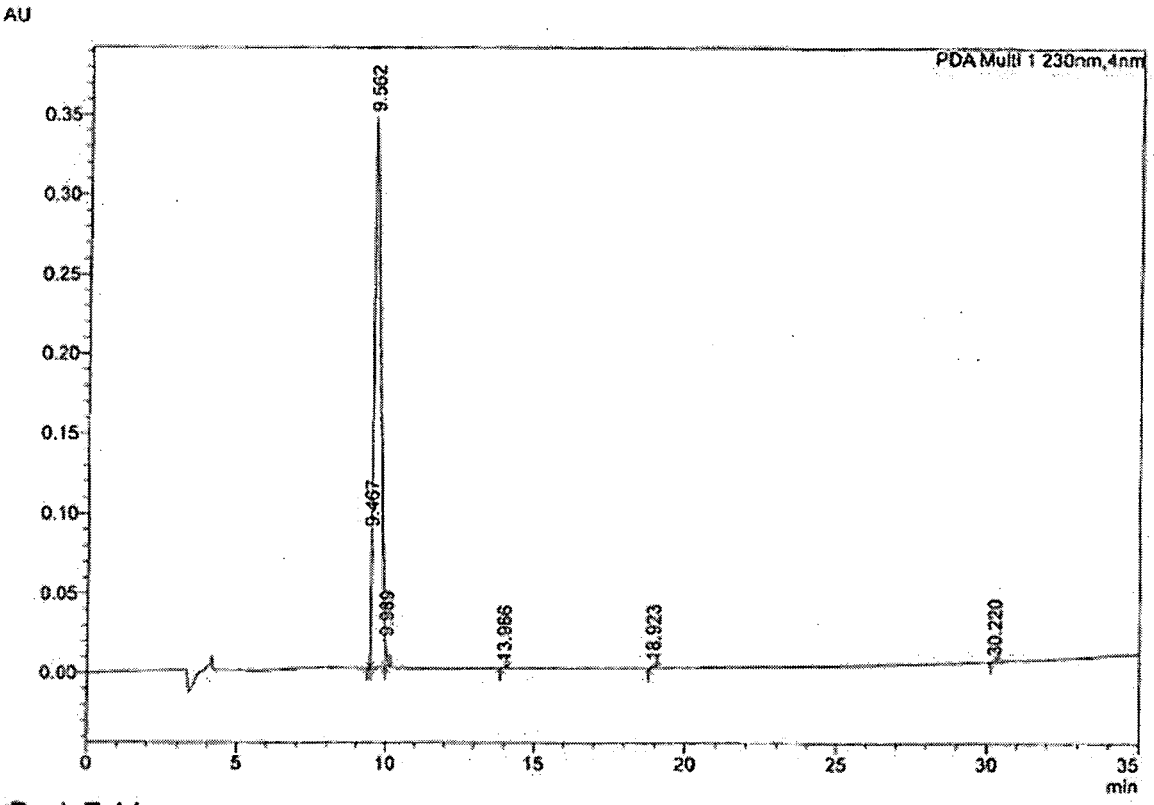
도 46

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name :K170695 (YDE-043)

<Chromatogram>



<Peak Table>

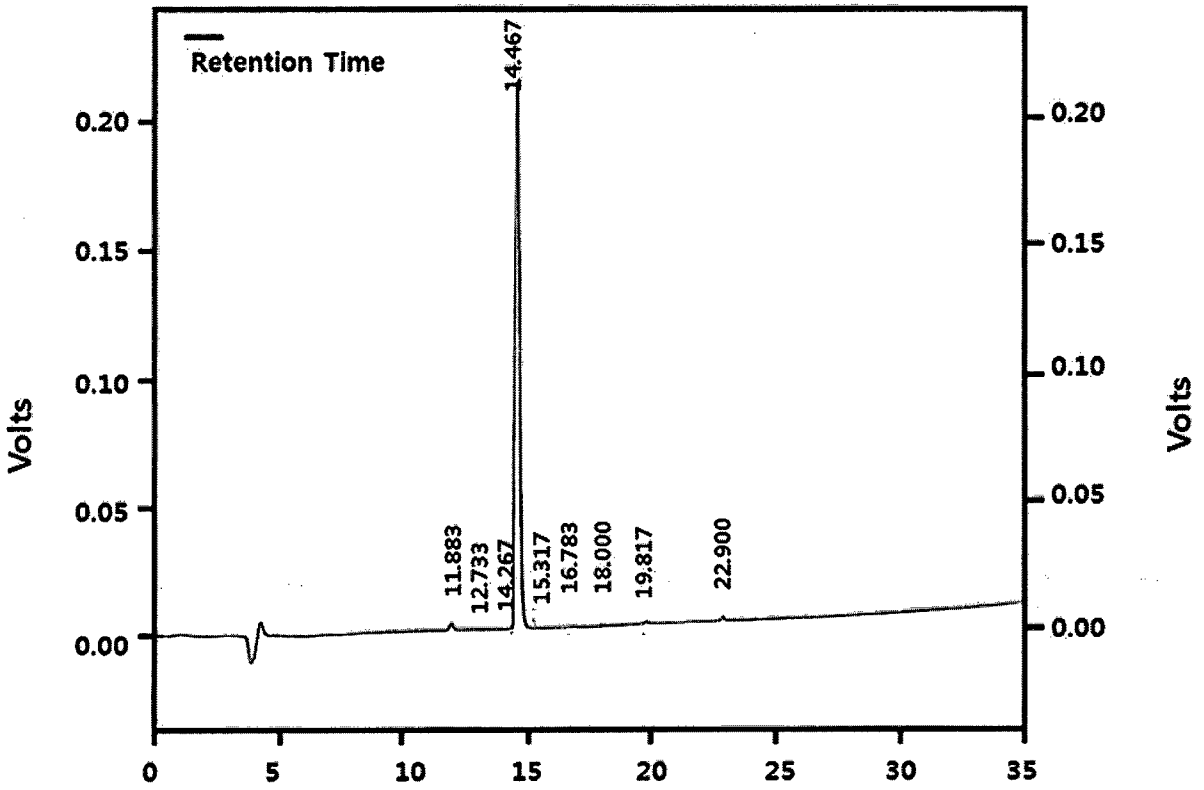
PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	9.467	2371	0.045
2	9.562	5211379	98.719
3	9.989	47144	0.893
4	13.966	4274	0.081
5	18.923	8330	0.158
6	30.220	5506	0.104
Total		5279004	100.000

도 47

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K171020 (YDE-044)

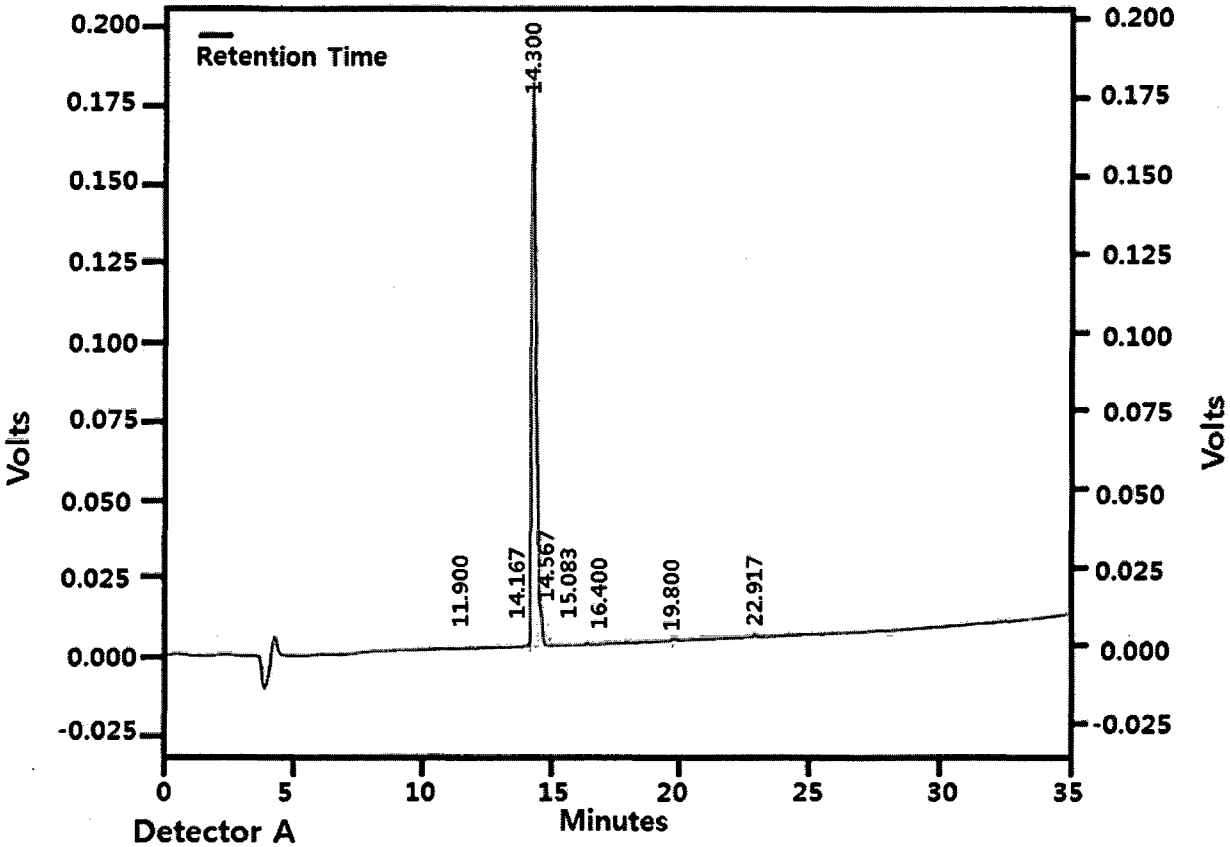


Detector A (230nm)	Retention Time	Area	Area %
1	11.883	27993	1.012
2	12.733	1286	0.047
3	14.267	2811	0.102
4	14.467	2704866	97.828
5	15.317	10992	0.398
6	16.783	4363	0.158
7	18.000	887	0.032
8	19.817	3279	0.119
9	22.900	8453	0.306
Totals		2764930	100.000

도 48

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K171021 (YDE-045)



Detector A (230nm)

Pk #	Retention Time	Area	Area %
1	11.900	636	0.029
2	14.167	5291	0.242
3	14.300	2089275	95.561
4	14.567	80787	3.695
5	15.083	1596	0.073
6	16.400	2393	0.109
7	19.800	2986	0.137
8	22.917	3361	0.154
Totals		2186325	100.000

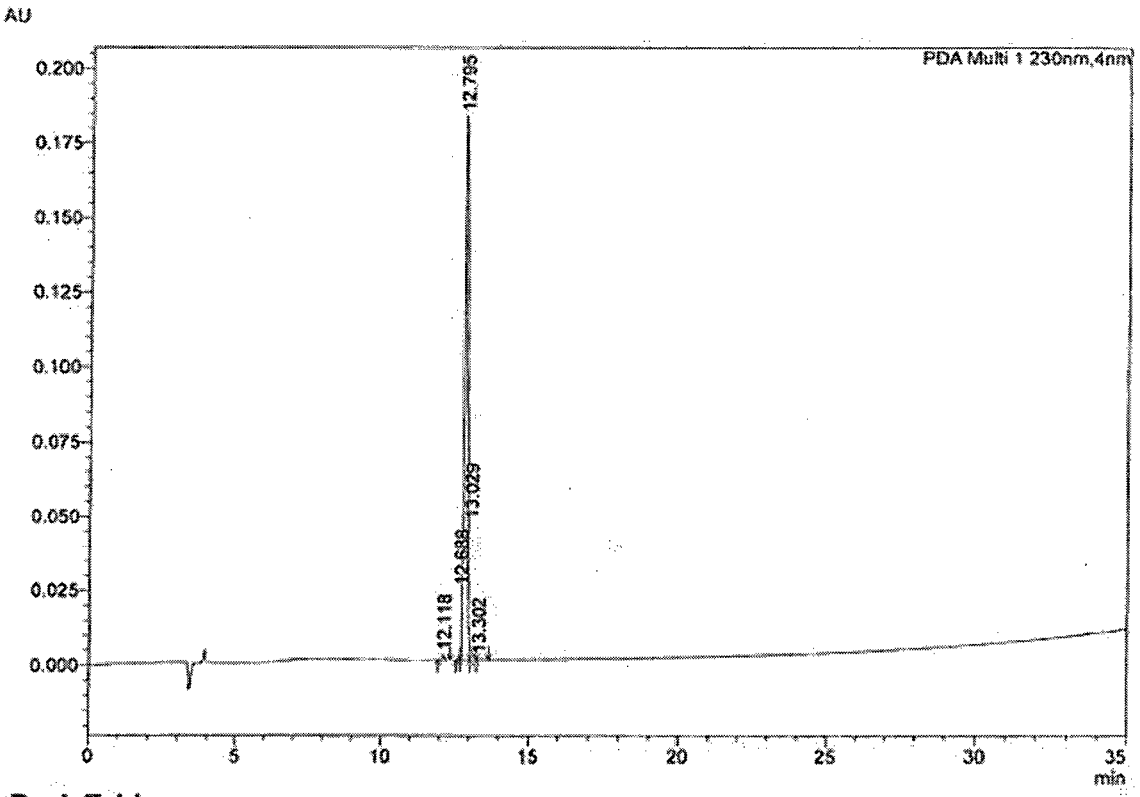
도 49

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name :K171849 (YDE-047)

<Chromatogram>



<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	12.118	8416	0.566
2	12.688	3751	0.252
3	12.795	1449638	97.513
4	13.029	22365	1.504
5	13.302	2443	0.164
Total		1486612	100.000

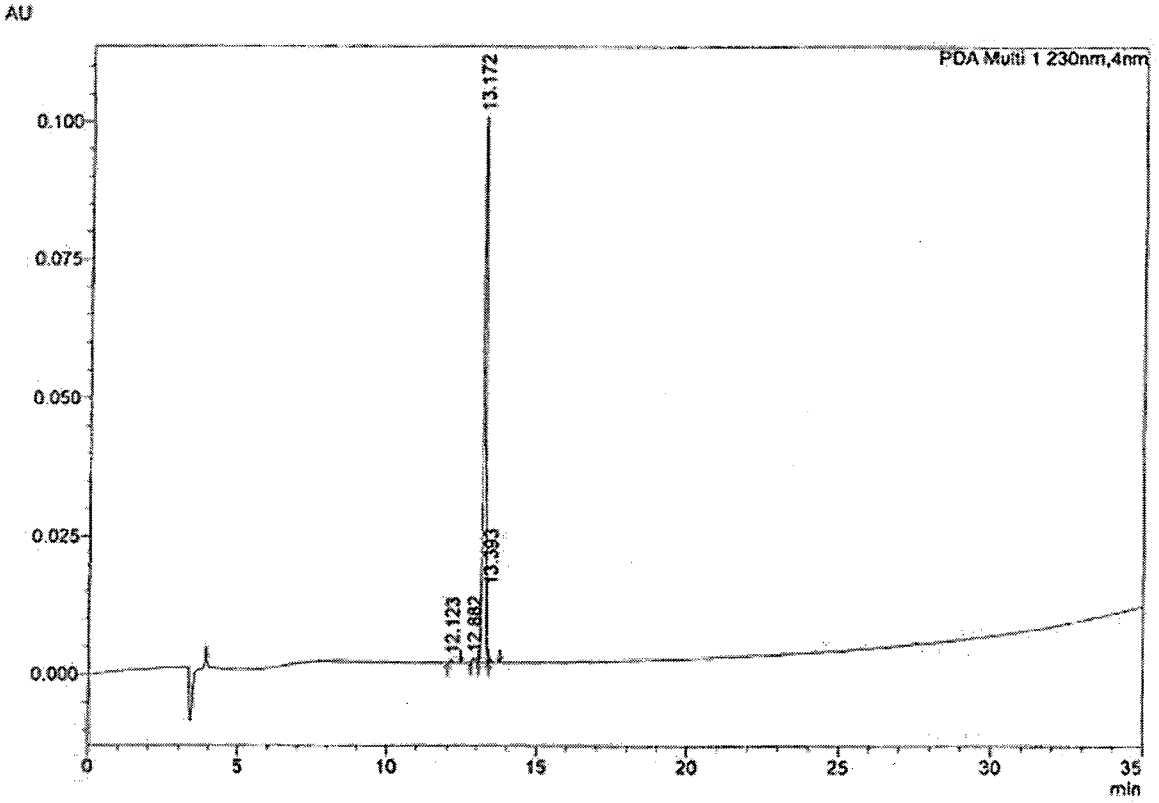
도 50

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name :K171850 (YDE-048)

<Chromatogram>



<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	12.123	3743	0.600
2	12.882	7696	1.234
3	13.172	606751	97.254
4	13.393	5695	0.913
Total		623885	100.000

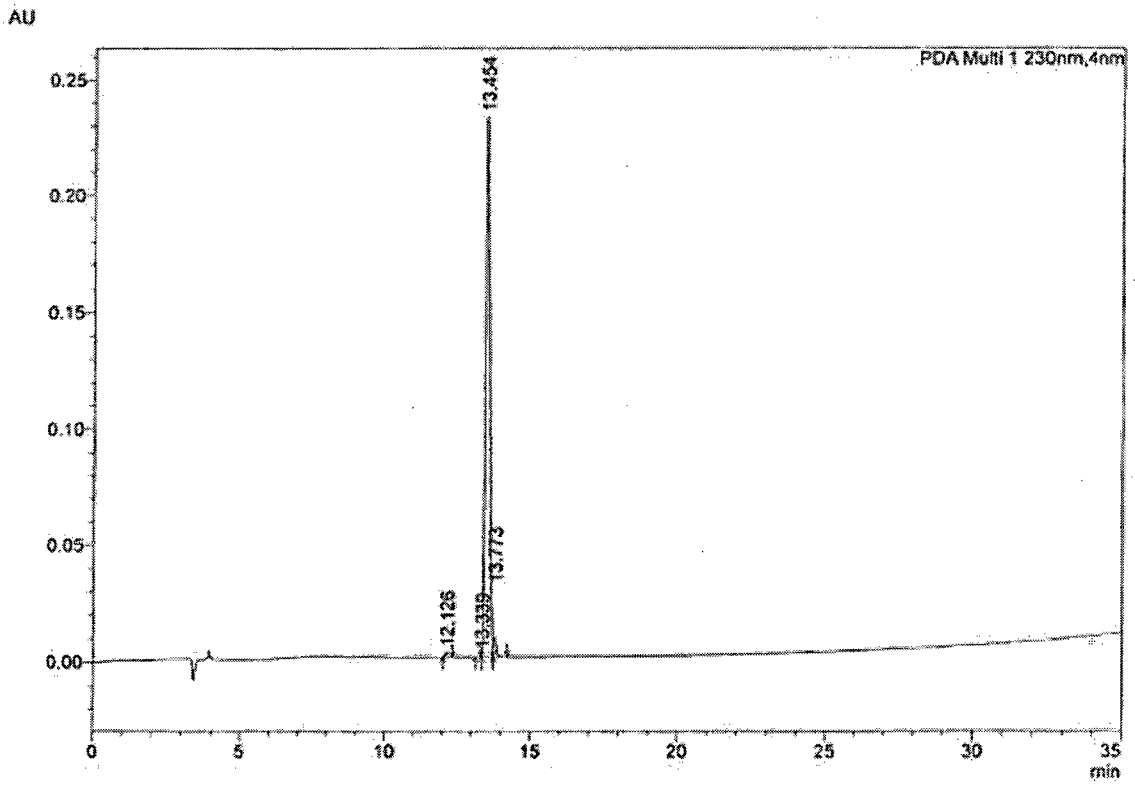
도 51

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name :K171851 (YDE-049)

<Chromatogram>



<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	12.126	12891	0.539
2	13.339	1756	0.073
3	13.454	2318972	96.924
4	13.773	58958	2.464
Total		2392577	100.000

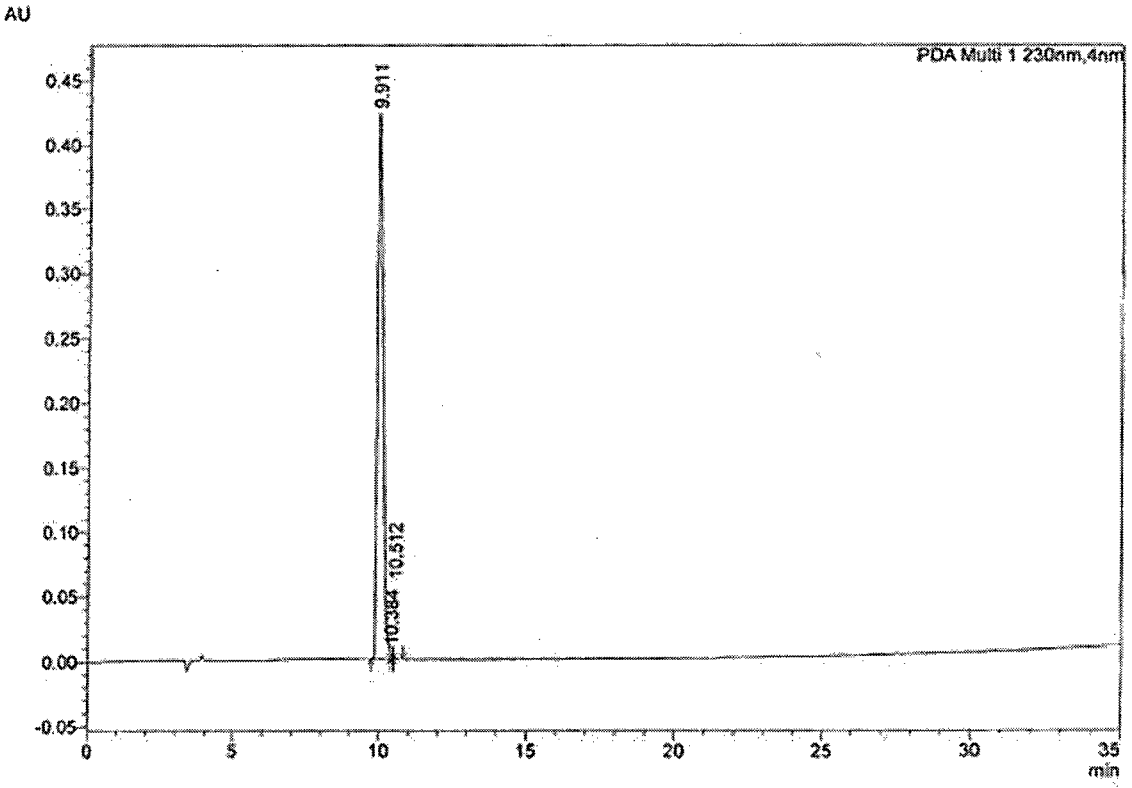
도 52

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name :K171852 (YDE-050)

<Chromatogram>



<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	9.911	5450324	99.329
2	10.384	20990	0.383
3	10.512	15843	0.289
Total		5487158	100.000

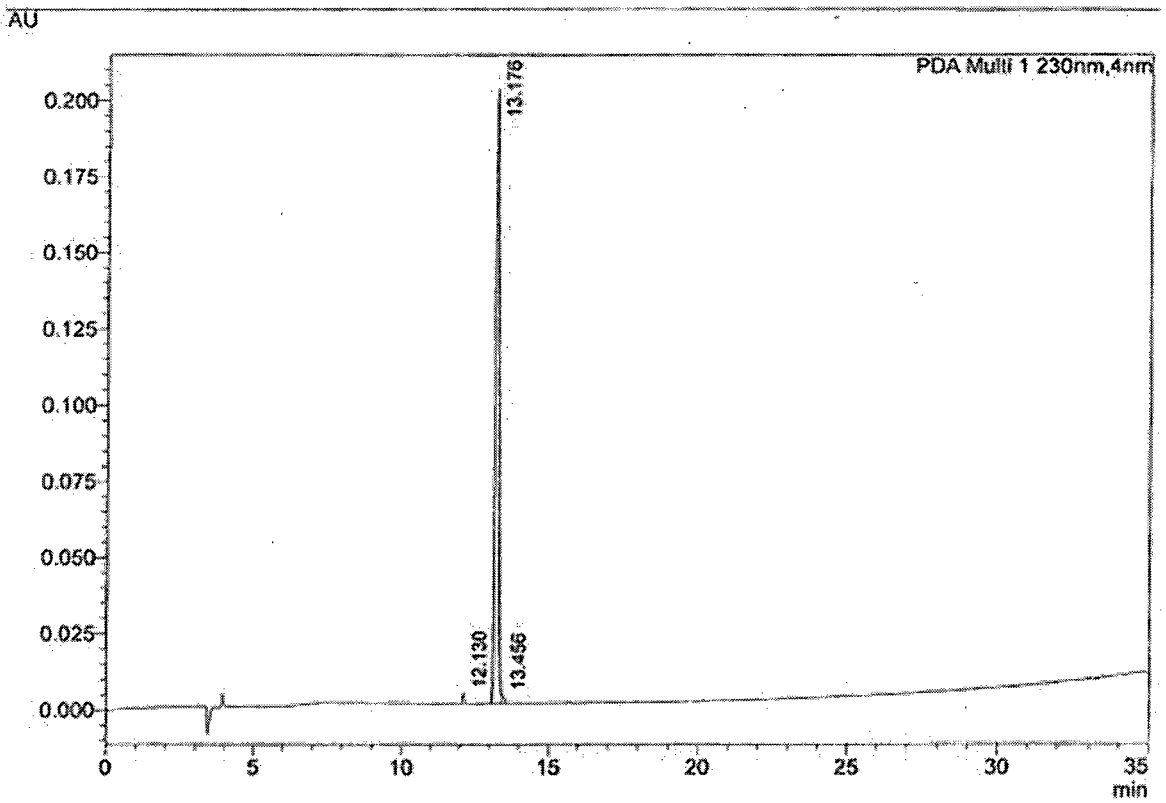
도 53

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name : K171853 (YDE-051)

<Chromatogram>



<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	12.130	18605	1.120
2	13.176	1627394	98.011
3	13.456	14421	0.869
Total		1660420	100.000

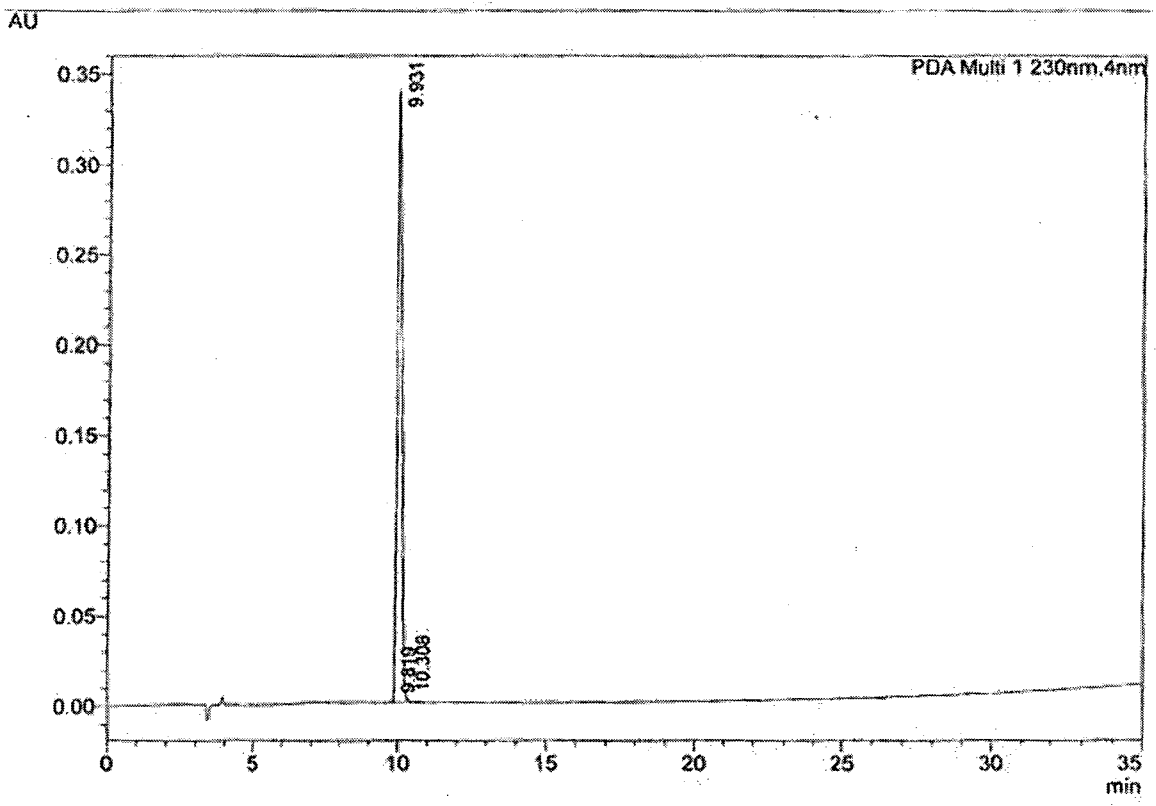
도 54

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name : K171854 (YDE-052)

<Chromatogram>



<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	9.819	2280	0.065
2	9.931	3486152	99.456
3	10.308	16804	0.479
Total		3505236	100.000

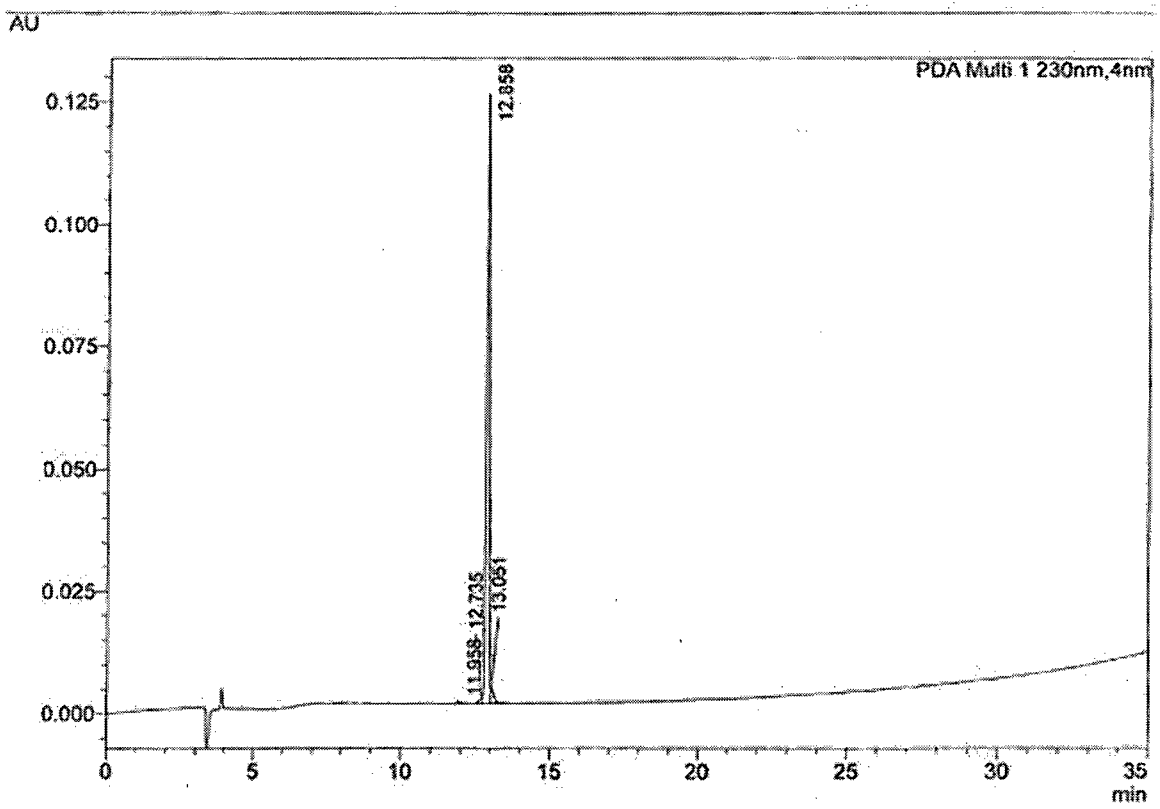
도 55

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name : K171855 (YDE-053)

<Chromatogram>



<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	11.958	3827	0.441
2	12.735	7134	0.822
3	12.858	836814	96.428
4	13.051	20034	2.309
Total		867809	100.000

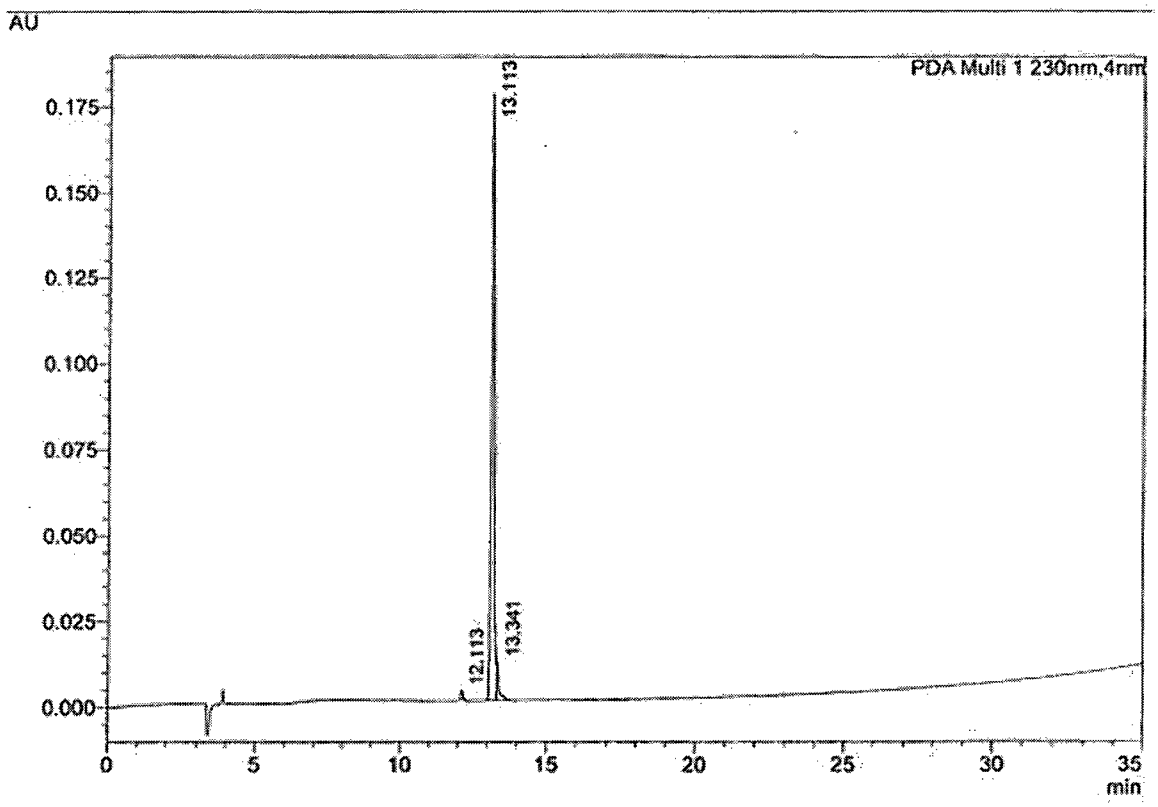
도 56

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name : K171856 (YDE-054)

<Chromatogram>



<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	12.113	9831	0.724
2	13.113	1291332	95.112
3	13.341	56534	4.164
Total		1357696	100.000

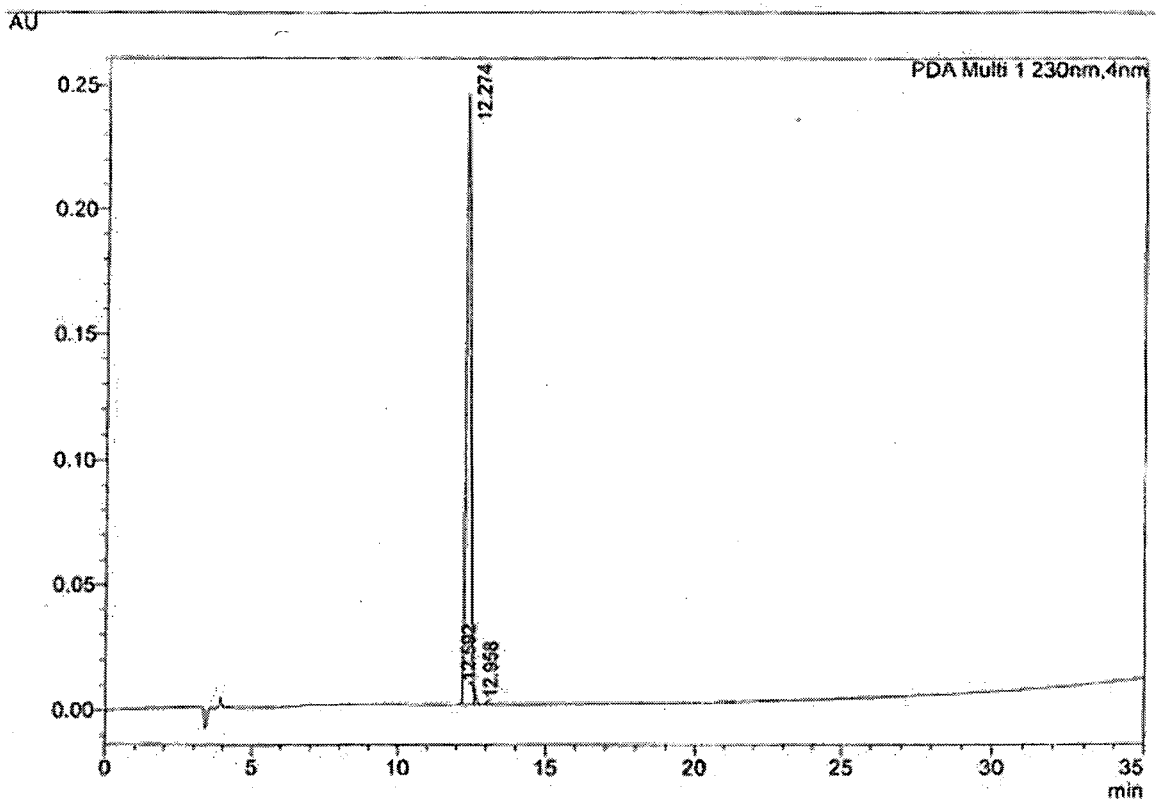
도 57

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name : K171857 (YDE-055)

<Chromatogram>



<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	12.274	2627179	98.689
2	12.592	31720	1.192
3	12.958	3175	0.119
Total		2662073	100.000

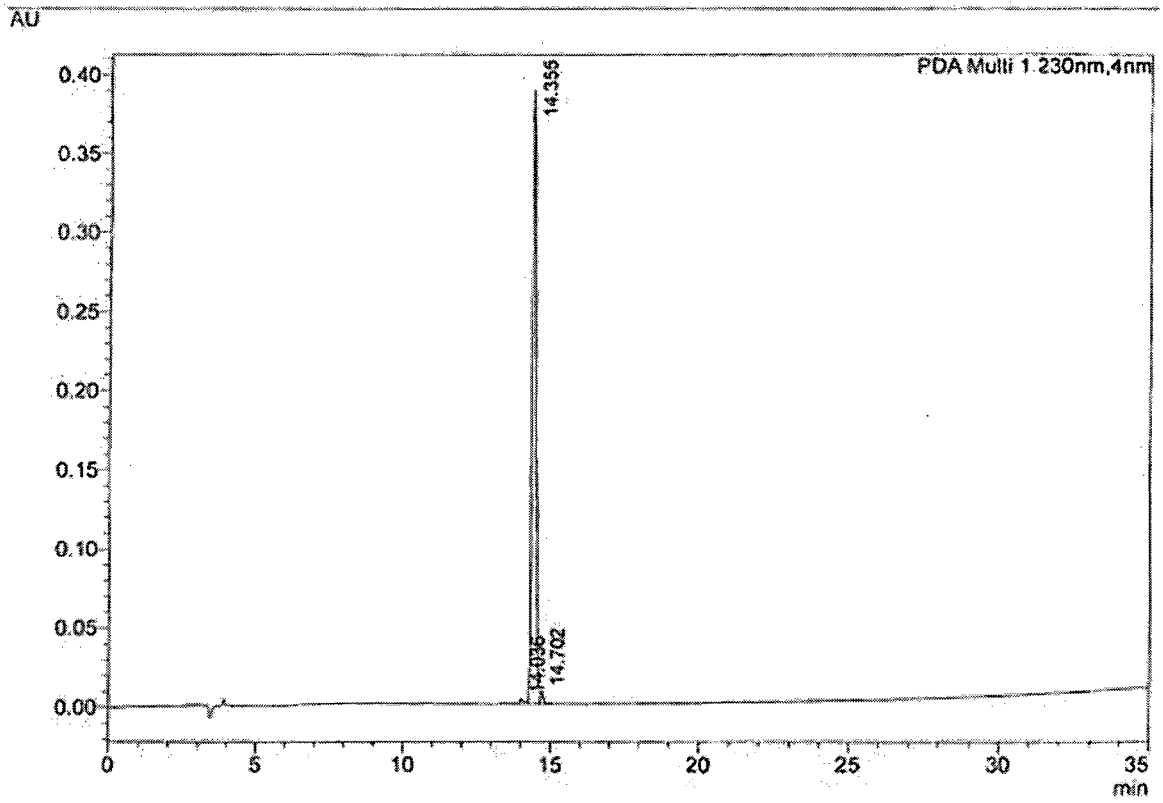
도 58

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name : K171858 (YDE-056)

<Chromatogram>



<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	14.036	36272	0.999
2	14.355	3537845	97.433
3	14.702	56951	1.568
Total		3631068	100.000

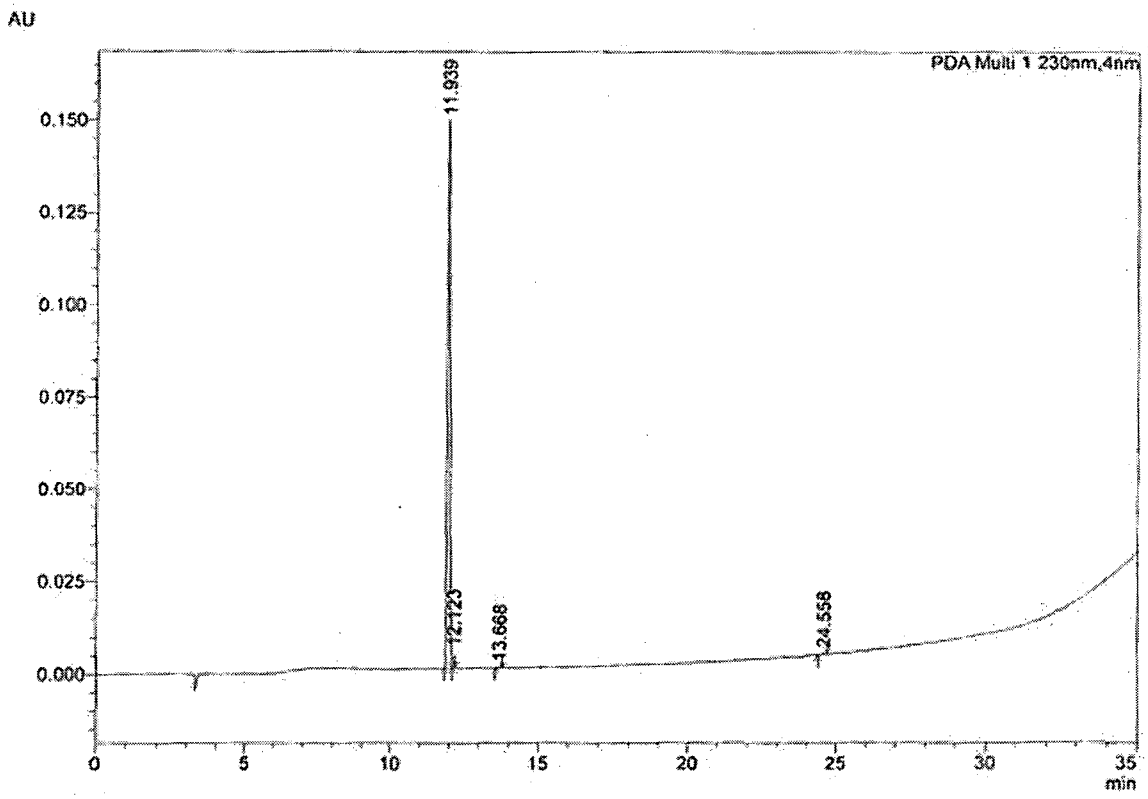
도 59

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name :K171869 (YDE-057)

<Chromatogram>



<Peak Table>

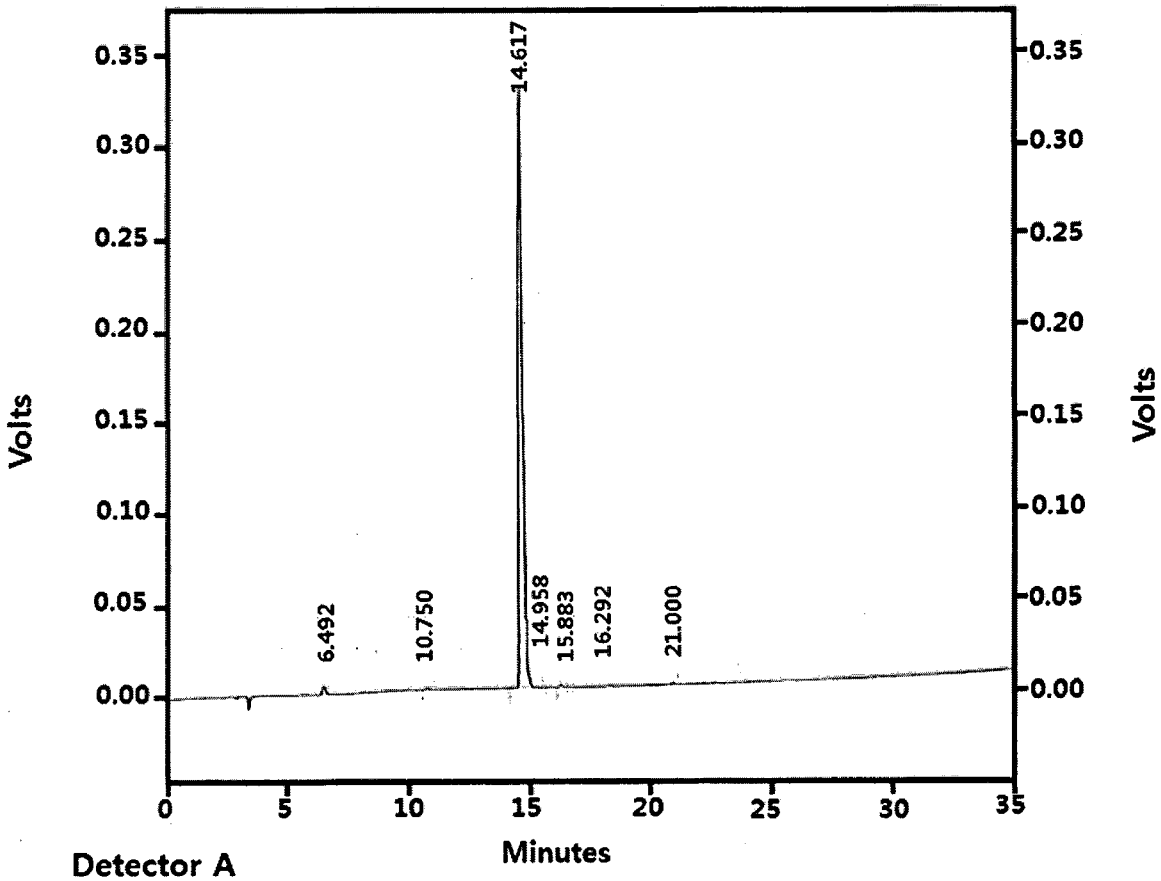
PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	11.939	945100	98.813
2	12.123	6524	0.682
3	13.668	2176	0.227
4	24.558	2651	0.277
Total		956452	100.000

도 60

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K171870 (YDE-058)

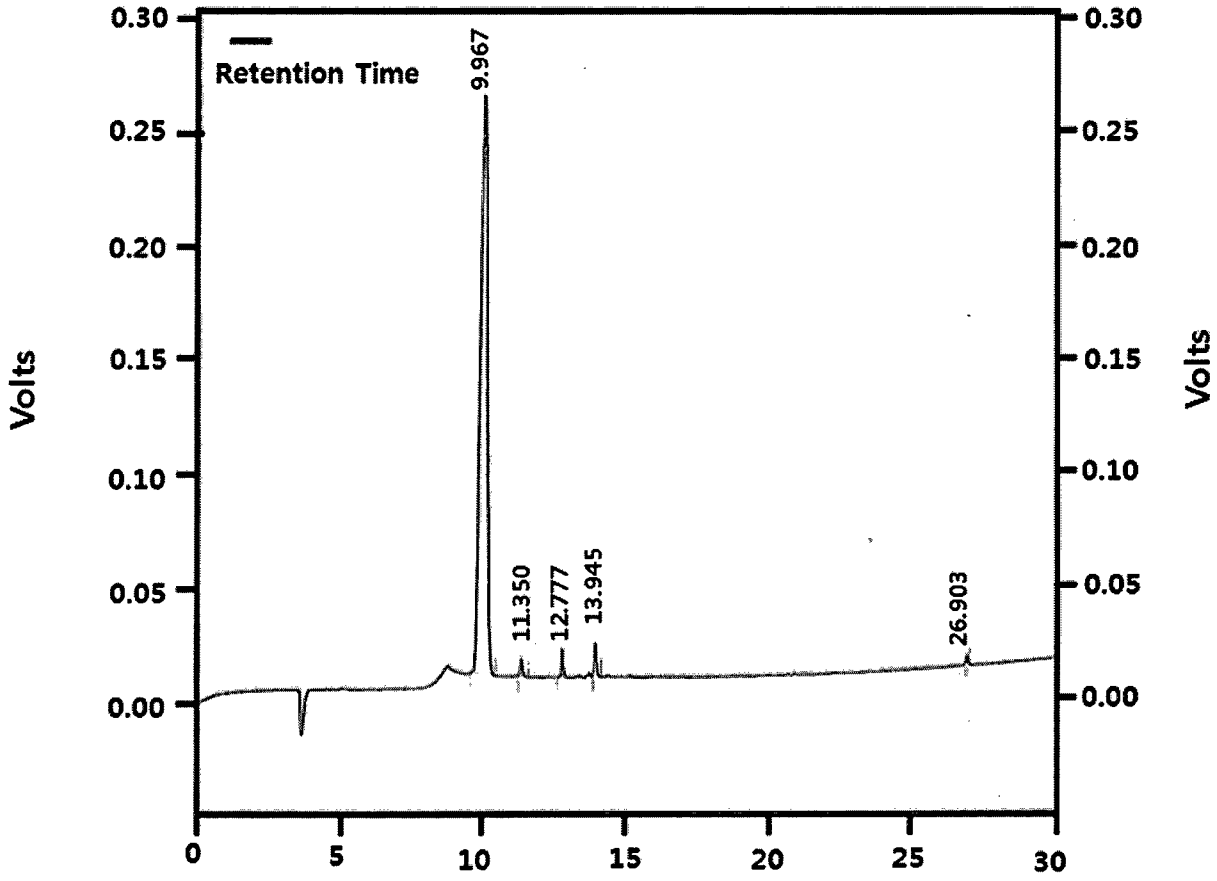


Detector A (230nm) Pk #	Retention Time	Area	Area %
1	6.492	36263	0.915
2	10.750	9609	0.243
3	14.617	3861560	97.473
4	14.958	33751	0.852
5	15.883	2210	0.056
6	16.292	13260	0.335
7	21.000	5001	0.126
Totals		3961654	100.000

도 61

Shimadzu CLASS-VP V6.14 SP1 new 10AVP *Area % Report* *Page of 1*

Sample ID : K171871 (YDE-059)



Detector A (230nm) Minutes

Pk #	Retention Time	Area	Area %
1	9.967	4241746	95.874
2	11.350	40399	0.913
3	12.777	52325	1.183
4	13.945	74918	1.693
5	26.903	14911	0.337
Totals		4424299	100.000

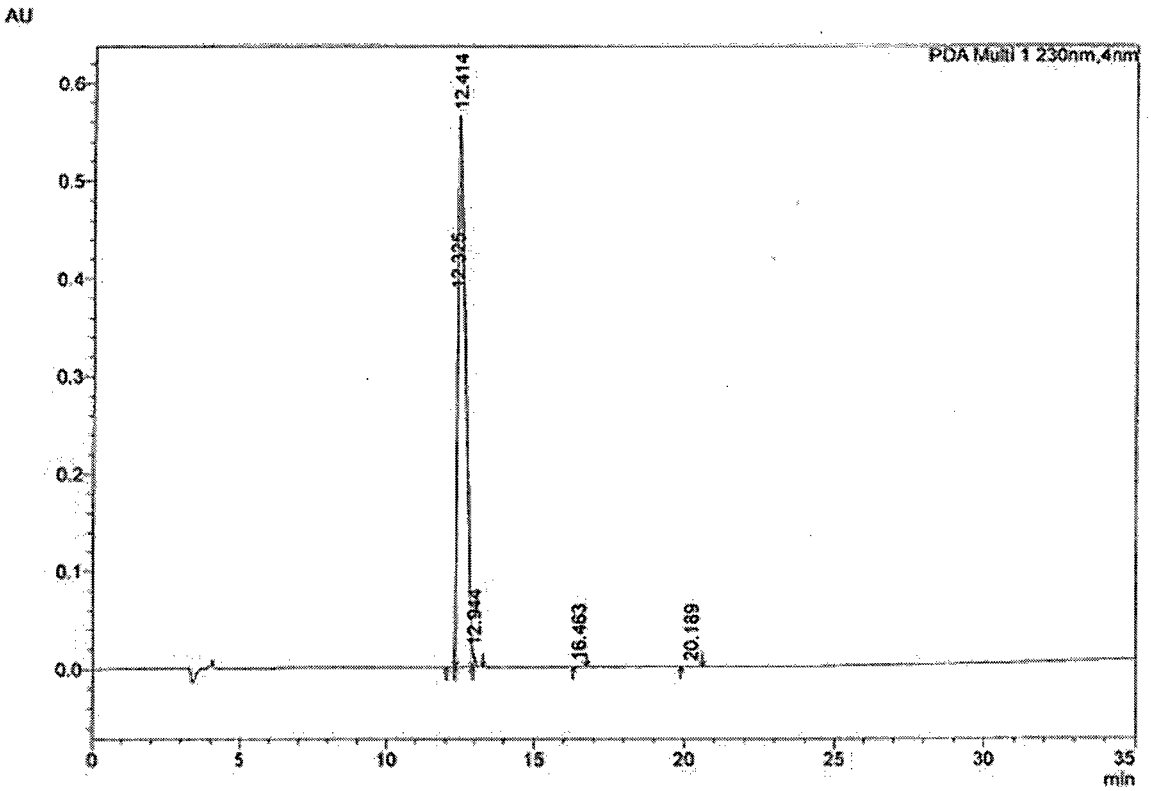
도 62

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name :K171872 (YDE-060)

<Chromatogram>



<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	12.325	21419	0.202
2	12.414	10477432	98.960
3	12.944	77001	0.727
4	16.463	6326	0.060
5	20.189	5396	0.051
Total		10587574	100.000

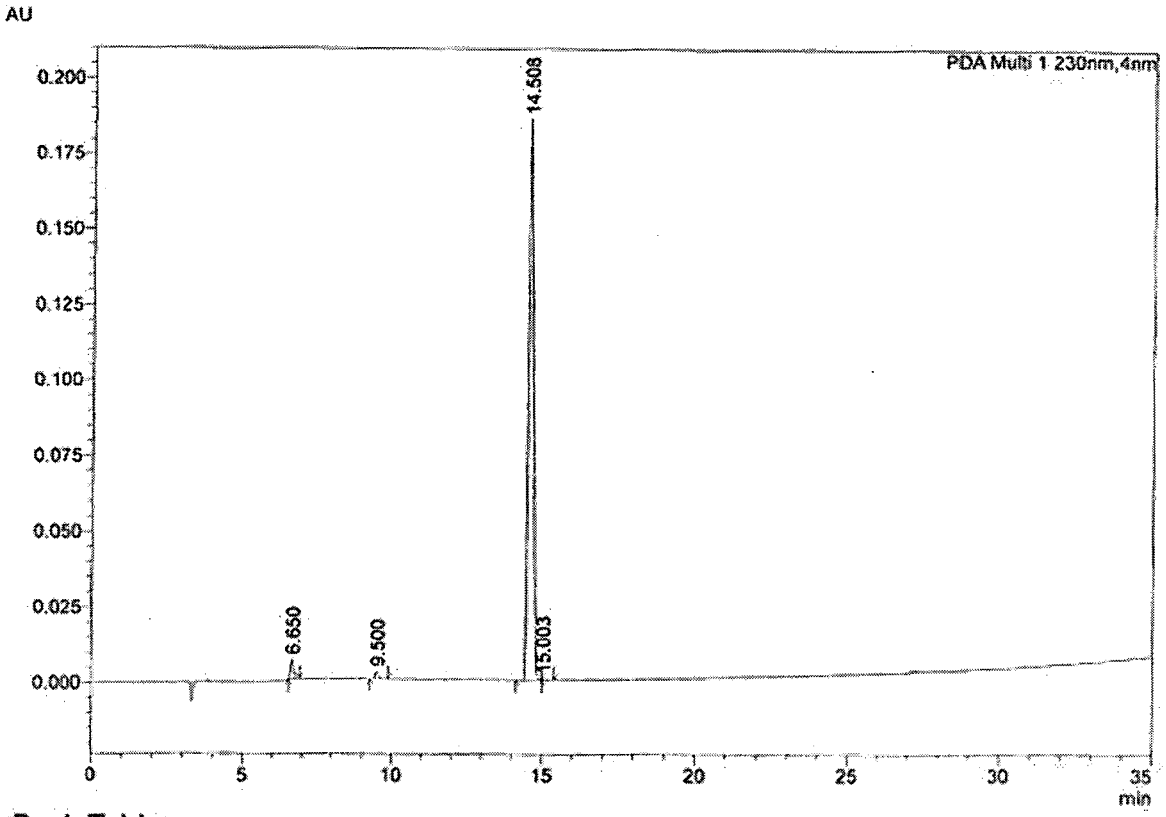
도 63

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name :K171987(YDE-064)

<Chromatogram>



<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	6.650	45425	2.187
2	9.500	15738	0.758
3	14.508	2014246	96.975
4	15.003	1669	0.080
Total		2077077	100.000

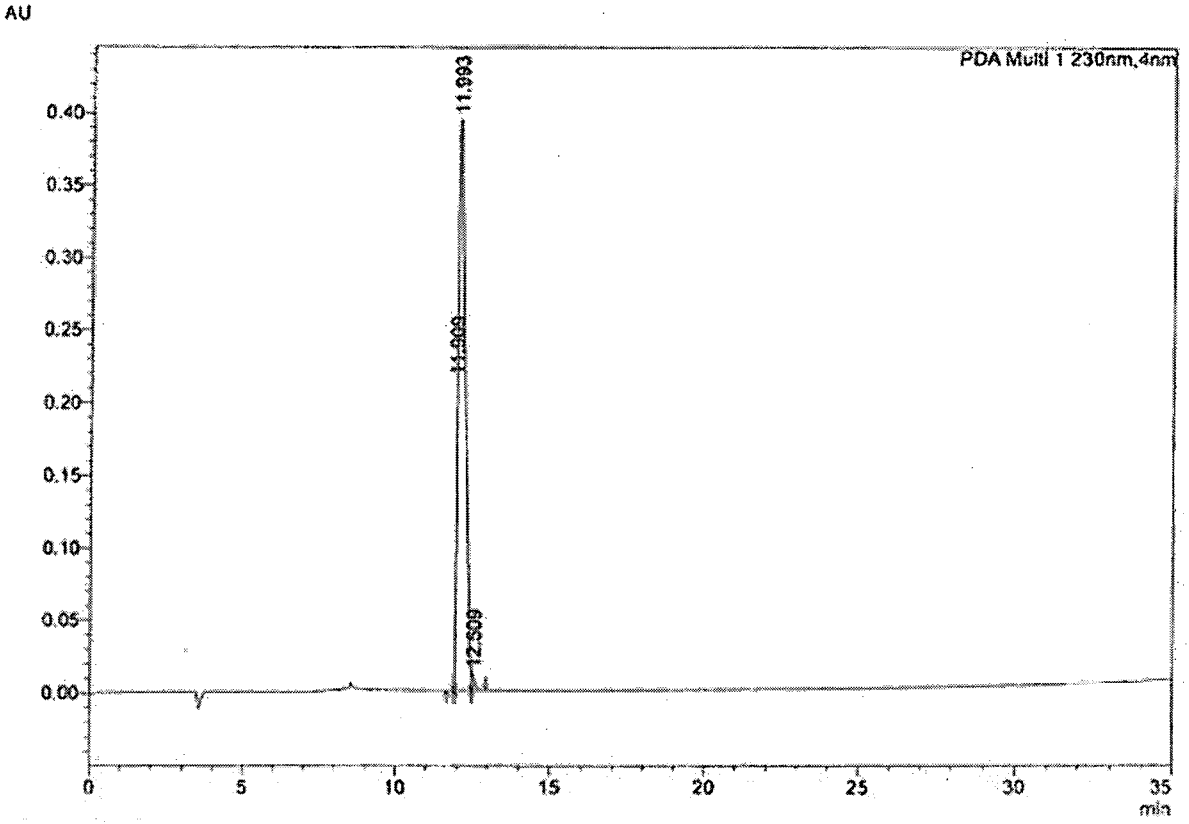
도 64

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name :K171989 (YDE-066)

<Chromatogram>



<Peak Table>

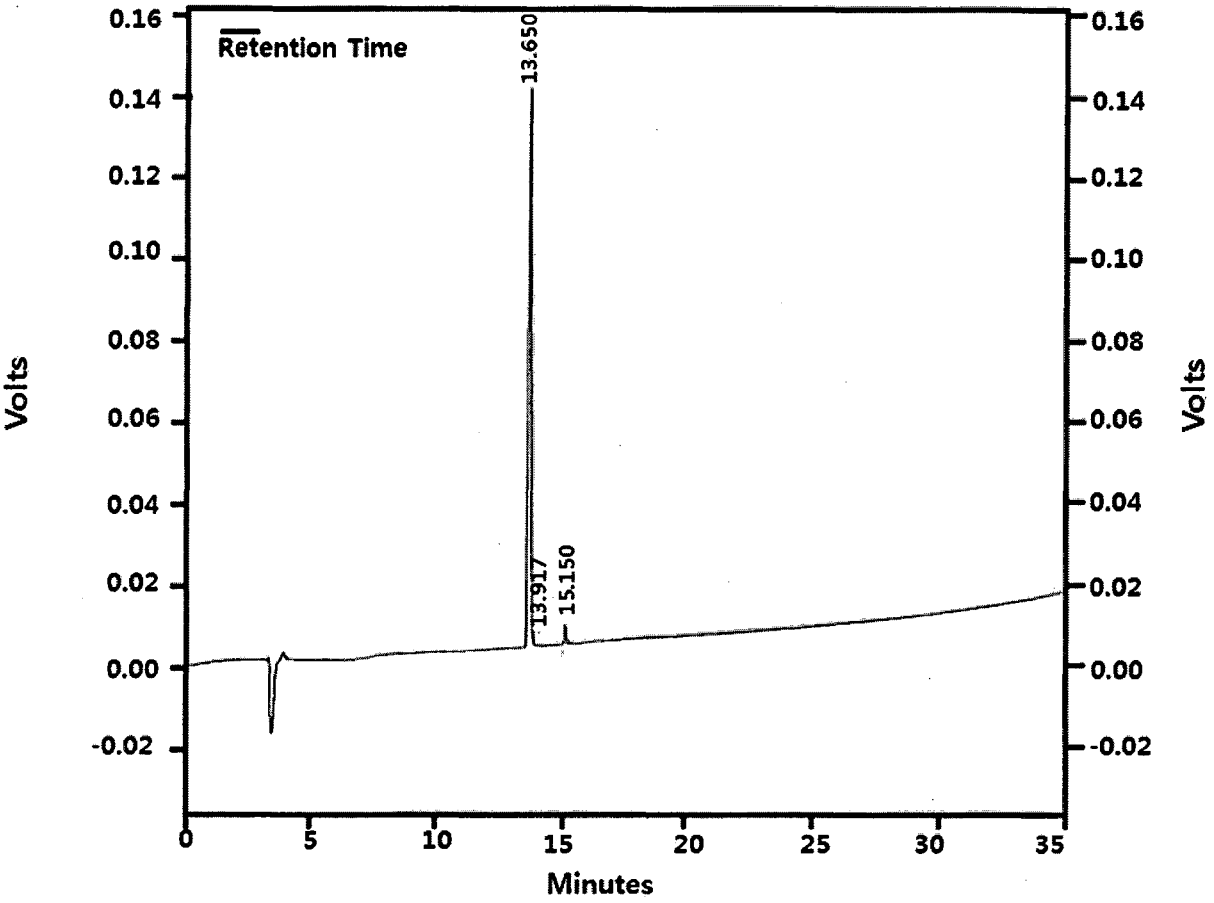
PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	11.909	1016	0.016
2	11.993	6411284	98.801
3	12.509	76758	1.183
Total		6489058	100.000

도 65

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K180115 (YDE-072)



Detector A (230nm)

Pk #	Retention Time	Area	Area %
1	13.650	1120198	97.732
2	13.917	1749	0.153
3	15.150	24243	2.115
Totals		1146190	100.000

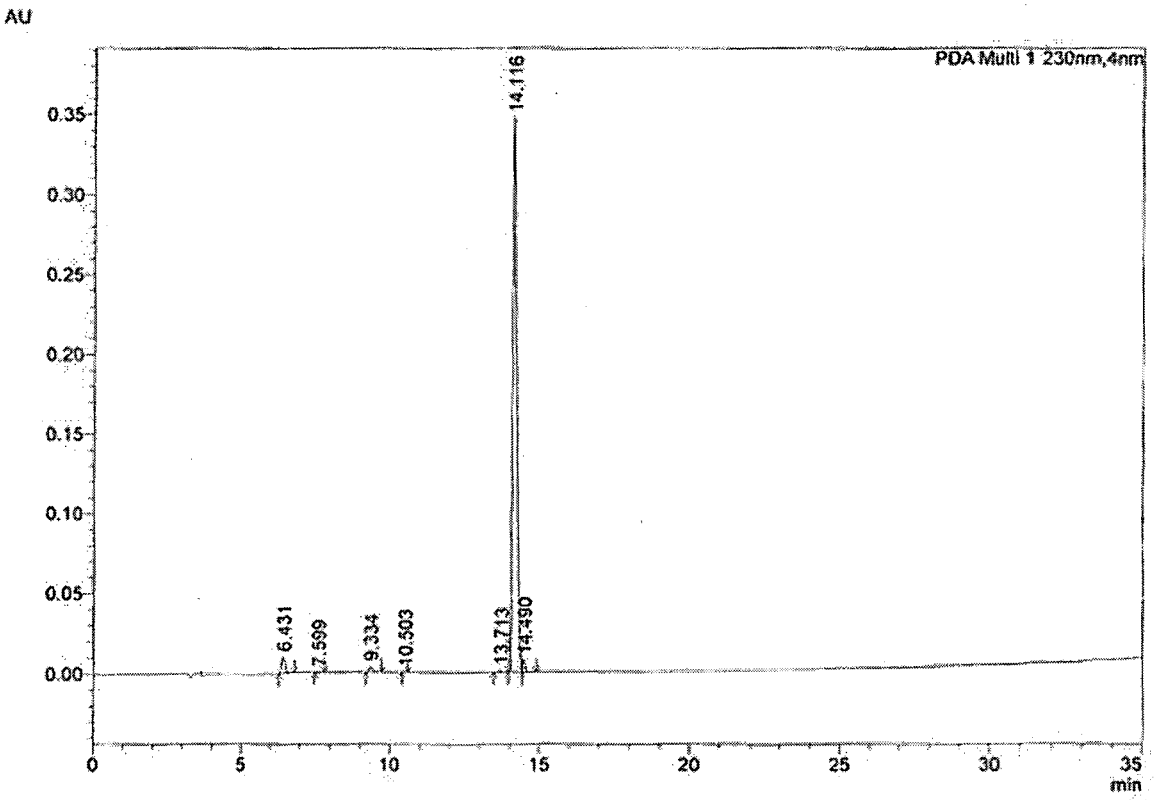
도 66

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name :K180116 (YDE-073)

<Chromatogram>



<Peak Table>

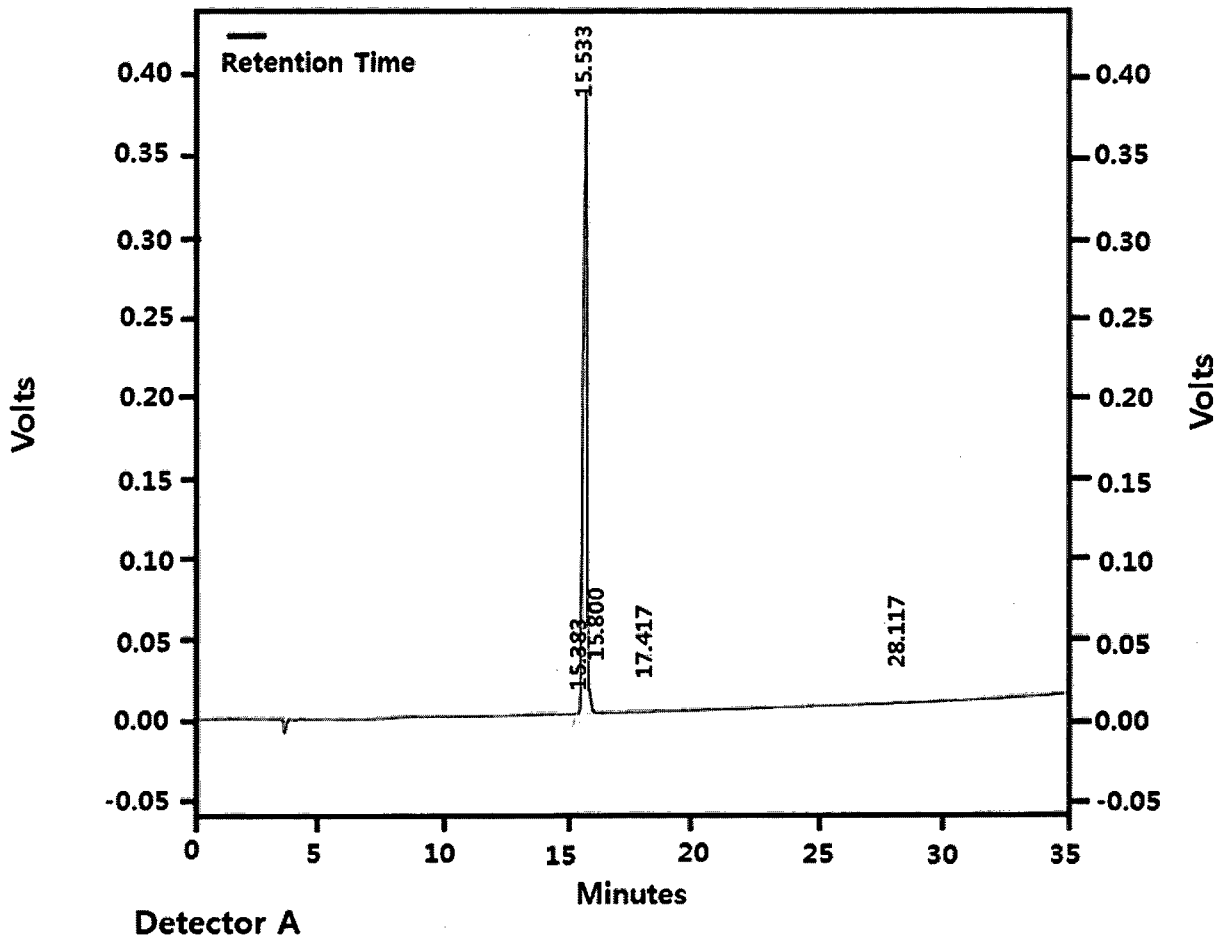
PDA Ch1 230nm

Peak#	Ret. Time	Area	Area%
1	6.431	84808	2.497
2	7.599	2612	0.077
3	9.334	26801	0.789
4	10.503	2243	0.066
5	13.713	11180	0.329
6	14.116	3228240	95.033
7	14.490	41081	1.209
Total		3396964	100.000

도 67

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

Sample ID : K180117 (YDE-074)



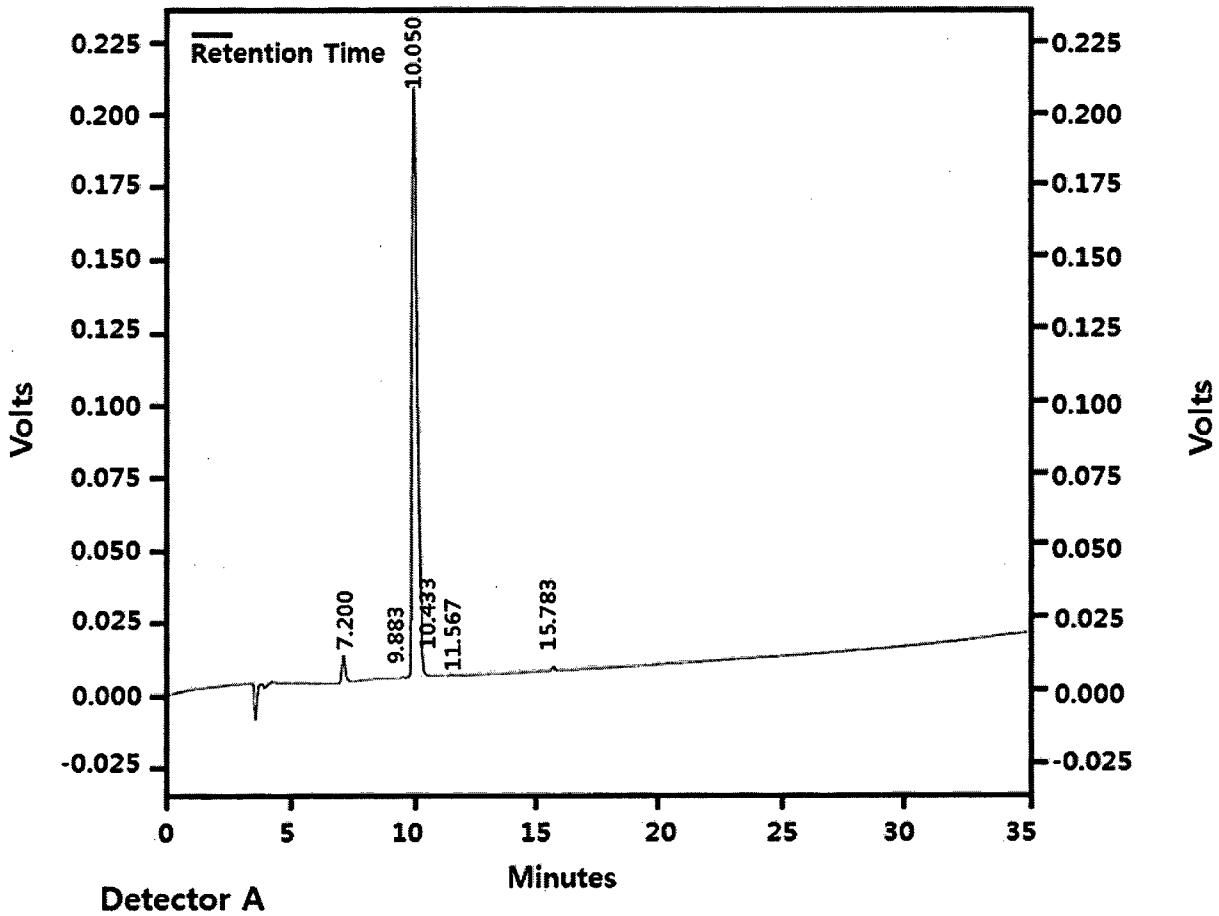
Detector A
(230nm)

Pk #	Retention Time	Area	Area %
1	15.383	1715	0.042
2	15.533	3991816	97.947
3	15.800	78057	1.915
4	17.417	1505	0.037
5	28.117	2389	0.059
Totals		4075482	100.000

도 68

Shimadzu CLASS-VP V6.14 SP1 20A_prep *Area % Report*

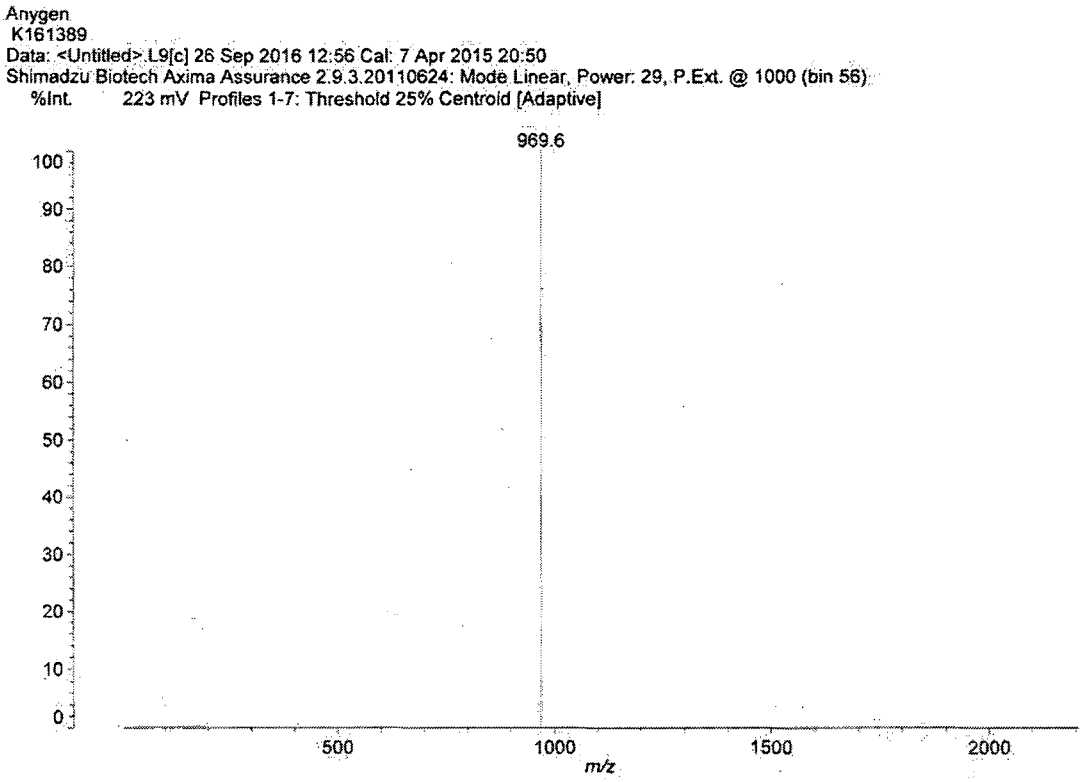
Sample ID : K180118 (YDE-075)



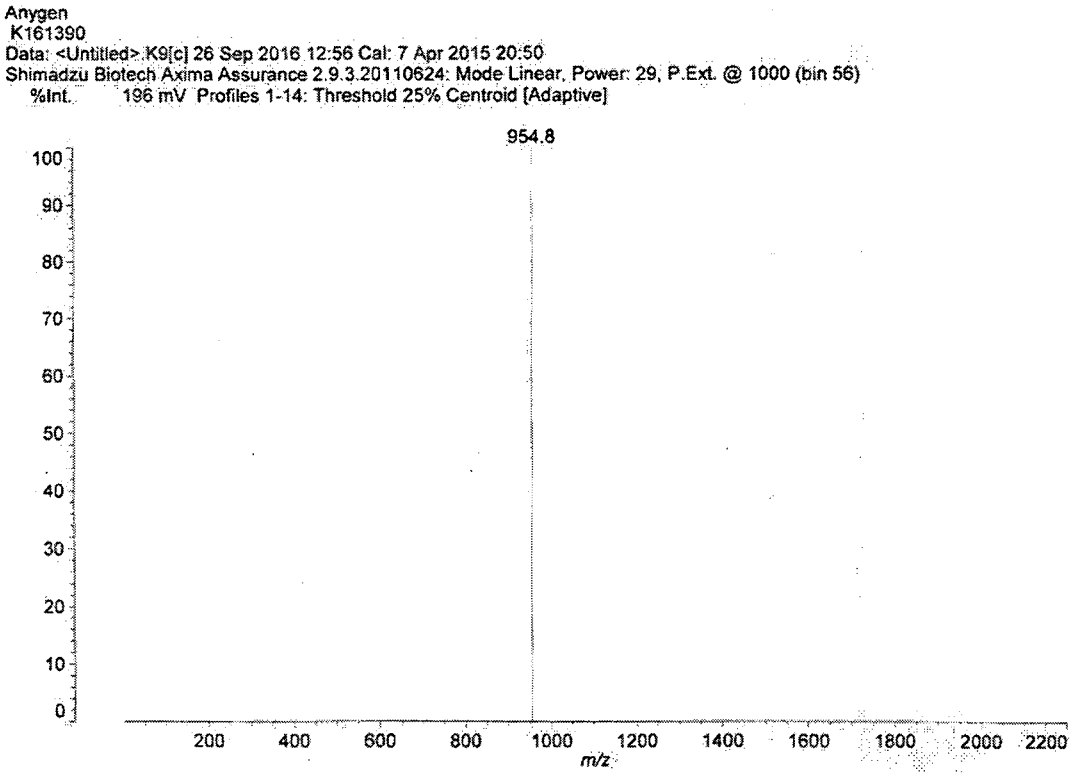
Detector A (230nm)

Pk #	Retention Time	Area	Area %
1	7.200	87289	2.762
2	9.883	1976	0.063
3	10.050	3045468	96.361
4	10.433	11869	0.376
5	11.567	3797	0.120
6	15.783	10067	0.319
Totals		3160466	100.000

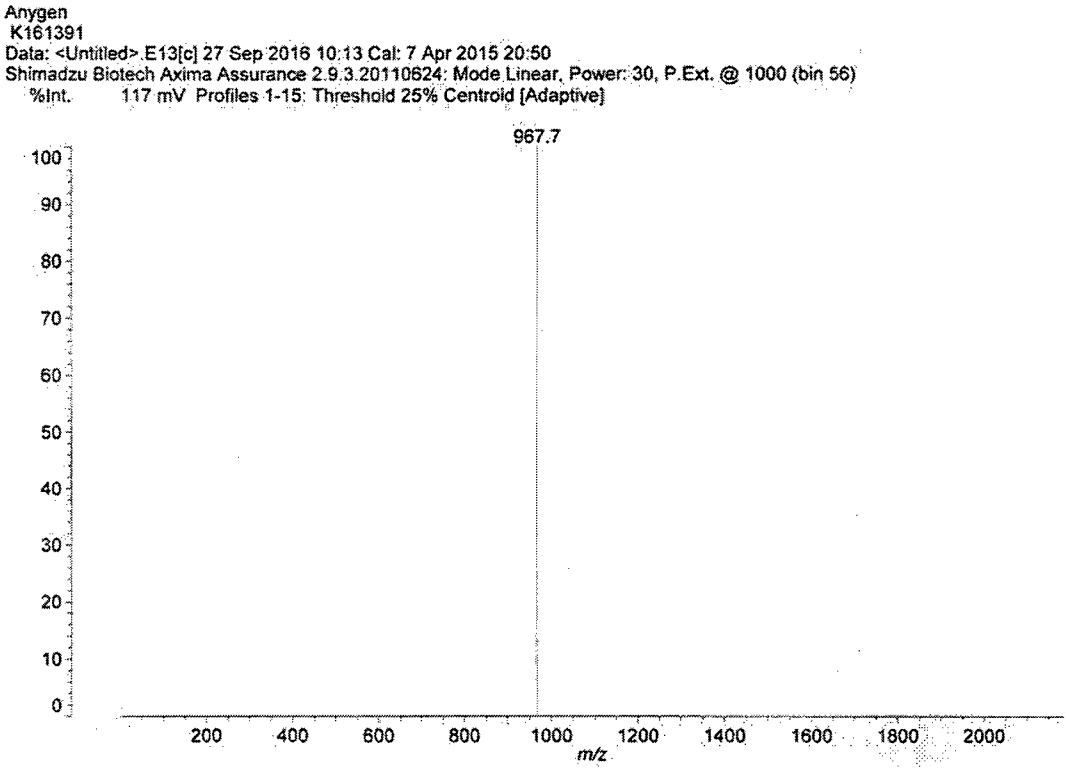
도 69


Anygen
K161389
Data: <Untitled> L9[c] 26 Sep 2016 12:56 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 29, P.Ext. @ 1000 (bin 56)
%Int. 223 mV Profiles 1-7: Threshold 25% Centroid [Adaptive]
969.6
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

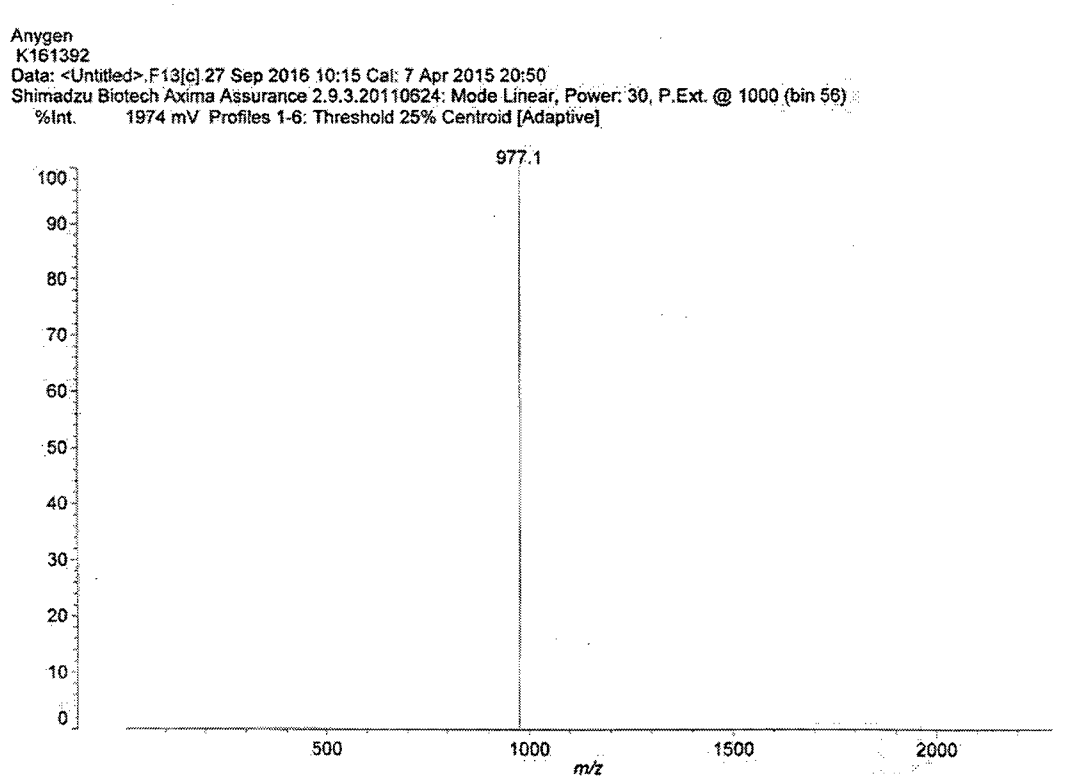
도 70


Anygen
K161390
Data: <Untitled> K9[c] 26 Sep 2016 12:56 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 29, P.Ext. @ 1000 (bin 56)
%Int. 196 mV Profiles 1-14: Threshold 25% Centroid [Adaptive]
954.8
100
90
80
70
60
50
40
30
20
10
0
200
400
600
800
1000
1200
1400
1600
1800
2000
2200
m/z

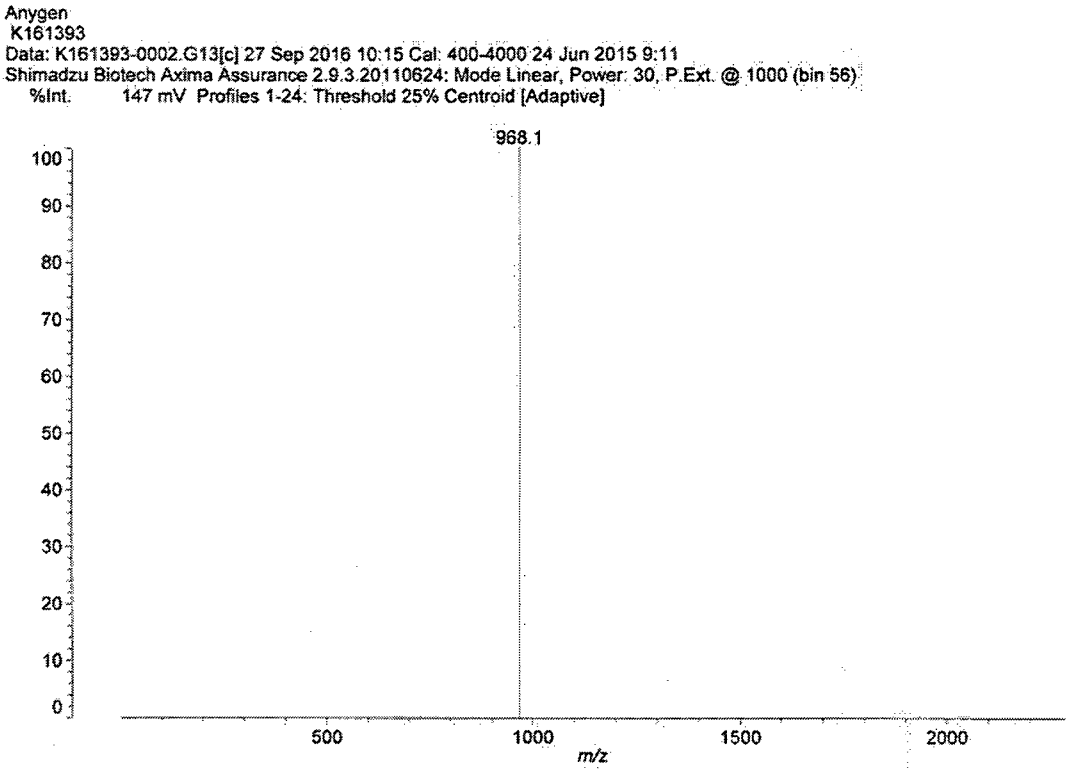
도 71


Anygen
K161391
Data: <Untitled>.E13[c] 27 Sep 2016 10:13 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 30, P.Ext. @ 1000 (bin 56)
%Int. 117 mV Profiles 1-15: Threshold 25% Centroid [Adaptive]
967.7
100
90
80
70
60
50
40
30
20
10
0
200
400
600
800
1000
1200
1400
1600
1800
2000
m/z

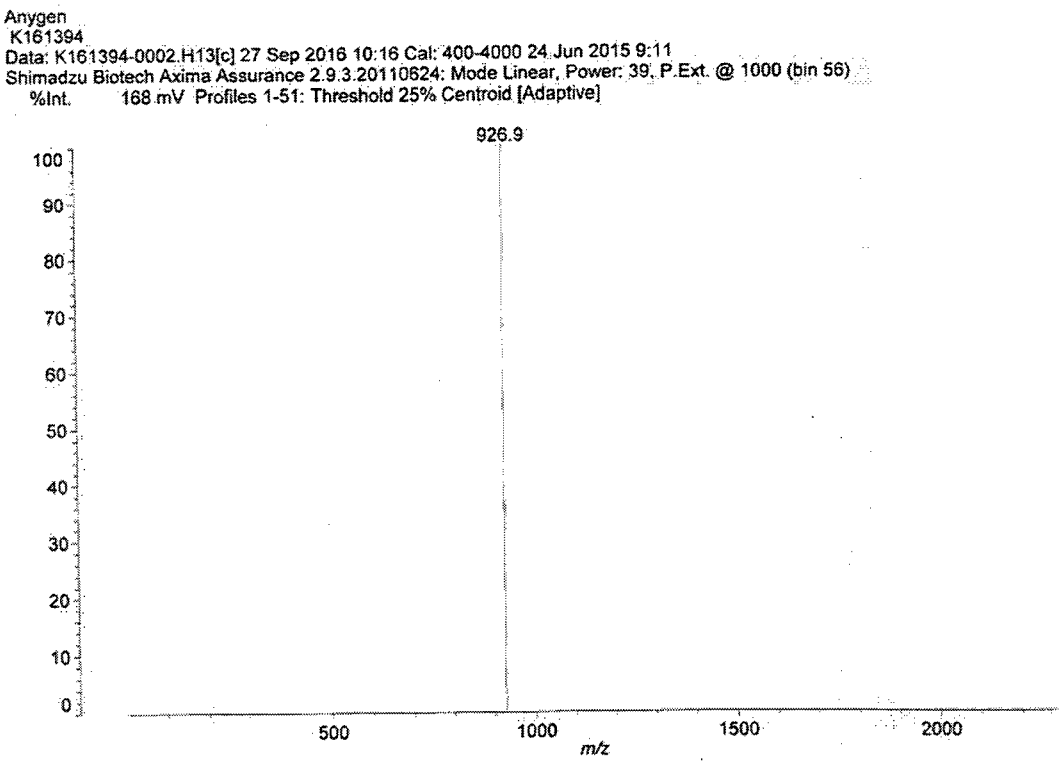
도 72


Anygen
K161392
Data: <Untitled>.F13[c] 27 Sep 2016 10:15 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 30, P.Ext. @ 1000 (bin 56)
%Int. 1974 mV Profiles 1-6: Threshold 25% Centroid [Adaptive]
977.1
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

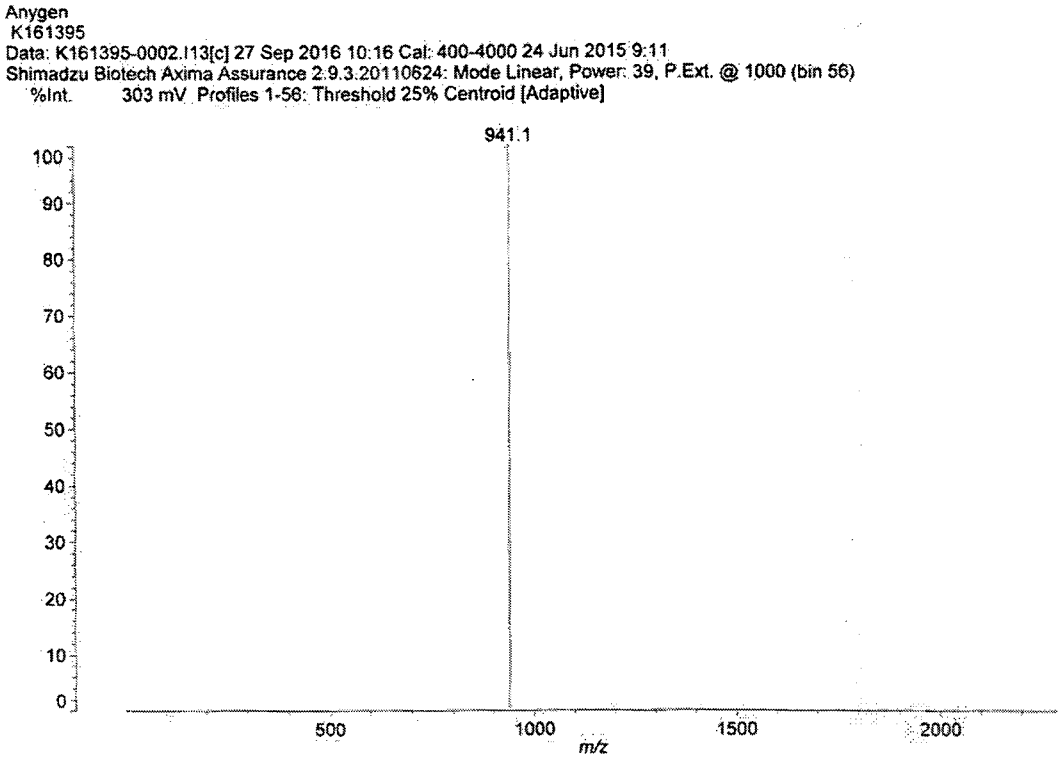
도 73


Anygen
K161393
Data: K161393-0002.G13[c] 27 Sep 2016 10:15 Cal: 400-4000 24 Jun 2015 9:11
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 30, P.Ext. @ 1000 (bin 56)
%Int. 147 mV Profiles 1-24: Threshold 25% Centroid [Adaptive]
968.1
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

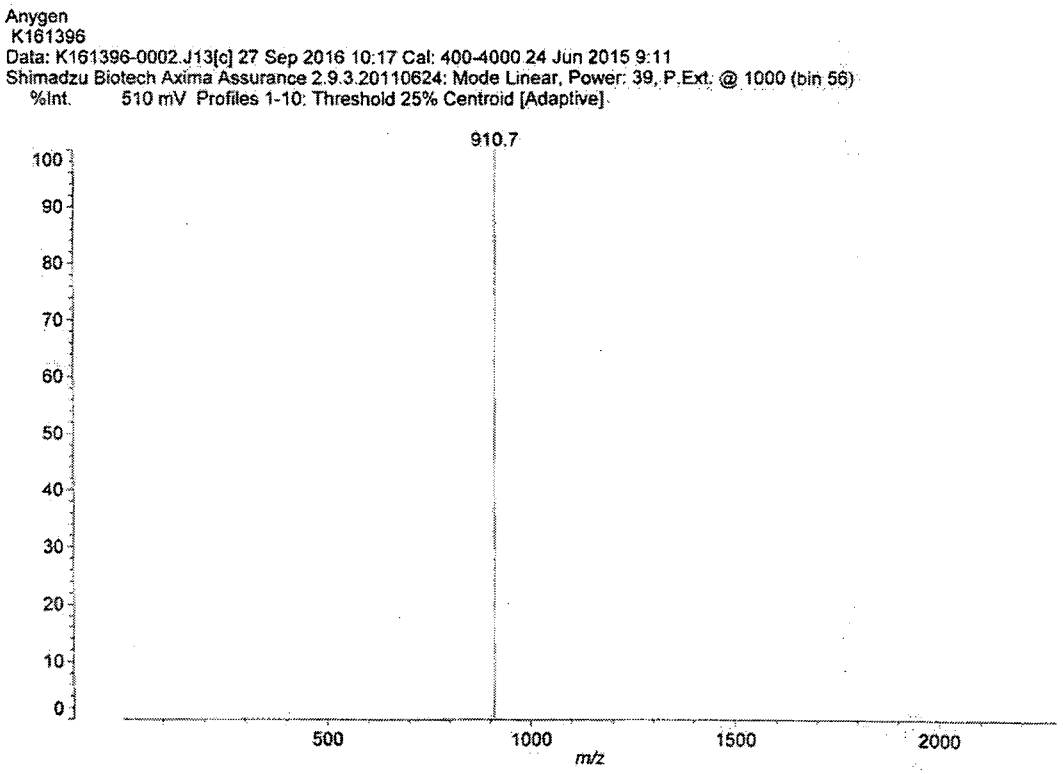
도 74


Anygen
K161394
Data: K161394-0002.H13[c] 27 Sep 2016 10:16 Cal: 400-4000 24 Jun 2015 9:11
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 39, P.Ext. @ 1000 (bin 56)
%Int. 168 mV Profiles 1-51: Threshold 25% Centroid [Adaptive]
926.9
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

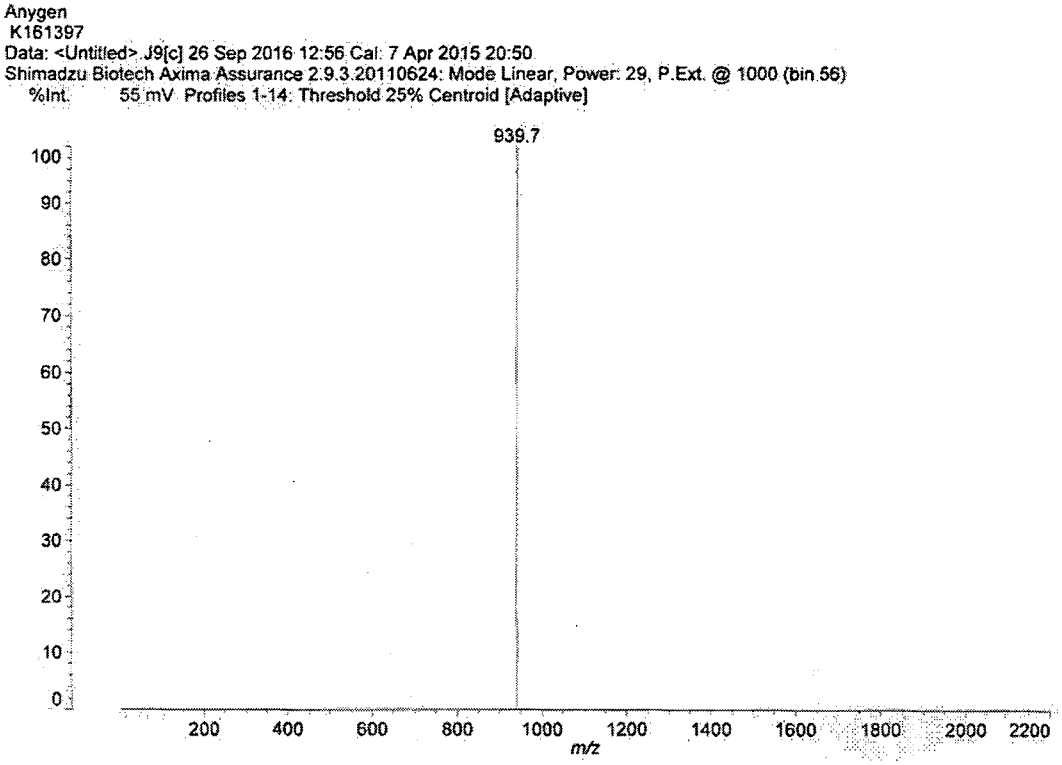
도 75


Anygen
K161395
Data: K161395-0002.I13[c] 27 Sep 2016 10:16 Cal: 400-4000 24 Jun 2015 9:11
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 39, P.Ext. @ 1000 (bin 56)
%Int. 303 mV Profiles 1-56: Threshold 25% Centroid [Adaptive]
941.1
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

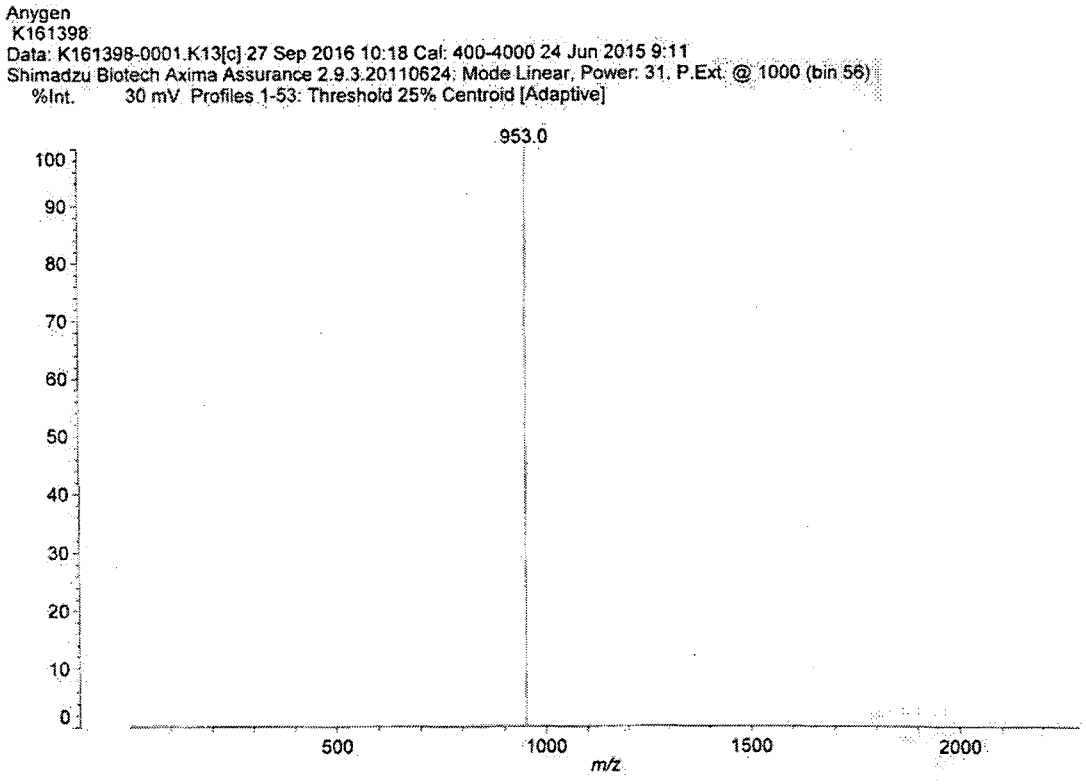
도 76


Anygen
K161396
Data: K161396-0002.J13[c] 27 Sep 2016 10:17 Cal: 400-4000 24 Jun 2015 9:11
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 39, P.Ext. @ 1000 (bin 56)
%Int. 510 mV Profiles 1-10: Threshold 25% Centroid [Adaptive]
910.7
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

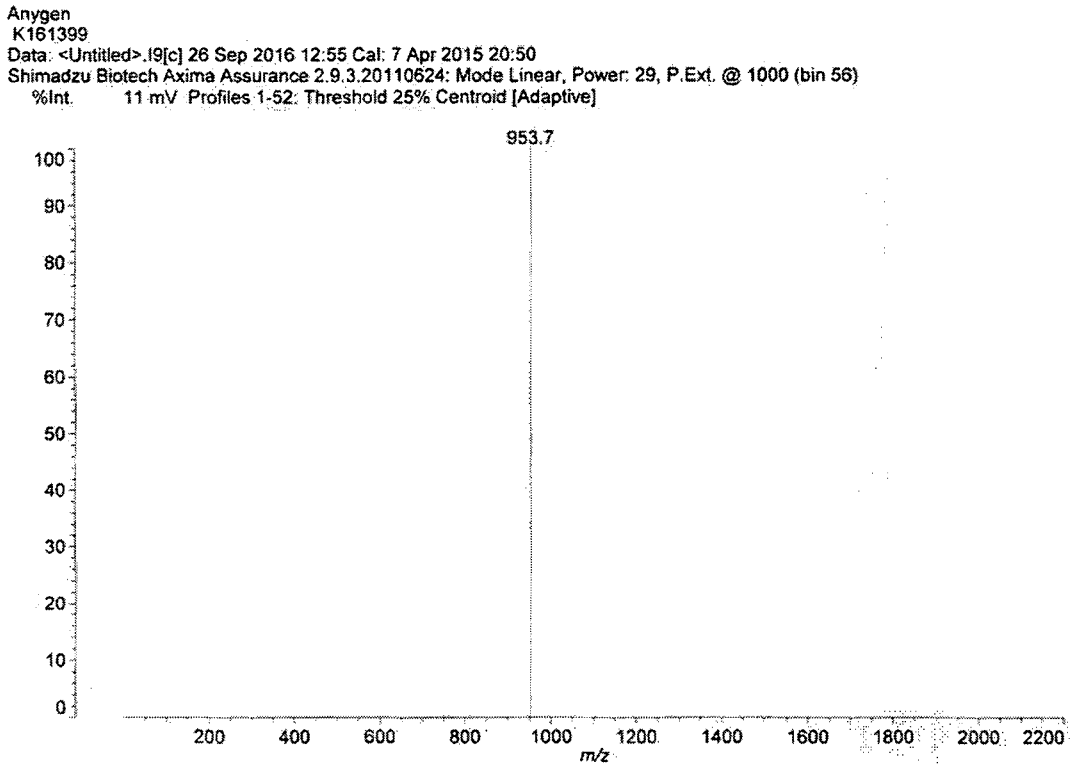
도 77


Anygen
K161397
Data: <Untitled> J9[c] 26 Sep 2016 12:56 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 29, P.Ext. @ 1000 (bin 56)
%Int. 55 mV Profiles 1-14: Threshold 25% Centroid [Adaptive]
939.7
100
90
80
70
60
50
40
30
20
10
0
200
400
600
800
1000
1200
1400
1600
1800
2000
2200
m/z

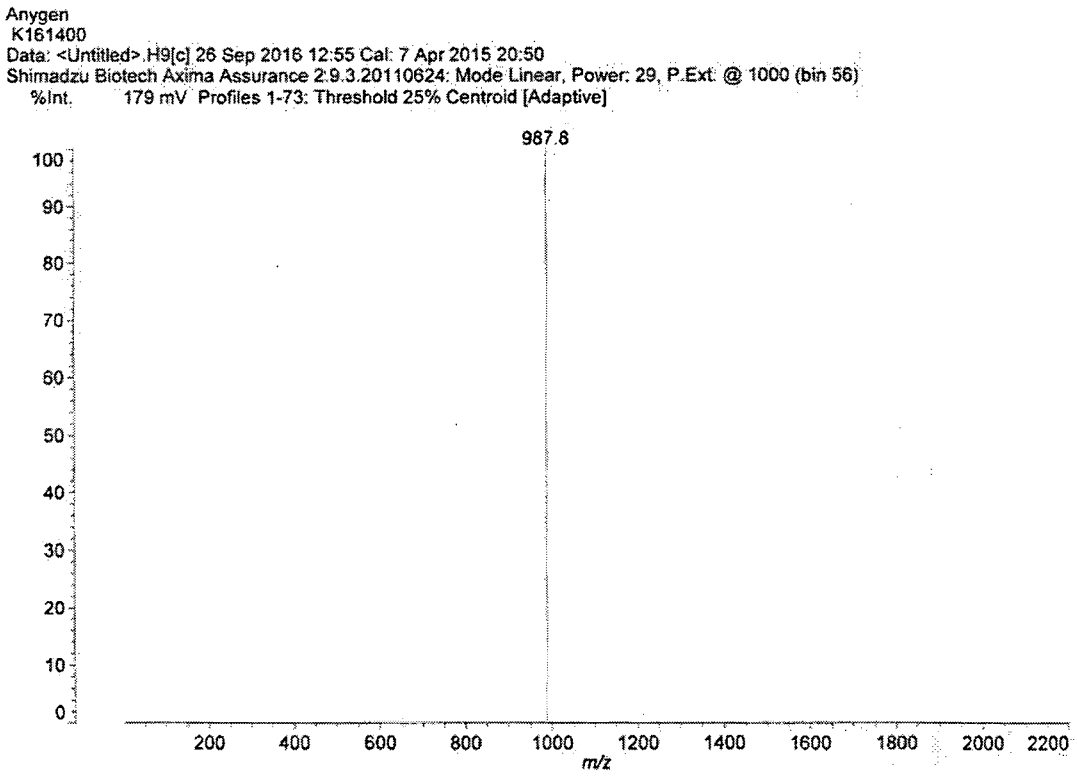
도 78


Anygen
K161398
Data: K161398-0001.K13[c] 27 Sep 2016 10:18 Cal: 400-4000 24 Jun 2015 9:11
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 31, P.Ext. @ 1000 (bin 56)
%Int. 30 mV Profiles 1-53: Threshold 25% Centroid [Adaptive]
953.0
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

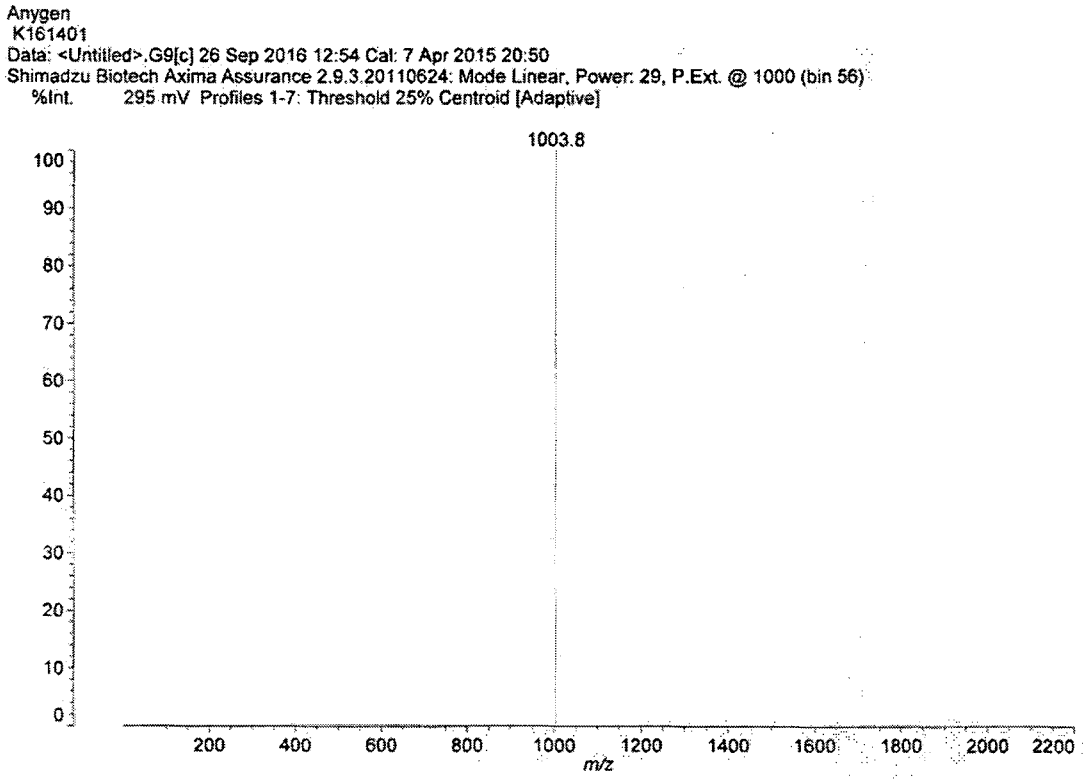
도 79


Anygen
K161399
Data: <Untitled>.I9[c] 26 Sep 2016 12:55 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 29, P.Ext. @ 1000 (bin 56)
%Int. 11 mV Profiles 1-52: Threshold 25% Centroid [Adaptive]
953.7
100
90
80
70
60
50
40
30
20
10
0
200
400
600
800
1000
1200
1400
1600
1800
2000
2200
m/z

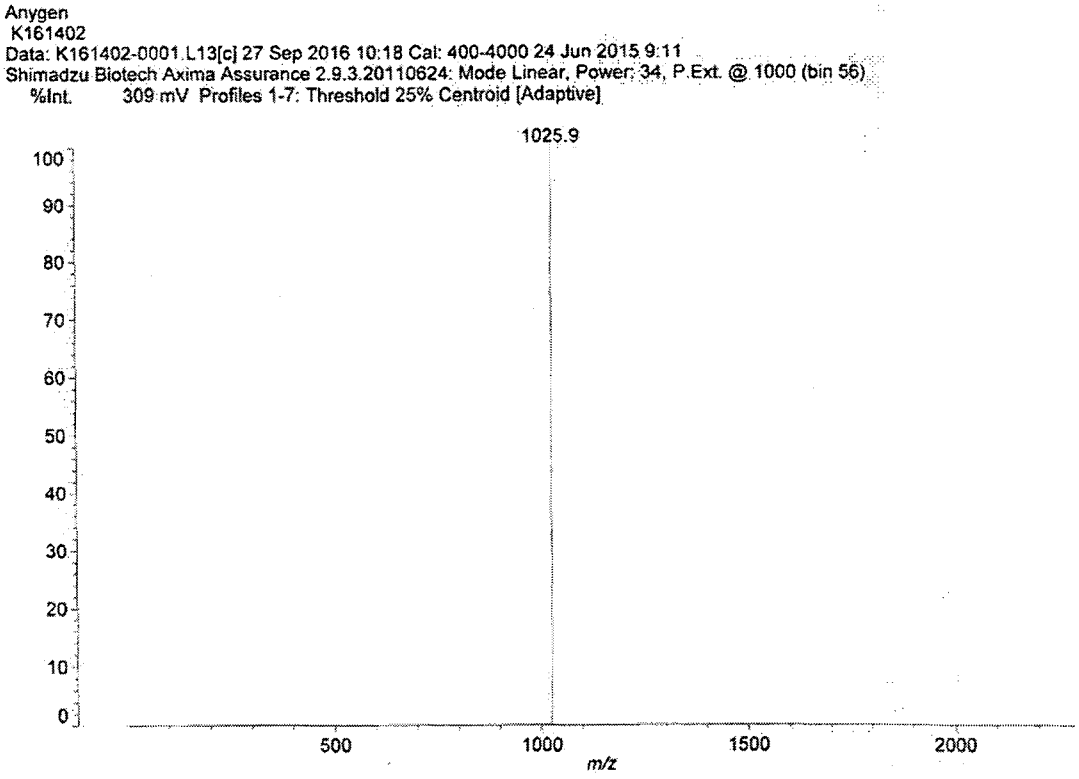
도 80


Anygen
K161400
Data: <Untitled>.I9[c] 26 Sep 2016 12:55 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 29, P.Ext. @ 1000 (bin 56)
%Int. 179 mV Profiles 1-73: Threshold 25% Centroid [Adaptive]
987.8
100
90
80
70
60
50
40
30
20
10
0
200
400
600
800
1000
1200
1400
1600
1800
2000
2200
m/z

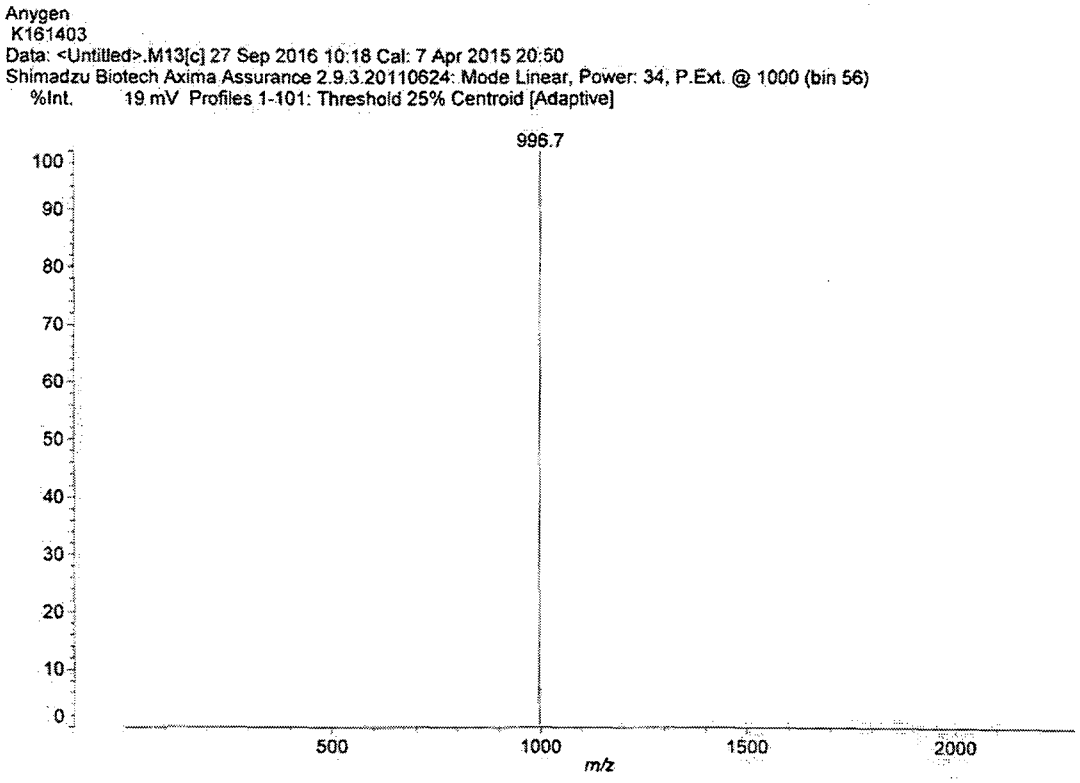
도 81


Anygen
K161401
Data: <Untitled>.G9[c] 26 Sep 2016 12:54 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 29, P.Ext. @ 1000 (bin 56)
%Int. 295 mV Profiles 1-7: Threshold 25% Centroid [Adaptive]
1003.8
100
90
80
70
60
50
40
30
20
10
0
200
400
600
800
1000
1200
1400
1600
1800
2000
2200
m/z

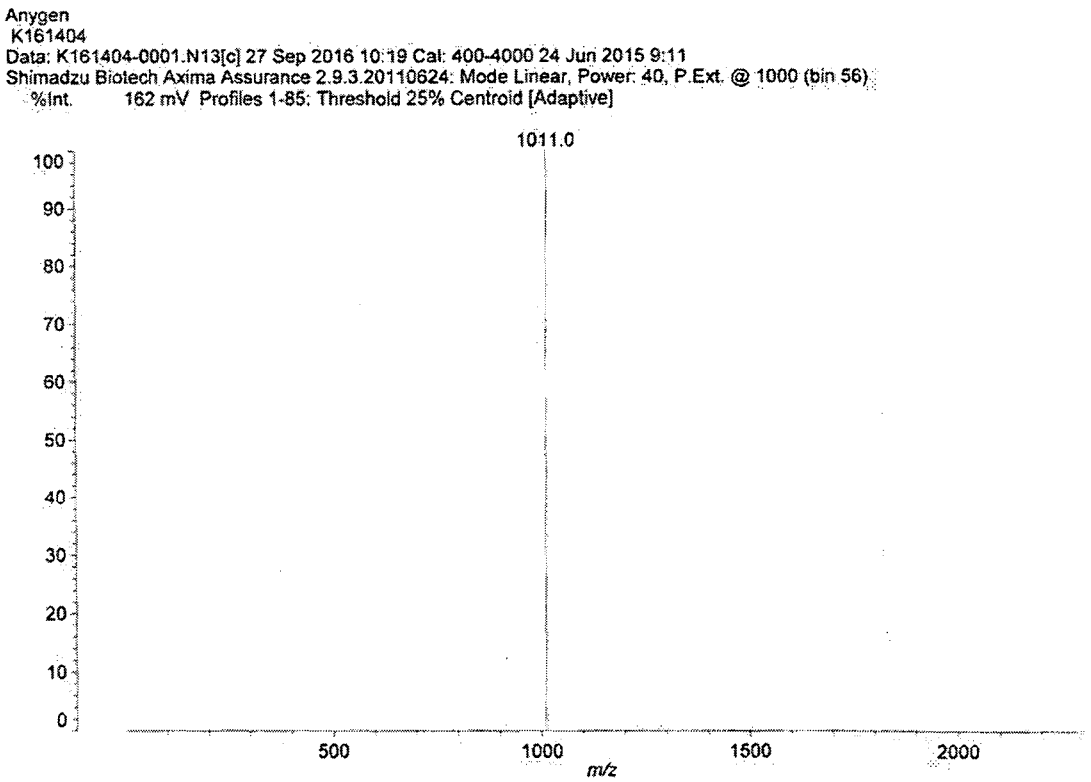
도 82


Anygen
K161402
Data: K161402-0001.L13[c] 27 Sep 2016 10:18 Cal: 400-4000 24 Jun 2015 9:11
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 34, P.Ext. @ 1000 (bin 56)
%Int. 309 mV Profiles 1-7: Threshold 25% Centroid [Adaptive]
1025.9
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

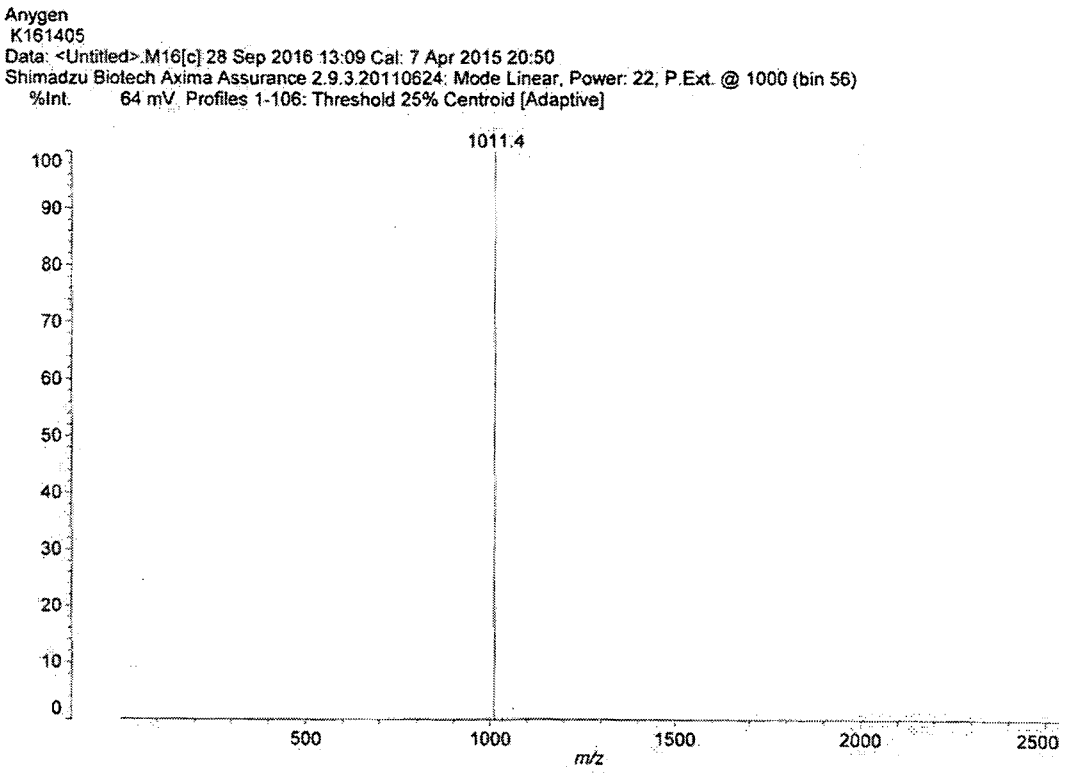
도 83


Anygen
K161403
Data: <Untitled>.M13[c] 27 Sep 2016 10:18 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 34, P.Ext. @ 1000 (bin 56)
%Int. 19 mV Profiles 1-101: Threshold 25% Centroid [Adaptive]
996.7
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

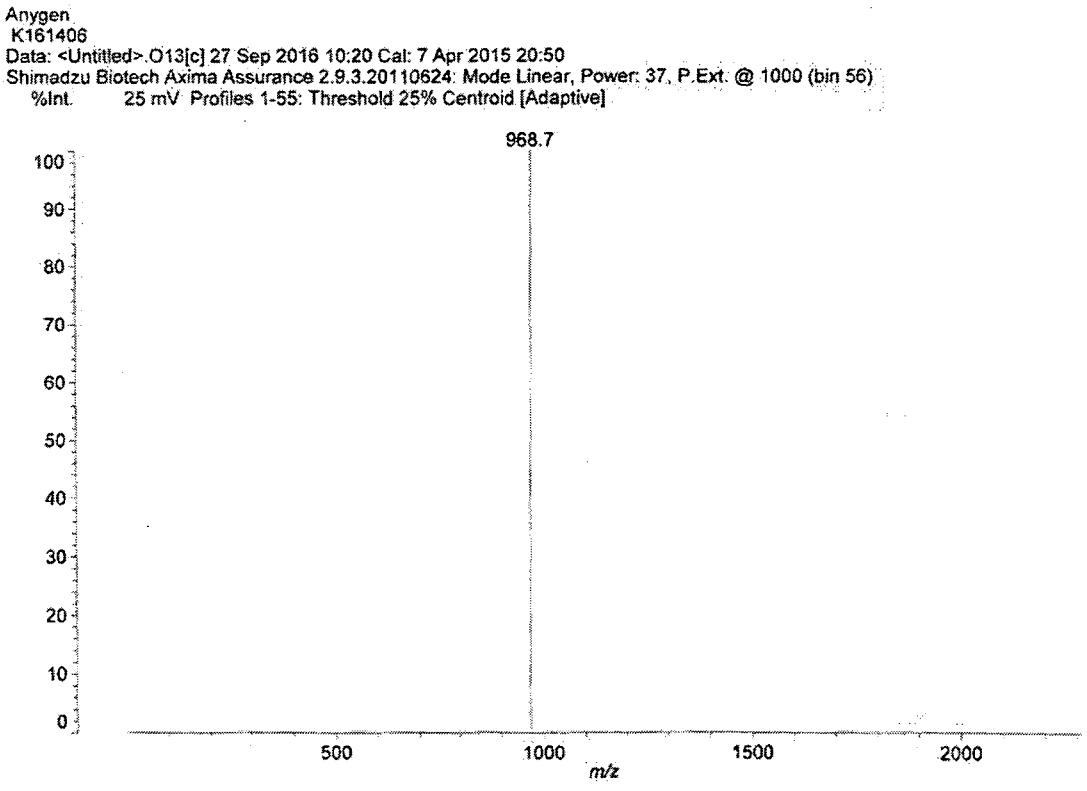
도 84


Anygen
K161404
Data: K161404-0001.N13[c] 27 Sep 2016 10:19 Cal: 400-4000 24 Jun 2015 9:11
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 40, P.Ext. @ 1000 (bin 56)
%Int. 162 mV Profiles 1-85: Threshold 25% Centroid [Adaptive]
1011.0
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

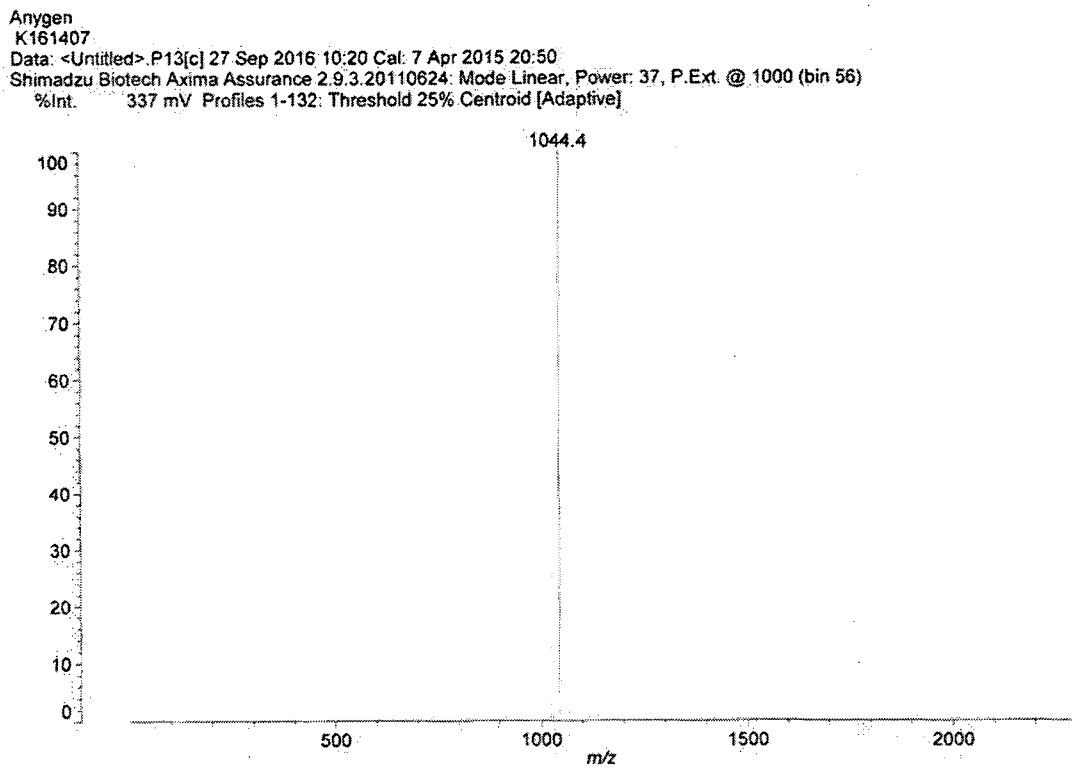
도 85


Anygen
K161405
Data: <Untitled>.M16[c] 28 Sep 2016 13:09 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 22, P.Ext. @ 1000 (bin 56)
%Int. 64 mV Profiles 1-106: Threshold 25% Centroid [Adaptive]
1011.4
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
2500
m/z

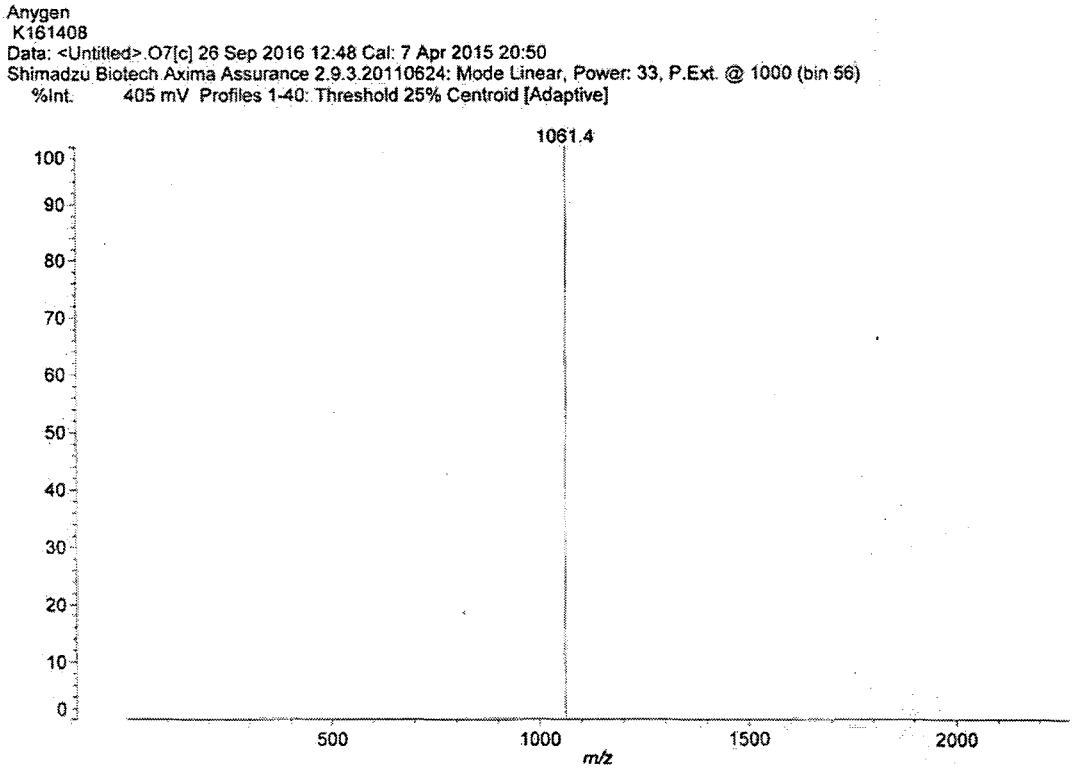
도 86


Anygen
K161406
Data: <Untitled>.O13[c] 27 Sep 2016 10:20 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 37, P.Ext. @ 1000 (bin 56)
%Int. 25 mV Profiles 1-55: Threshold 25% Centroid [Adaptive]
968.7
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

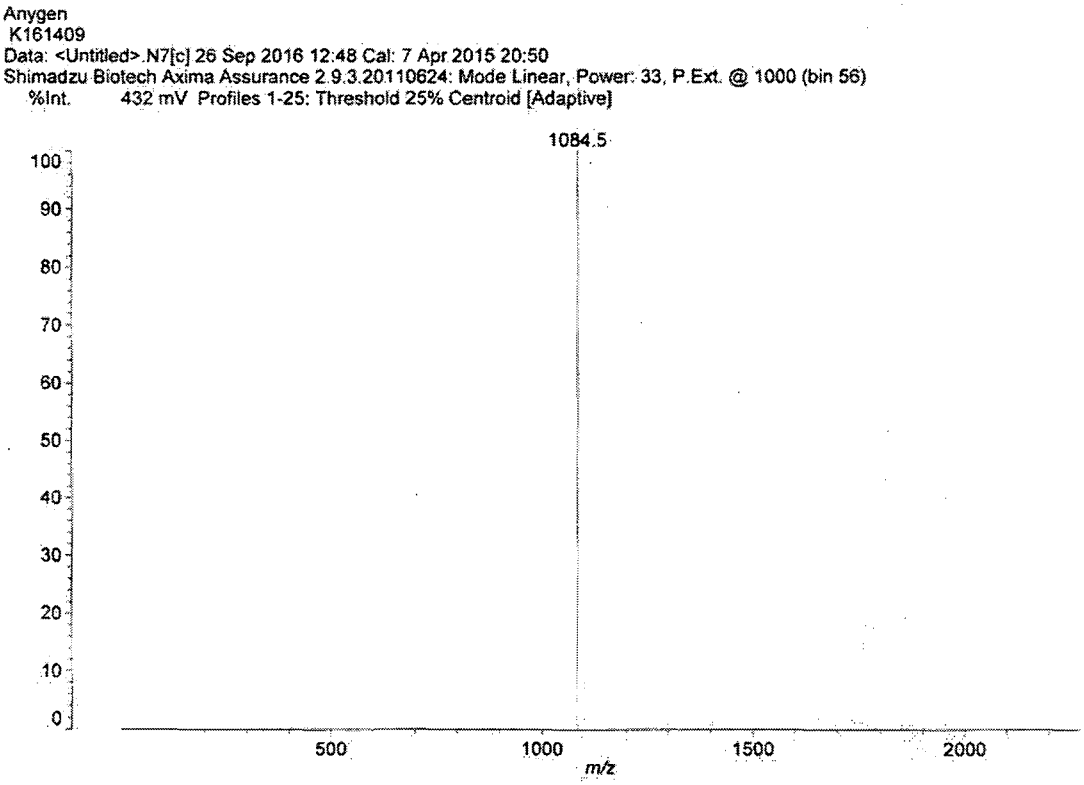
도 87


Anygen
K161407
Data: <Untitled>.P13[c] 27 Sep 2016 10:20 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 37, P.Ext. @ 1000 (bin 56)
%Int. 337 mV Profiles 1-132: Threshold 25% Centroid [Adaptive]
1044.4
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

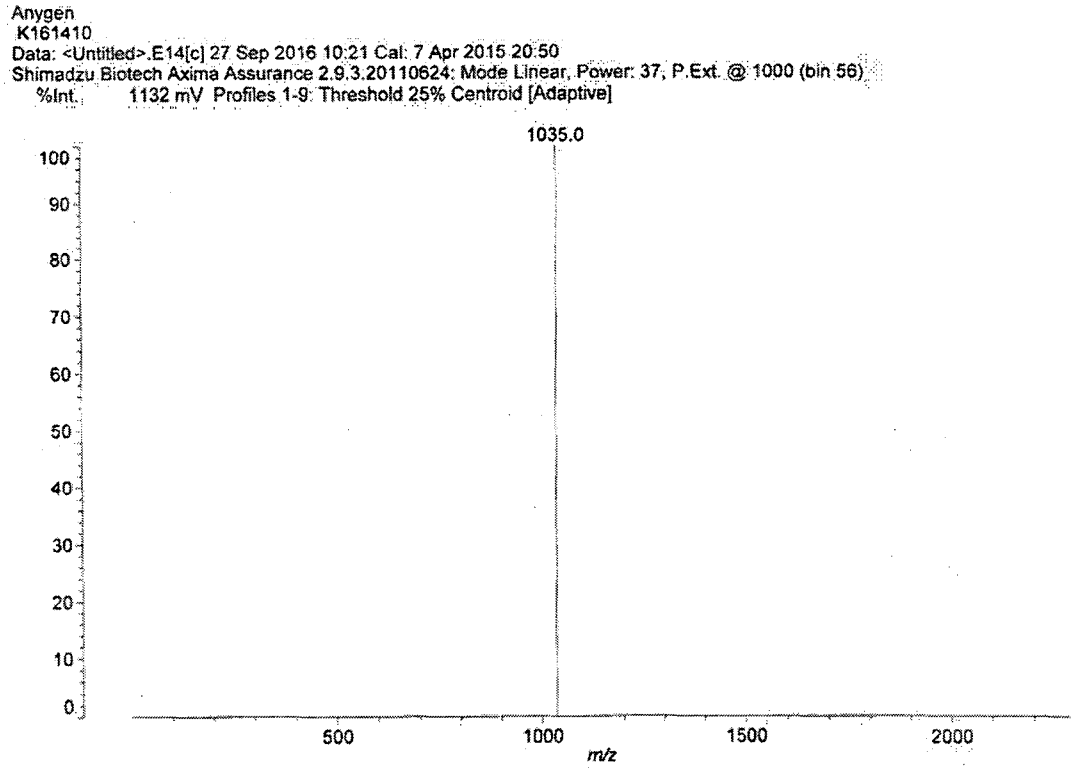
도 88


Anygen
K161408
Data: <Untitled>.O7[c] 26 Sep 2016 12:48 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 33, P.Ext. @ 1000 (bin 56)
%Int. 405 mV Profiles 1-40: Threshold 25% Centroid [Adaptive]
1061.4
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

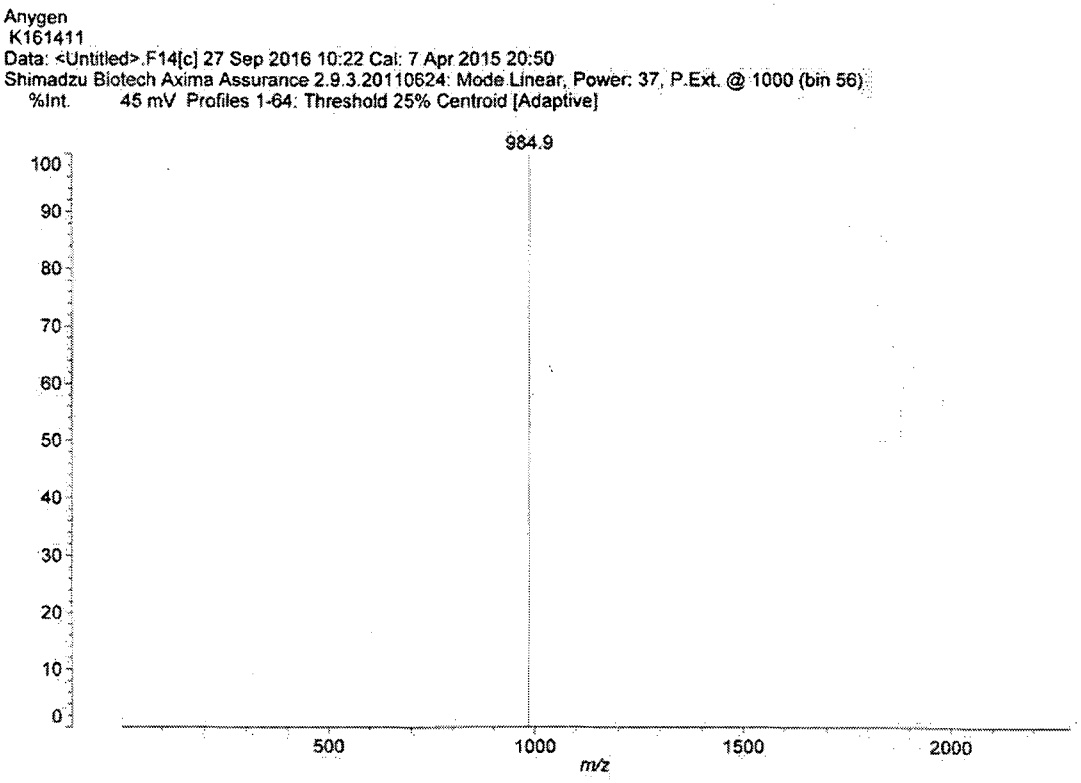
도 89


Anygen
K161409
Data: <Untitled>.N7[c] 26 Sep 2016 12:48 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 33, P.Ext. @ 1000 (bin 56)
%Int. 432 mV Profiles 1-25: Threshold 25% Centroid [Adaptive]
1084.5
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

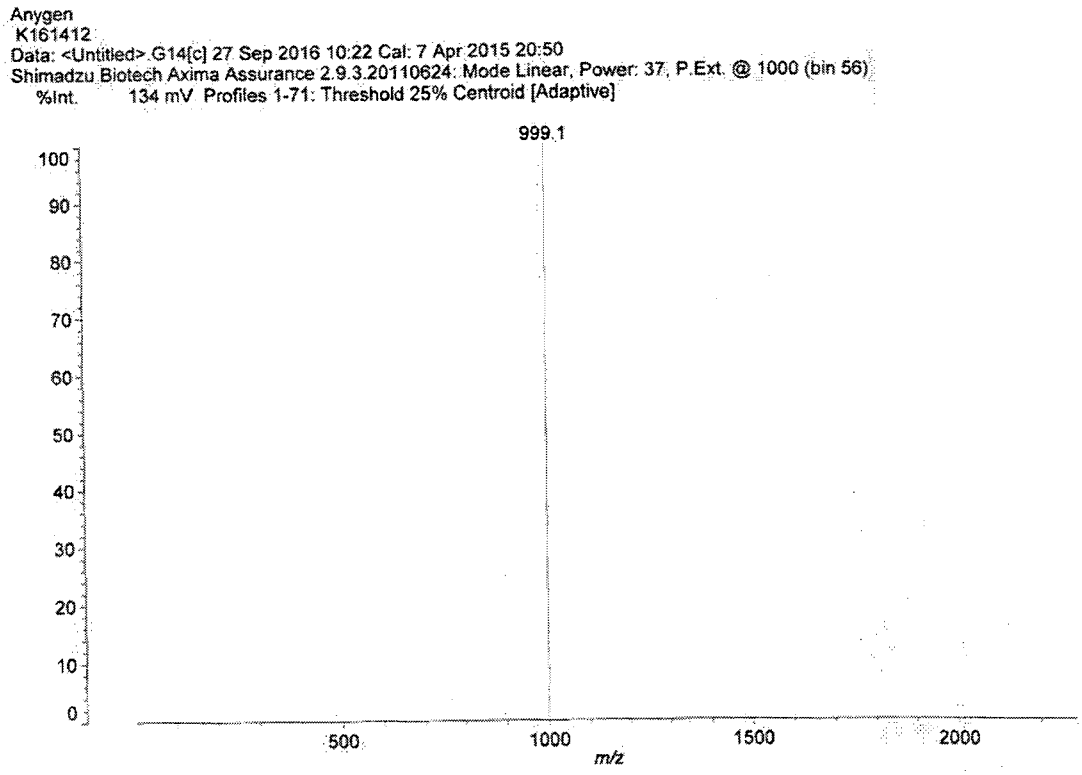
도 90


Anygen
K161410
Data: <Untitled>.E14[c] 27 Sep 2016 10:21 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 37, P.Ext. @ 1000 (bin 56)
%Int. 1132 mV Profiles 1-9: Threshold 25% Centroid [Adaptive]
1035.0
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

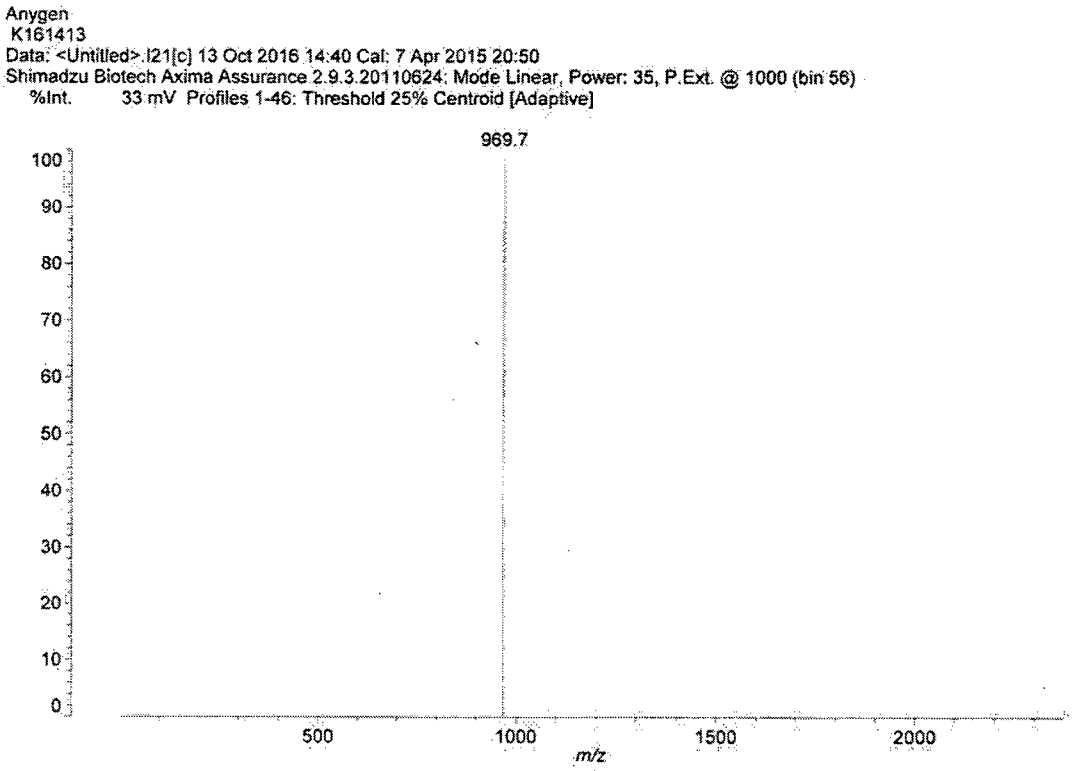
도 91


Anygen
K161411
Data: <Untitled>.F14[c] 27 Sep 2016 10:22 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 37, P.Ext. @ 1000 (bin 56)
%Int. 45 mV Profiles 1-64: Threshold 25% Centroid [Adaptive]
984.9
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

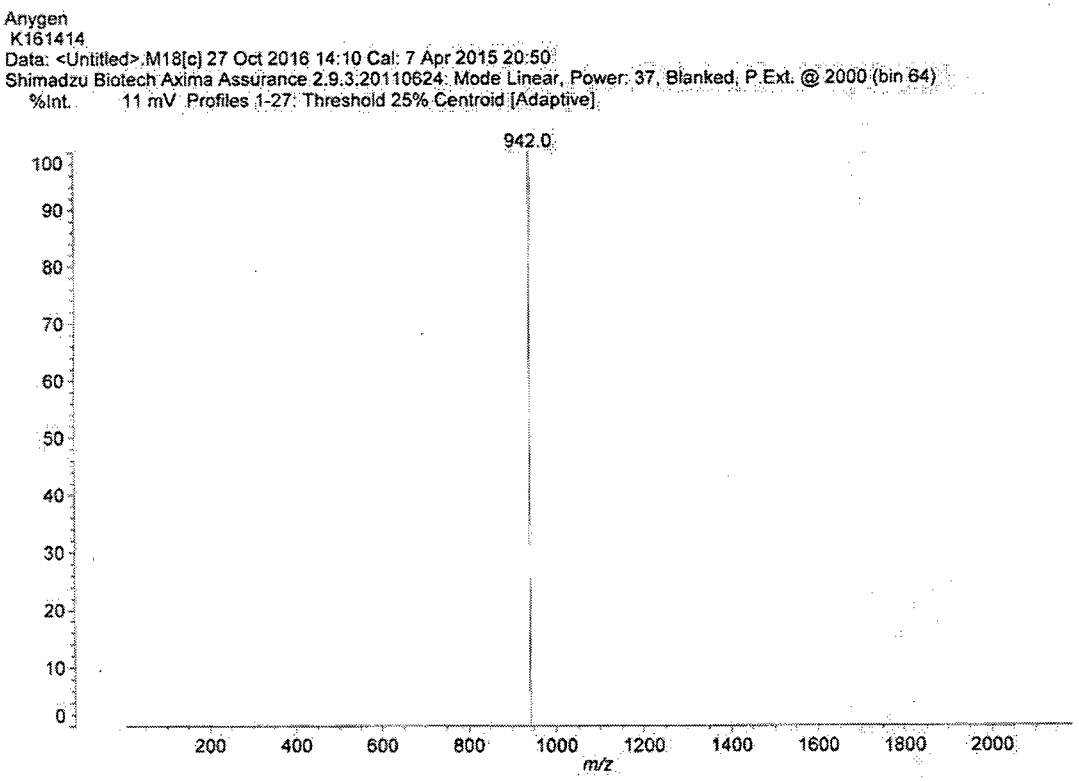
도 92


Anygen
K161412
Data: <Untitled>.G14[c] 27 Sep 2016 10:22 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 37, P.Ext. @ 1000 (bin 56)
%Int. 134 mV Profiles 1-71: Threshold 25% Centroid [Adaptive]
999.1
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

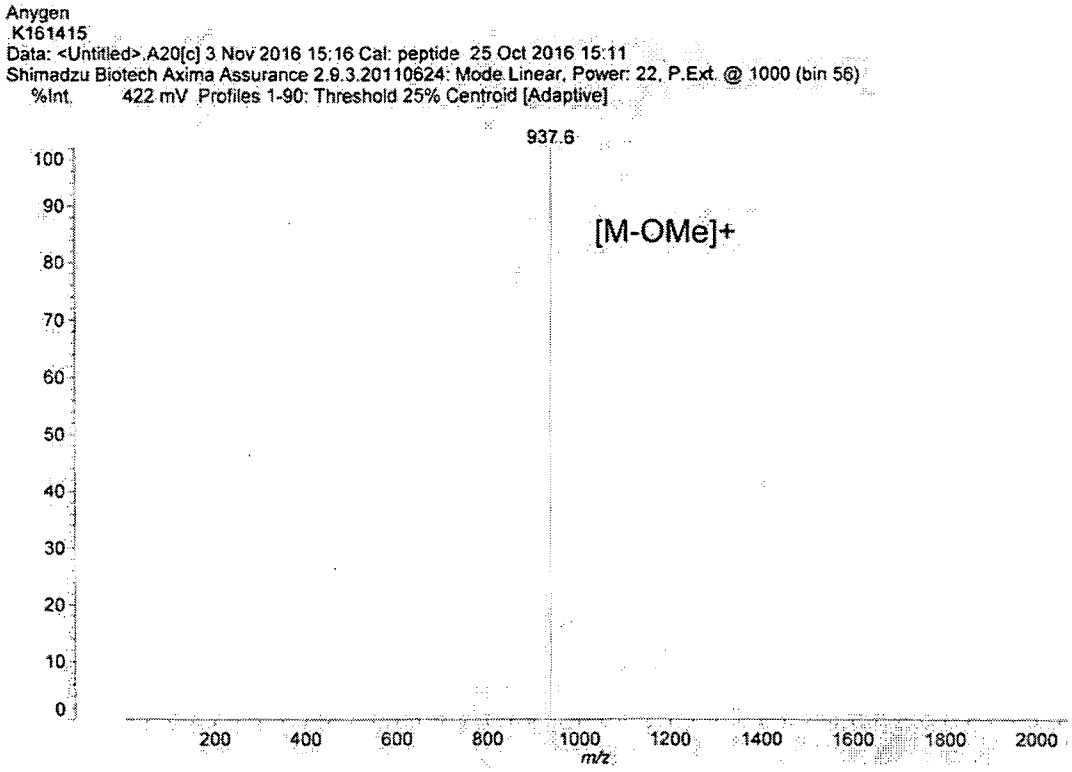
도 93


Anygen
K161413
Data: <Untitled>.I21[c] 13 Oct 2016 14:40 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 35, P.Ext. @ 1000 (bin 56)
%Int. 33 mV Profiles 1-46: Threshold 25% Centroid [Adaptive]
969.7
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

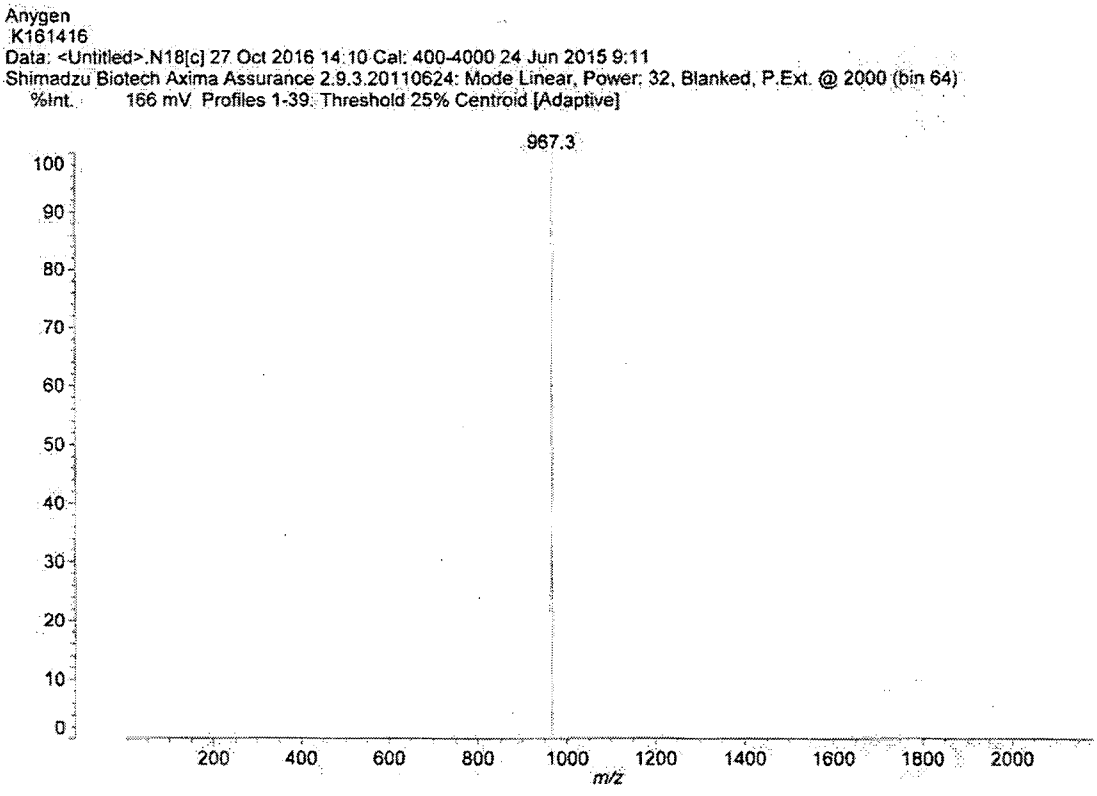
도 94


Anygen
K161414
Data: <Untitled>.M18[c] 27 Oct 2016 14:10 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 37, Blanked, P.Ext. @ 2000 (bin 64)
%Int. 11 mV Profiles 1-27: Threshold 25% Centroid [Adaptive]
942.0
100
90
80
70
60
50
40
30
20
10
0
200
400
600
800
1000
1200
1400
1600
1800
2000
m/z

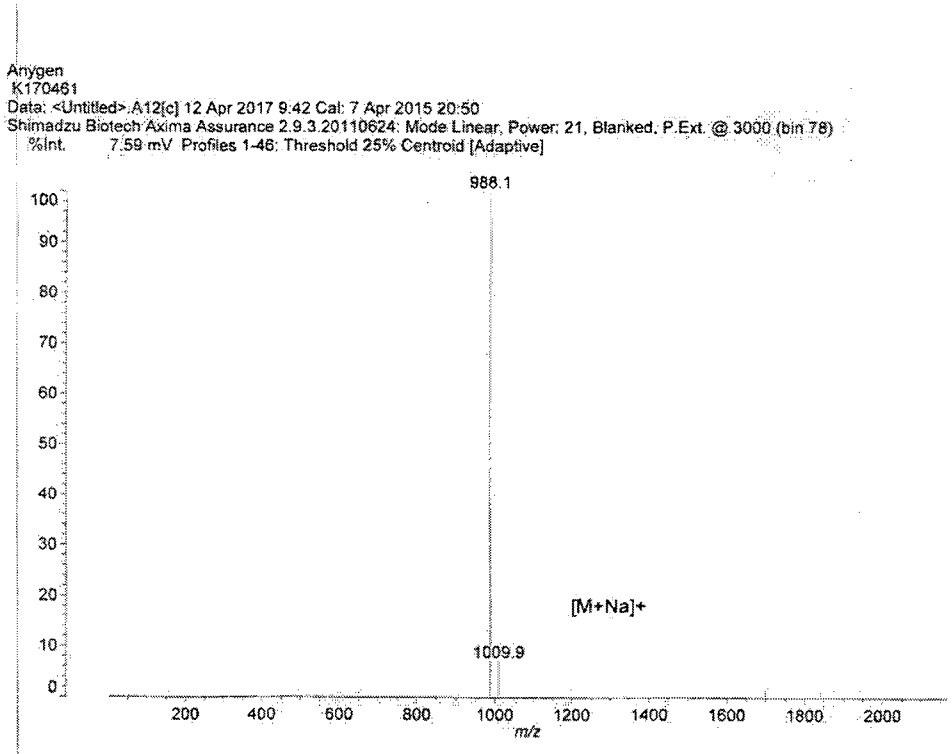
도 95


Anygen
K161415
Data: <Untitled>.A20[c] 3 Nov 2016 15:16 Cal: peptide 25 Oct 2016 15:11
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 22, P.Ext. @ 1000 (bin 56)
%Int. 422 mV Profiles 1-90: Threshold 25% Centroid [Adaptive]
937.6
[M-OMe]+
100
90
80
70
60
50
40
30
20
10
0
200
400
600
800
1000
1200
1400
1600
1800
2000
m/z

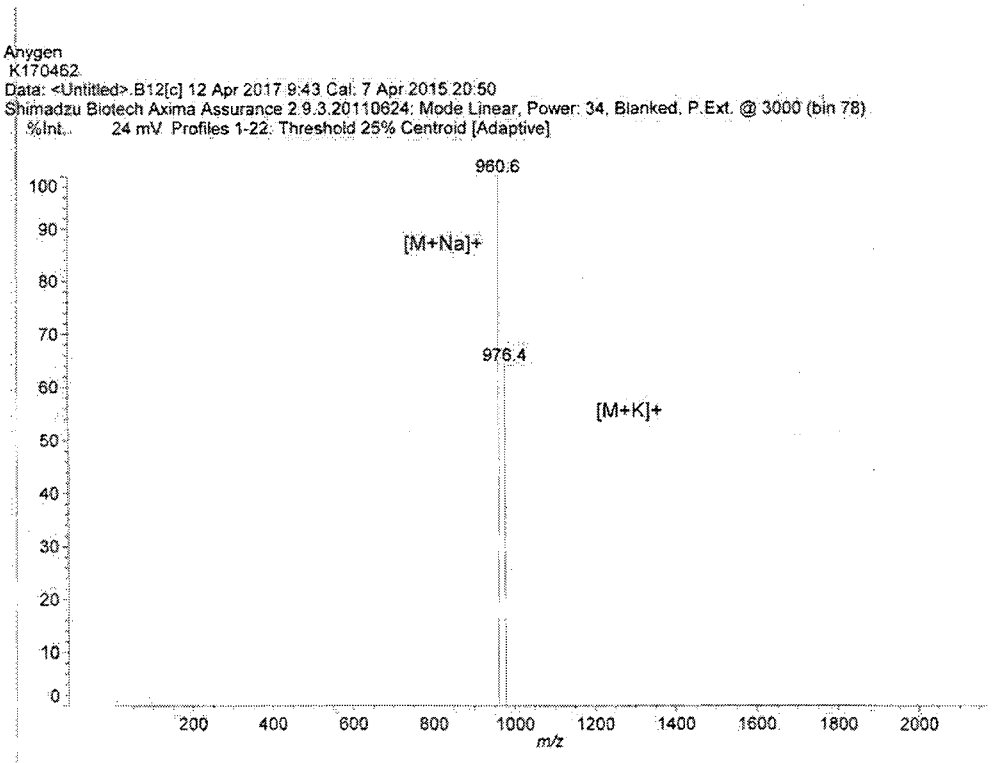
도 96


Anygen
K161416
Data: <Untitled>.N18[c] 27 Oct 2016 14:10 Cal: 400-4000 24 Jun 2015 9:11
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 32, Blanked, P.Ext. @ 2000 (bin 64)
%Int. 166 mV Profiles 1-39: Threshold 25% Centroid [Adaptive]
967.3
100
90
80
70
60
50
40
30
20
10
0
200
400
600
800
1000
1200
1400
1600
1800
2000
m/z

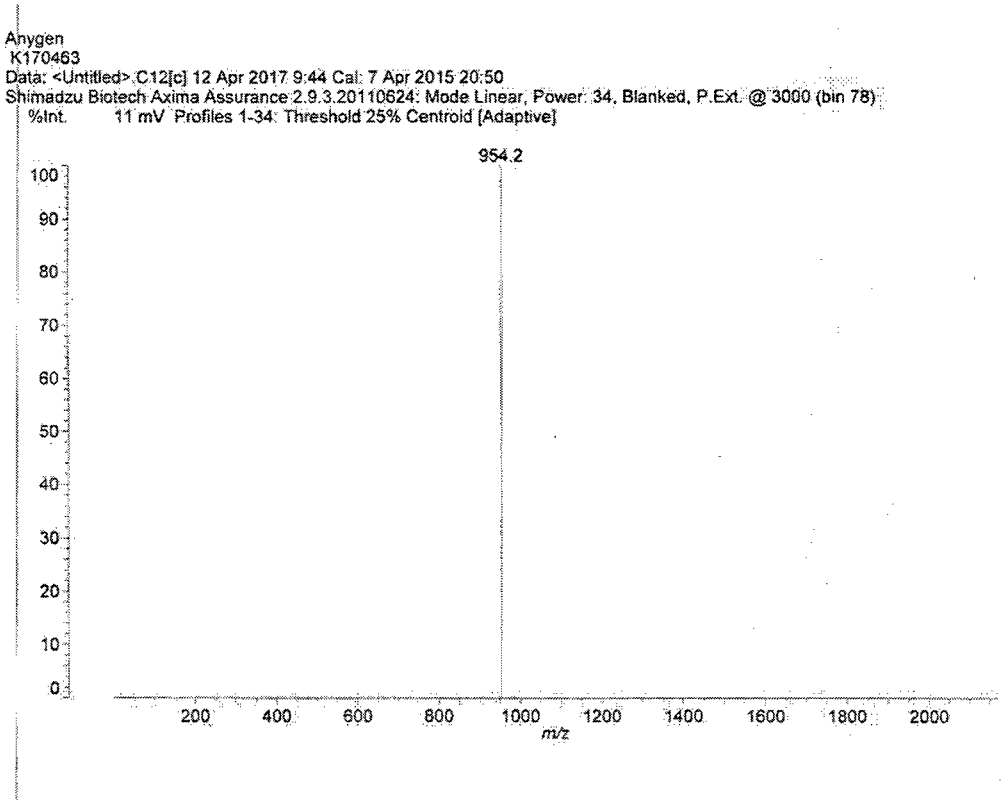
도 97


Anygen
K170461
Data: <Untitled>.A12[c] 12 Apr 2017 9:42 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 21, Blanked, P.Ext. @ 3000 (bin 78)
%Int. 7.59 mV Profiles 1-46: Threshold 25% Centroid [Adaptive]
988.1
[M+Na]+
1009.9
m/z

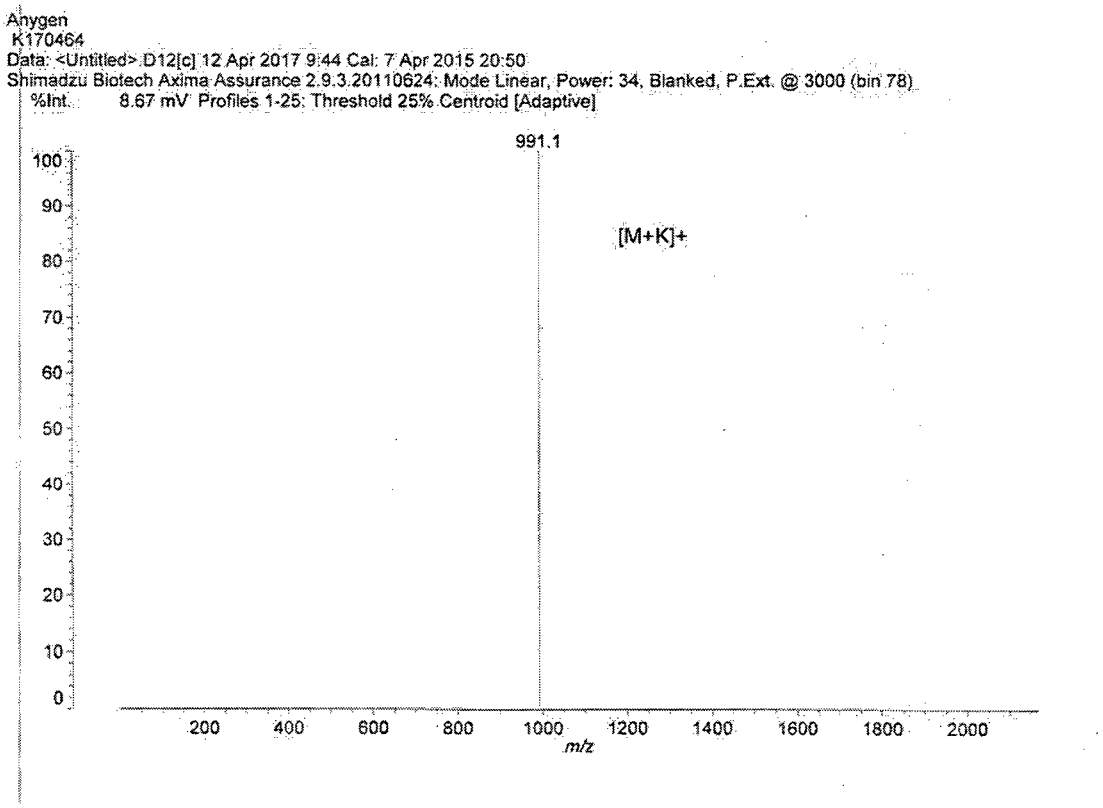
도 98


Anygen
K170462
Data: <Untitled>.B12[c] 12 Apr 2017 9:43 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 34, Blanked, P.Ext. @ 3000 (bin 78)
%Int. 24 mV Profiles 1-22: Threshold 25% Centroid [Adaptive]
960.6
[M+Na]+
976.4
[M+K]+
m/z

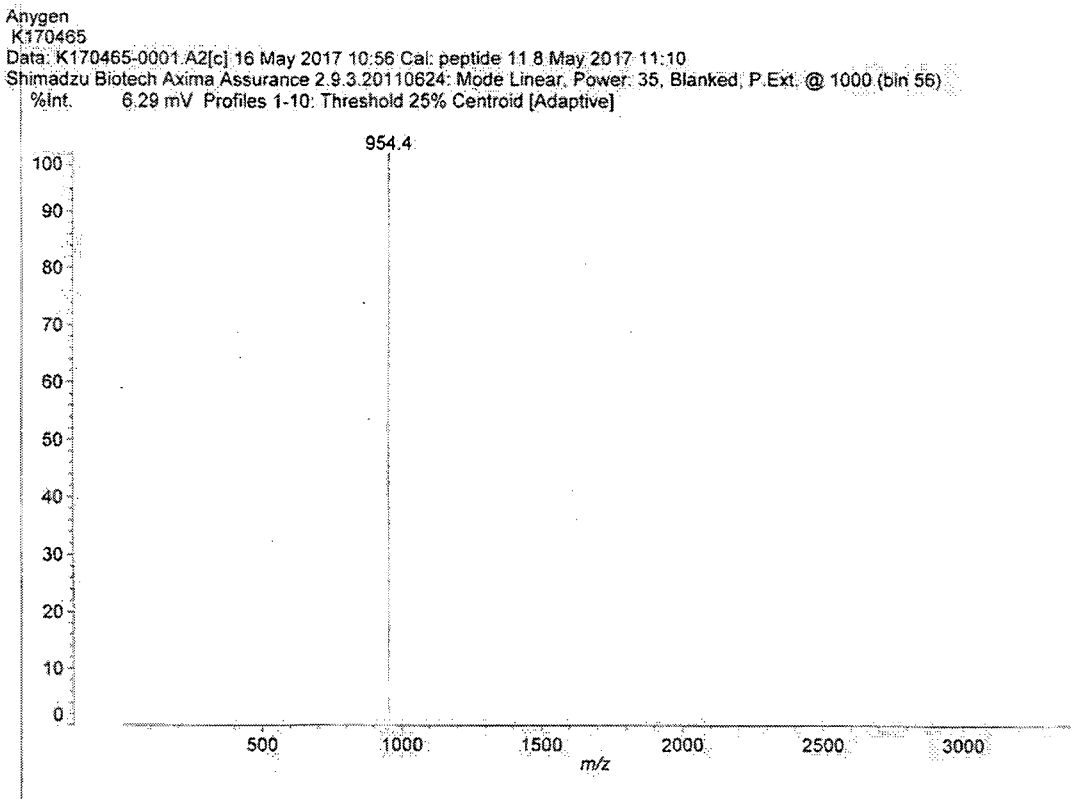
도 99


Anygen
K170463
Data: <Untitled> C12[c] 12 Apr 2017 9:44 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 34, Blanked, P.Ext. @ 3000 (bin 78)
%Int. 11 mV Profiles 1-34: Threshold 25% Centroid [Adaptive]
954.2
100
90
80
70
60
50
40
30
20
10
0
200
400
600
800
1000
1200
1400
1600
1800
2000
m/z

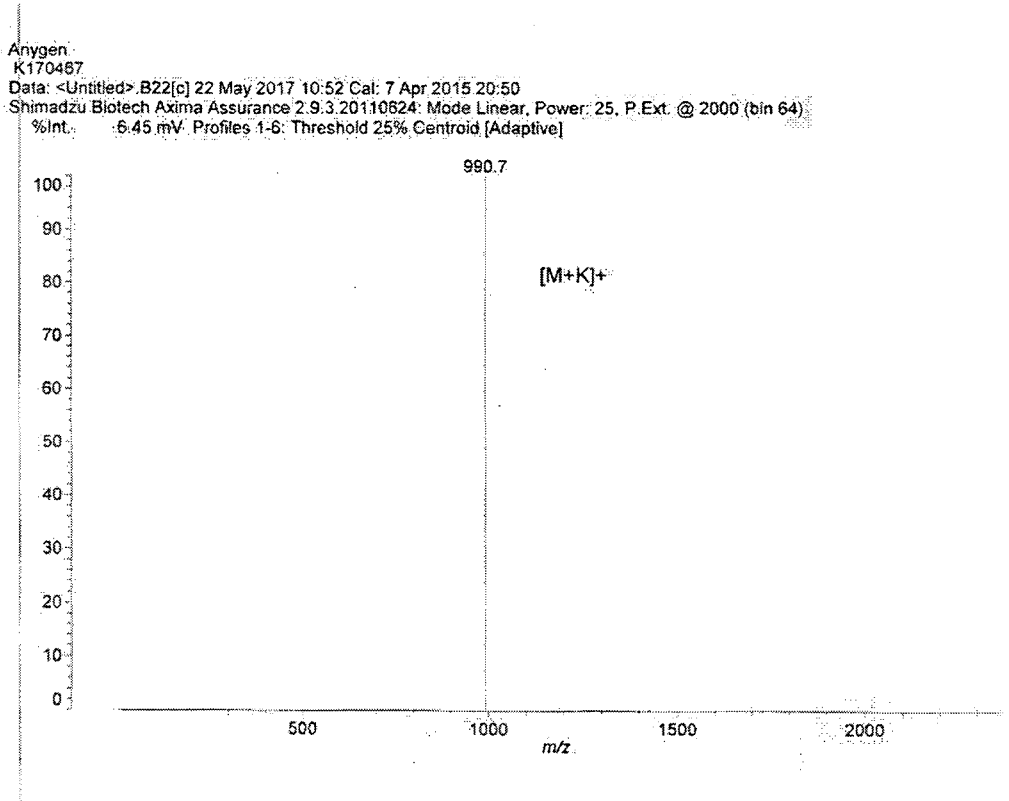
도 100


Anygen
K170464
Data: <Untitled> D12[c] 12 Apr 2017 9:44 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 34, Blanked, P.Ext. @ 3000 (bin 78)
%Int. 8.67 mV Profiles 1-25: Threshold 25% Centroid [Adaptive]
991.1
[M+K]+
100
90
80
70
60
50
40
30
20
10
0
200
400
600
800
1000
1200
1400
1600
1800
2000
m/z

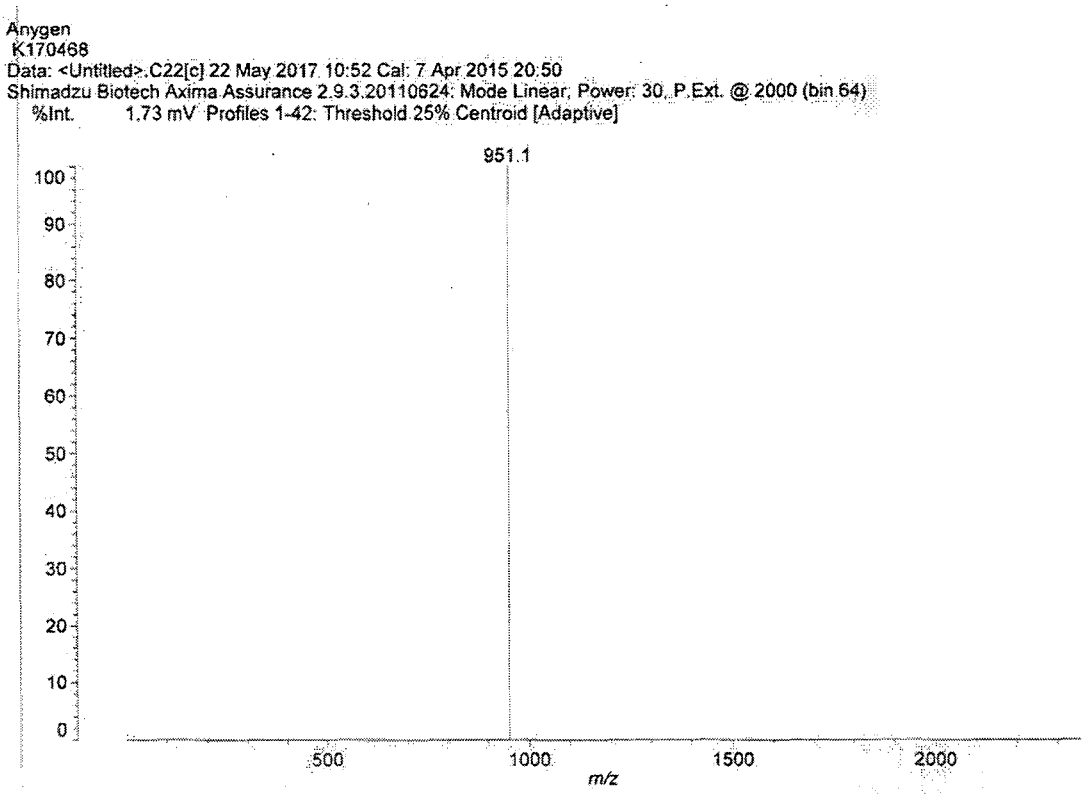
도 101


Anygen
K170465
Data: K170465-0001.A2[c] 16 May 2017 10:56 Cal: peptide 11 8 May 2017 11:10
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 35, Blanked, P.Ext. @ 1000 (bin 56)
%Int. 6.29 mV Profiles 1-10: Threshold 25% Centroid [Adaptive]
954.4
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
2500
3000
m/z

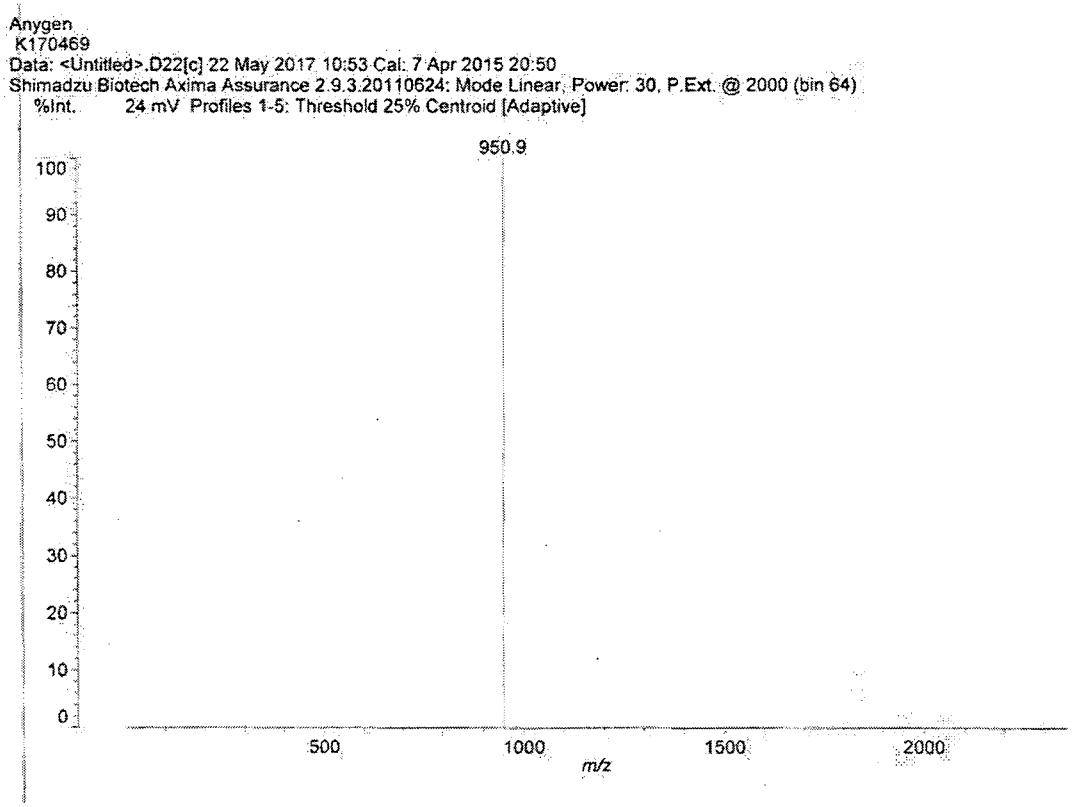
도 102


Anygen
K170467
Data: <Untitled> B22[c] 22 May 2017 10:52 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 25, P.Ext. @ 2000 (bin 64)
%Int. 6.45 mV Profiles 1-6: Threshold 25% Centroid [Adaptive]
990.7
[M+K]+
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

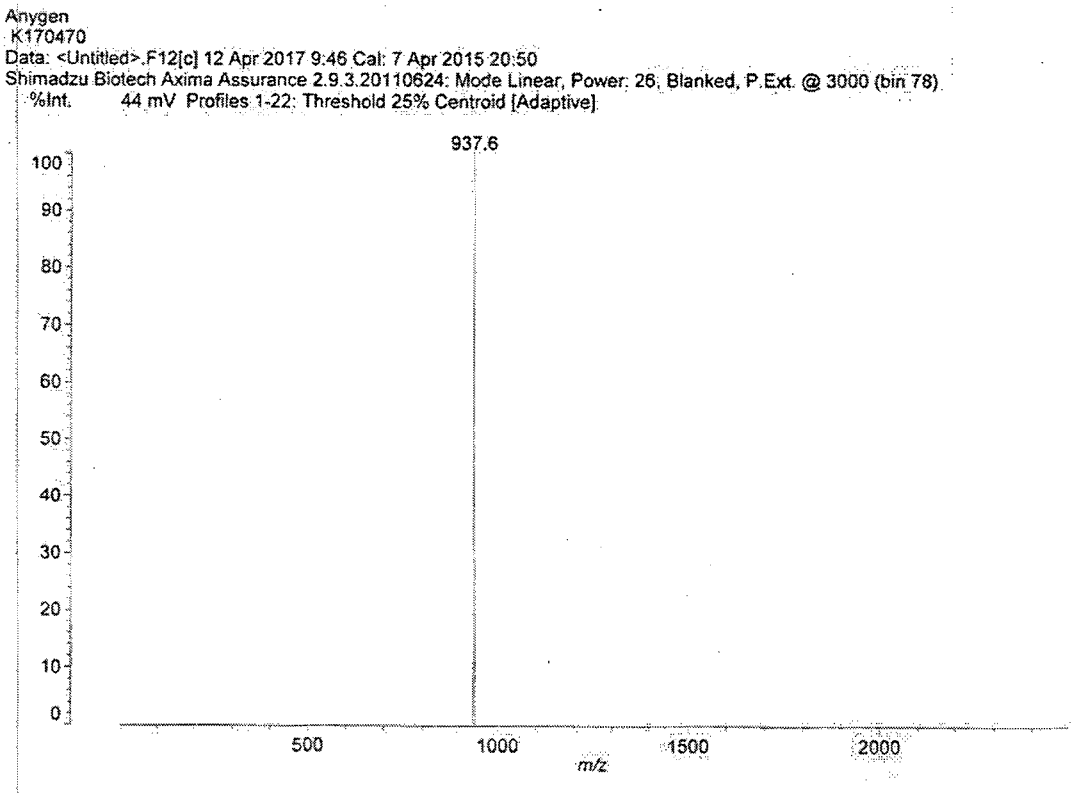
도 103


Anygen
K170468
Data: <Untitled>.C22[c] 22 May 2017 10:52 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 30, P.Ext. @ 2000 (bin 64)
%Int. 1.73 mV Profiles 1-42: Threshold 25% Centroid [Adaptive]
951.1
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

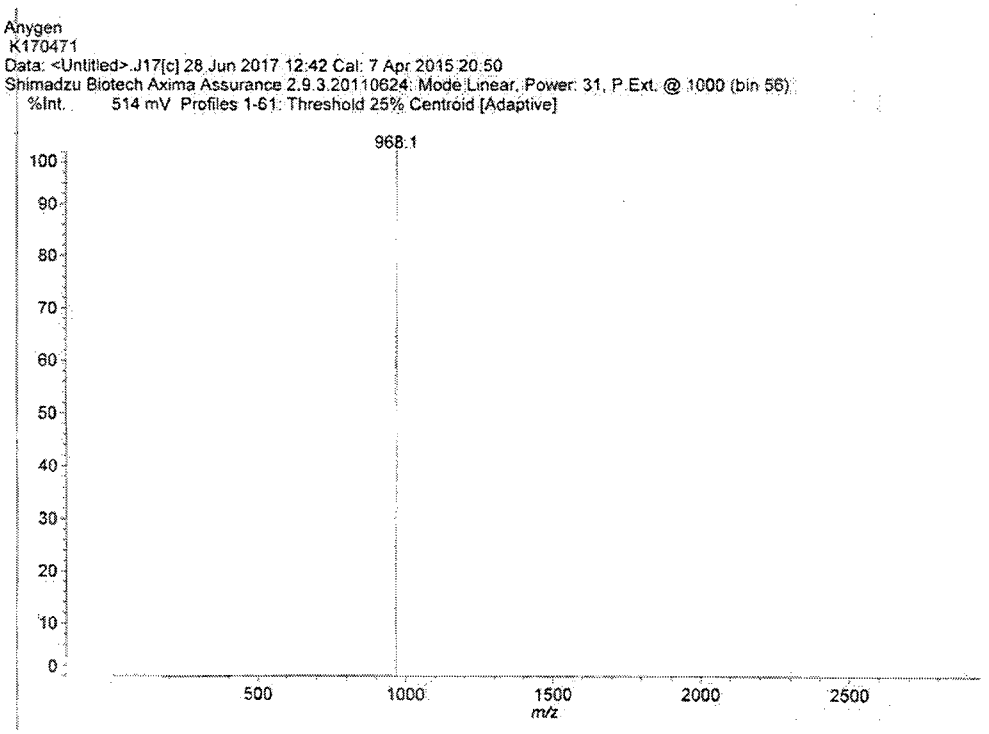
도 104


Anygen
K170469
Data: <Untitled>.D22[c] 22 May 2017 10:53 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 30, P.Ext. @ 2000 (bin 64)
%Int. 24 mV Profiles 1-5: Threshold 25% Centroid [Adaptive]
950.9
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

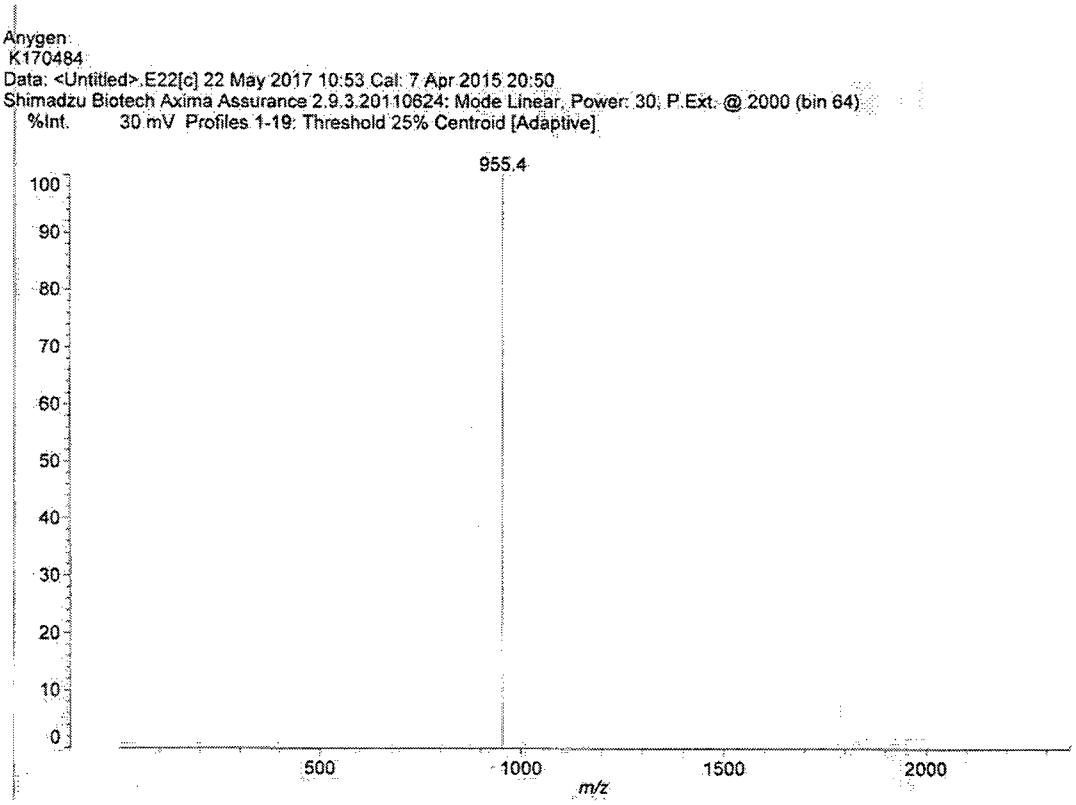
도 105


Anygen
K170470
Data: <Untitled>.F12[c] 12 Apr 2017 9:46 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 26, Blanked, P.Ext. @ 3000 (bin 78)
%Int. 44 mV Profiles 1-22: Threshold 25% Centroid [Adaptive]
937.6
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

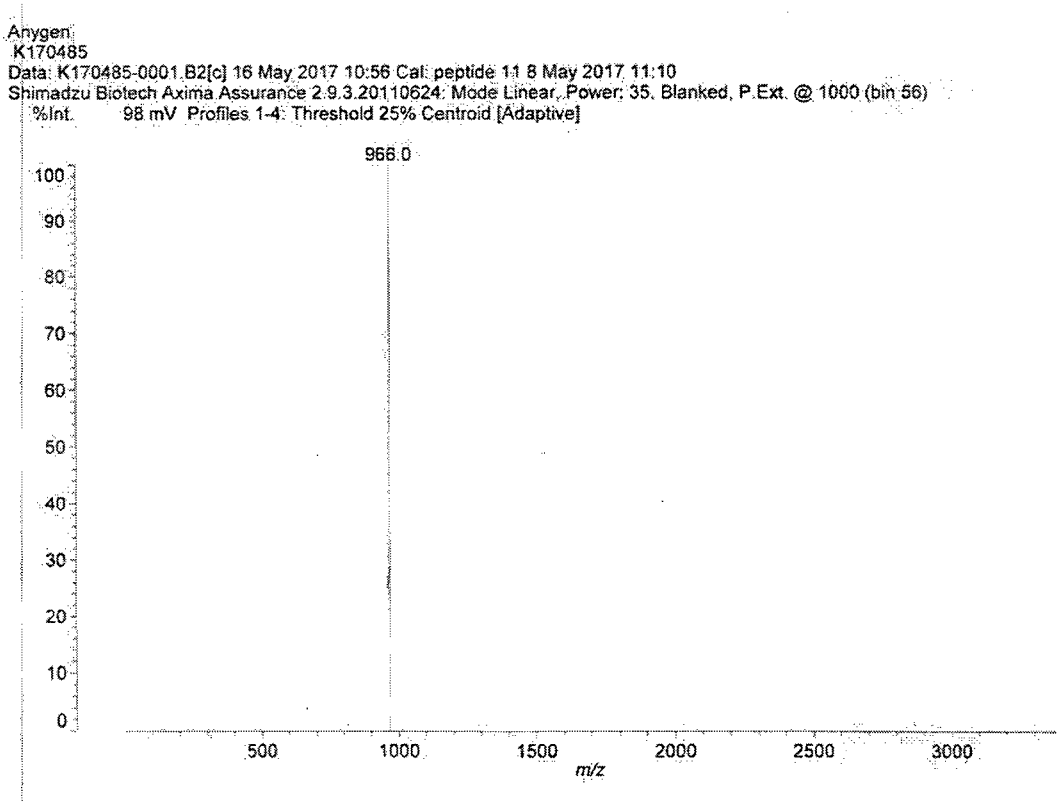
도 106


Anygen
K170471
Data: <Untitled>.J17[c] 28 Jun 2017 12:42 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 31, P.Ext. @ 1000 (bin 56)
%Int. 514 mV Profiles 1-61: Threshold 25% Centroid [Adaptive]
968.1
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
2500
m/z

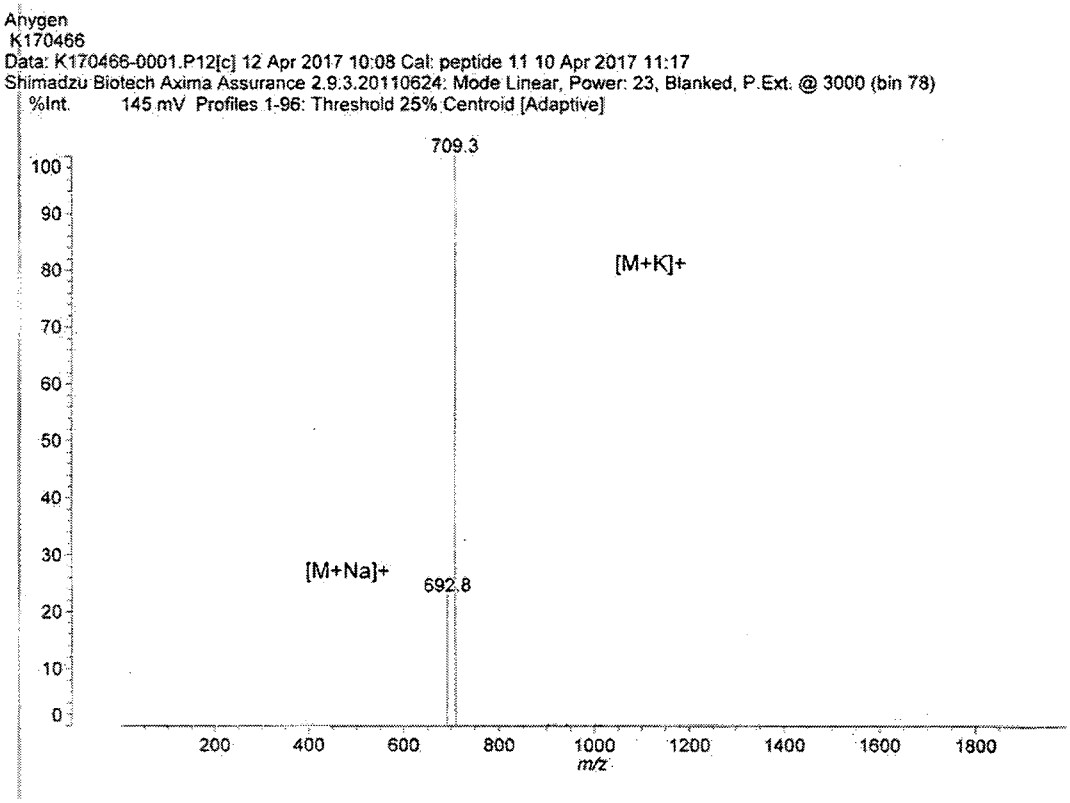
도 107


Anygen
K170484
Data: <Untitled>.E22[c] 22 May 2017 10:53 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 30, P.Ext. @ 2000 (bin 64)
%Int. 30 mV Profiles 1-19: Threshold 25% Centroid [Adaptive]
955.4
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

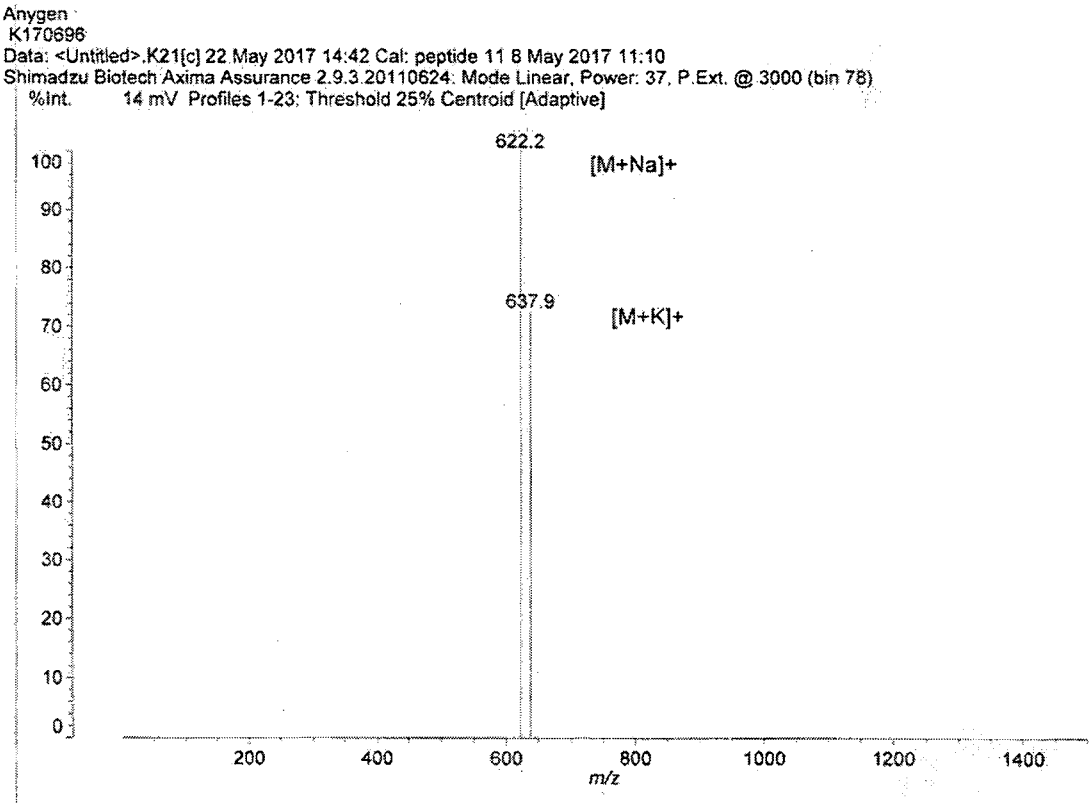
도 108


Anygen
K170485
Data: K170485-0001.B2[c] 16 May 2017 10:56 Cal: peptide 11 8 May 2017 11:10
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 35, Blanked, P.Ext. @ 1000 (bin 56)
%Int. 98 mV Profiles 1-4: Threshold 25% Centroid [Adaptive]
966.0
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
2500
3000
m/z

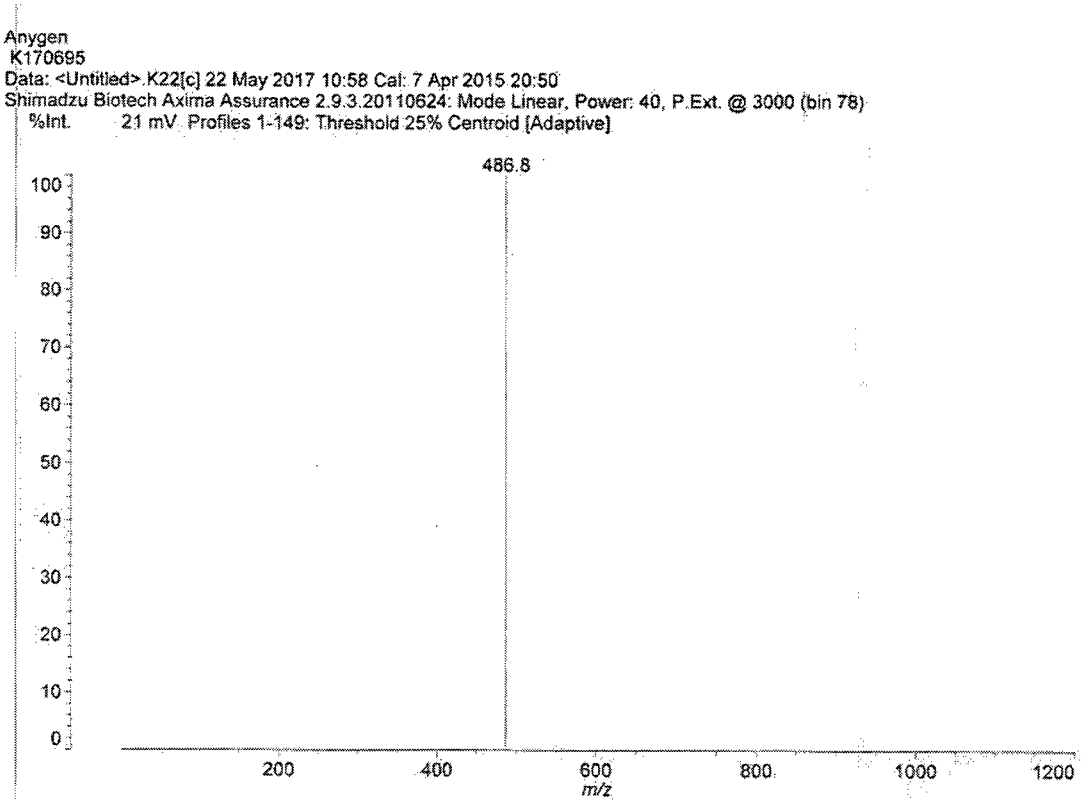
도 109


Anygen
K170466
Data: K170466-0001.P12[c] 12 Apr 2017 10:08 Cal: peptide 11 10 Apr 2017 11:17
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 23, Blanked, P.Ext. @ 3000 (bin 78)
%Int. 145 mV Profiles 1-96: Threshold 25% Centroid [Adaptive]
709.3
[M+K]+
[M+Na]+
692.8
m/z

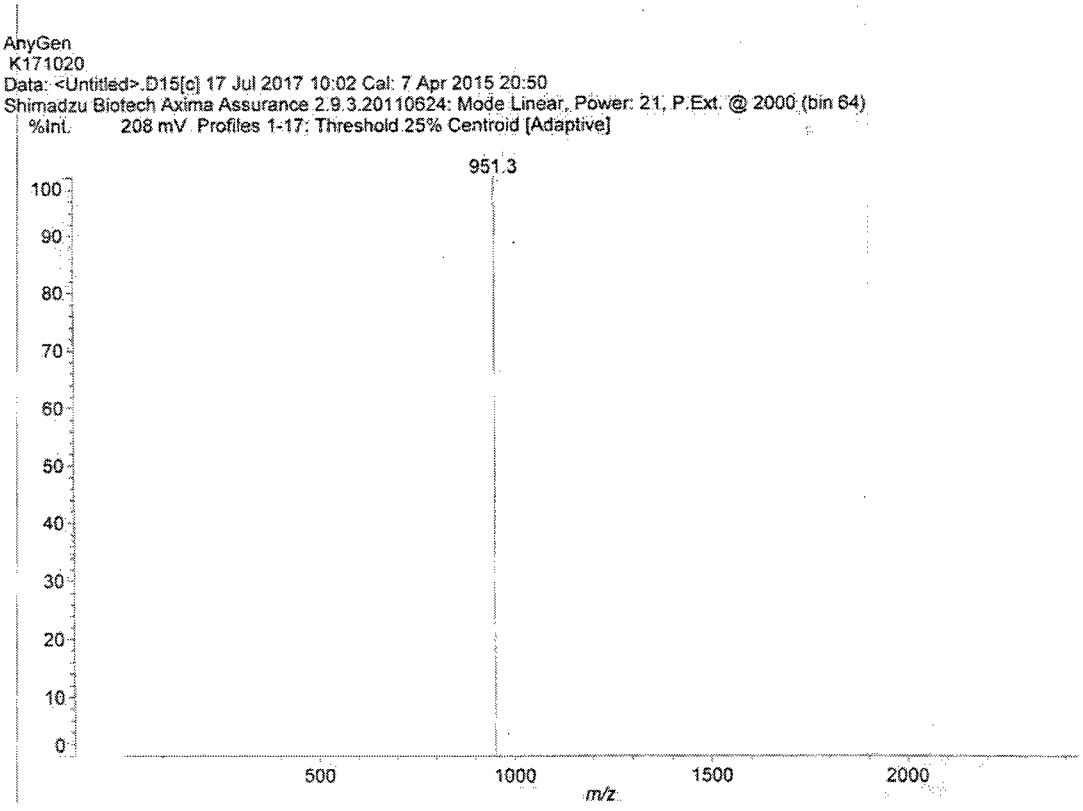
도 110


Anygen
K170696
Data: <Untitled>.K21[c] 22 May 2017 14:42 Cal: peptide 11 8 May 2017 11:10
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 37, P.Ext. @ 3000 (bin 78)
%Int. 14 mV Profiles 1-23: Threshold 25% Centroid [Adaptive]
622.2
[M+Na]+
637.9
[M+K]+
m/z

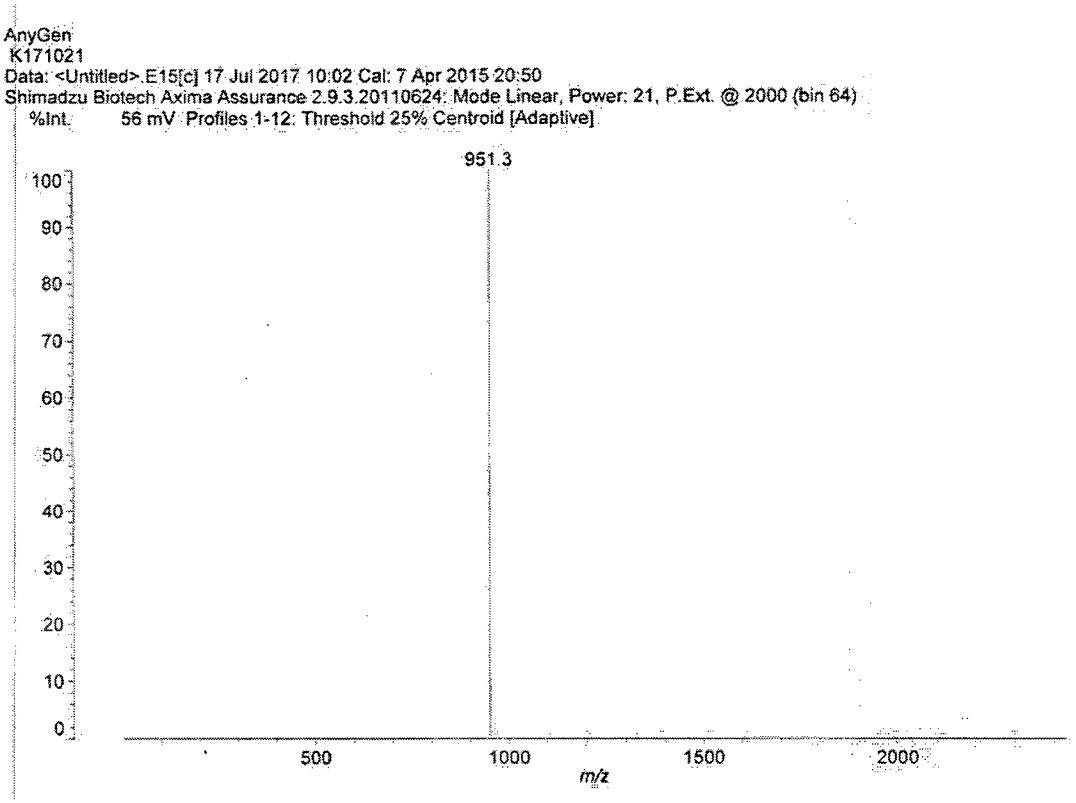
도 111


Anygen
K170695
Data: <Untitled>.K22[c] 22 May 2017 10:58 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 40, P.Ext. @ 3000 (bin 78)
%Int. 21 mV Profiles 1-149: Threshold 25% Centroid [Adaptive]
486.8
100
90
80
70
60
50
40
30
20
10
0
200
400
600
800
1000
1200
m/z

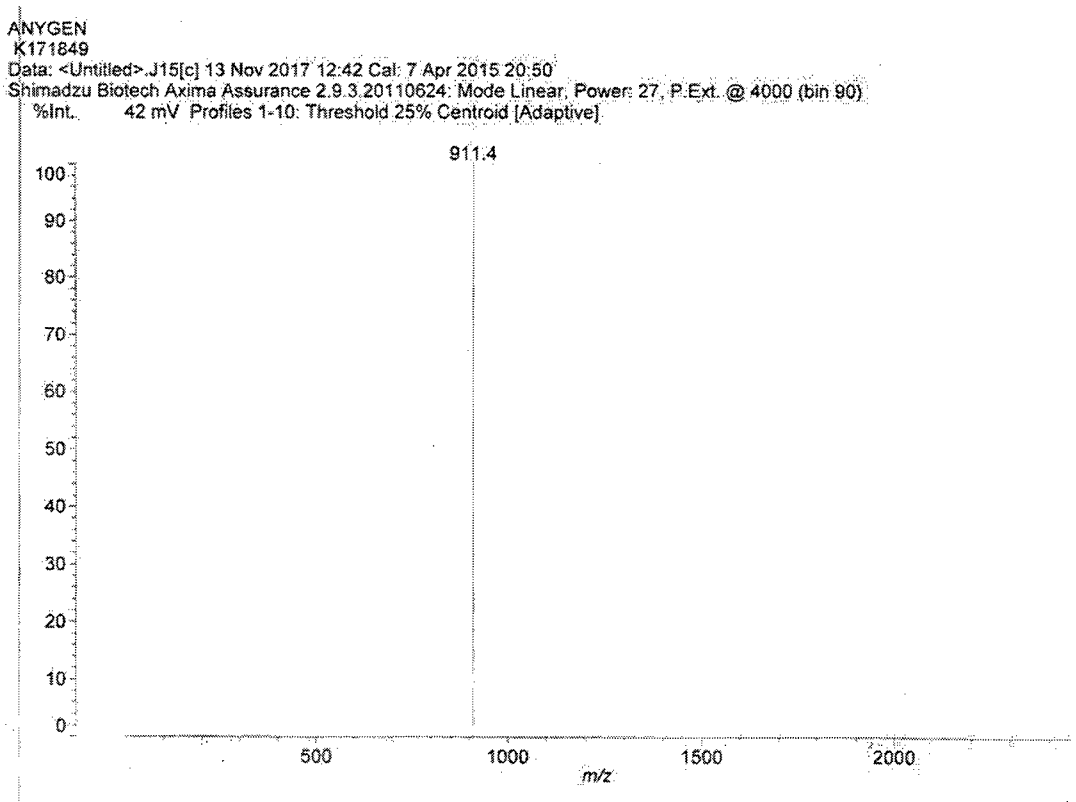
도 112


AnyGen
K171020
Data: <Untitled>.D15[c] 17 Jul 2017 10:02 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 21, P.Ext. @ 2000 (bin 64)
%Int. 208 mV Profiles 1-17: Threshold 25% Centroid [Adaptive]
951.3
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

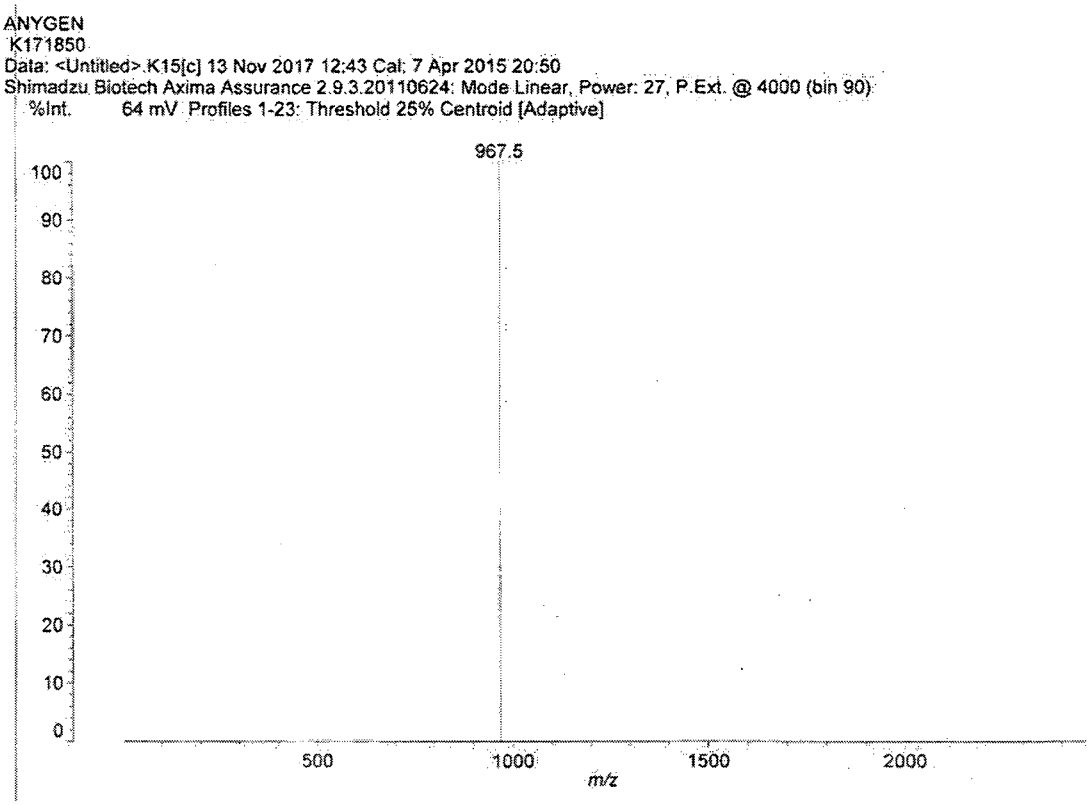
도 113


AnyGen
K171021
Data: <Untitled>.E15[c] 17 Jul 2017 10:02 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 21, P.Ext. @ 2000 (bin 64)
%Int. 56 mV Profiles 1-12: Threshold 25% Centroid [Adaptive]
951.3
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

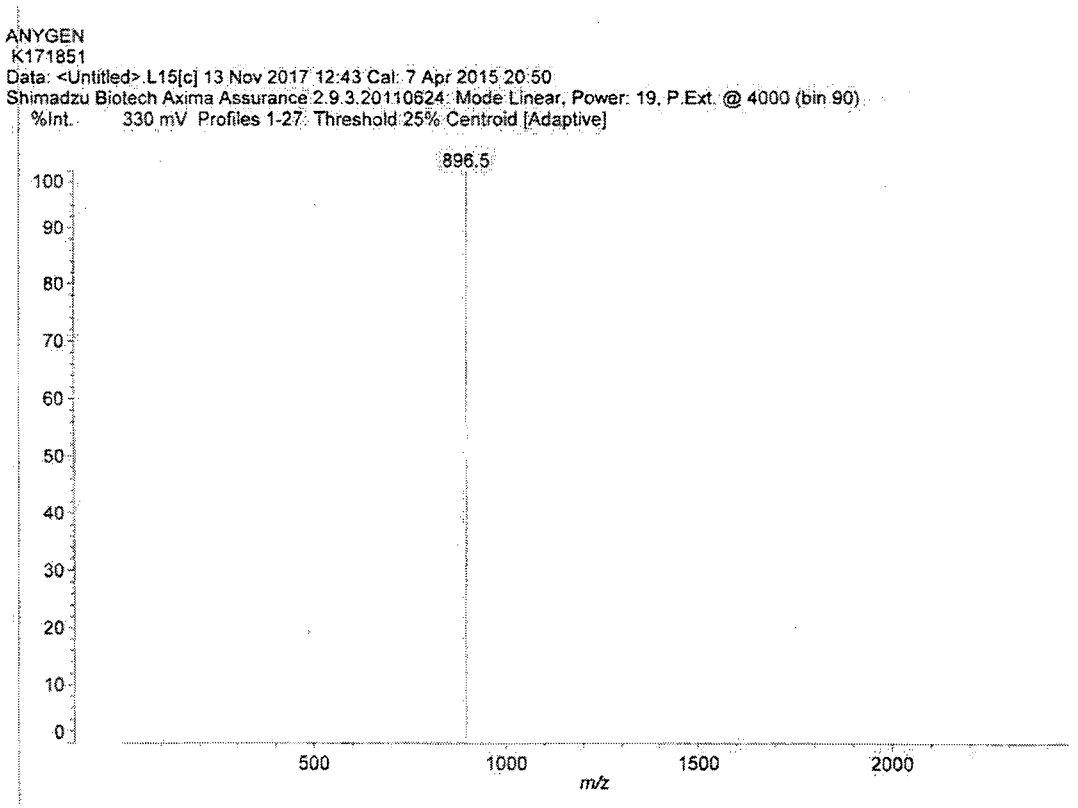
도 114


ANYGEN
K171849
Data: <Untitled>.J15[c] 13 Nov 2017 12:42 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 27, P.Ext. @ 4000 (bin 90)
%Int. 42 mV Profiles 1-10: Threshold 25% Centroid [Adaptive]
911.4
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

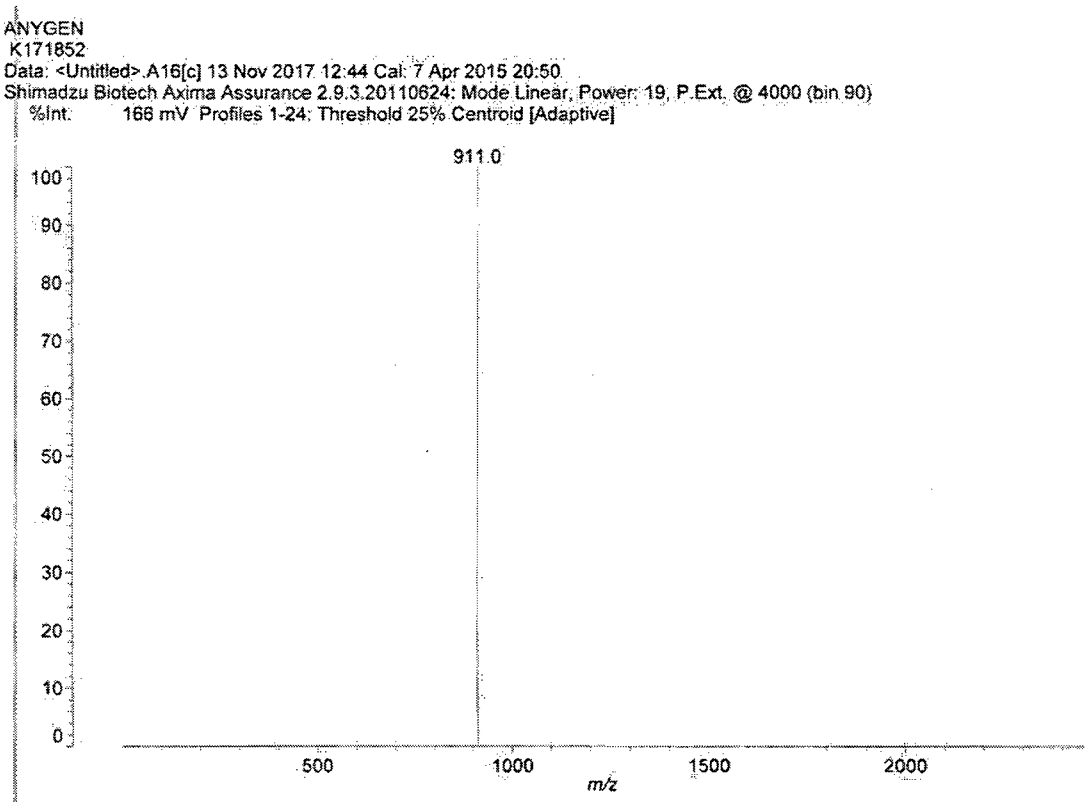
도 115


ANYGEN
K171850
Data: <Untitled> K15[c] 13 Nov 2017 12:43 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 27, P.Ext. @ 4000 (bin 90)
%Int. 64 mV Profiles 1-23: Threshold 25% Centroid [Adaptive]
967.5
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

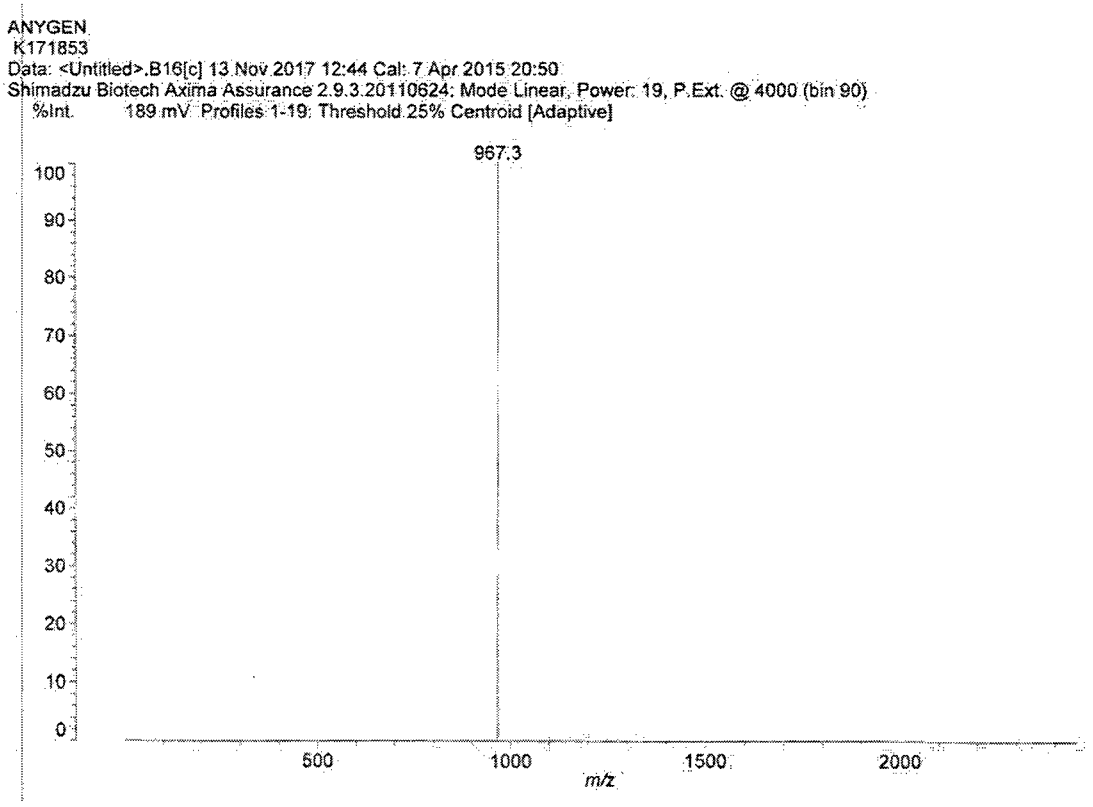
도 116


ANYGEN
K171851
Data: <Untitled> L15[c] 13 Nov 2017 12:43 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 19, P.Ext. @ 4000 (bin 90)
%Int. 330 mV Profiles 1-27: Threshold 25% Centroid [Adaptive]
896.5
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

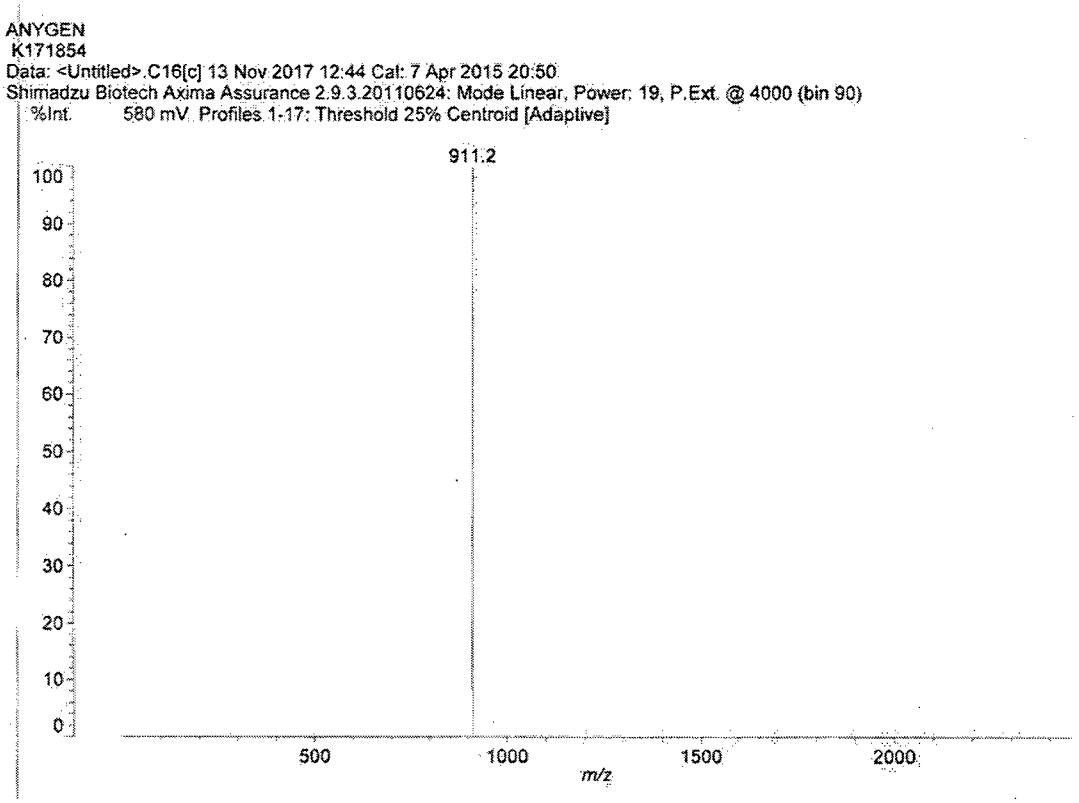
도 117


ANYGEN
K171852
Data: <Untitled>.A16[c] 13 Nov 2017 12:44 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 19, P.Ext. @ 4000 (bin 90)
%Int. 166 mV Profiles 1-24: Threshold 25% Centroid [Adaptive]
911.0
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

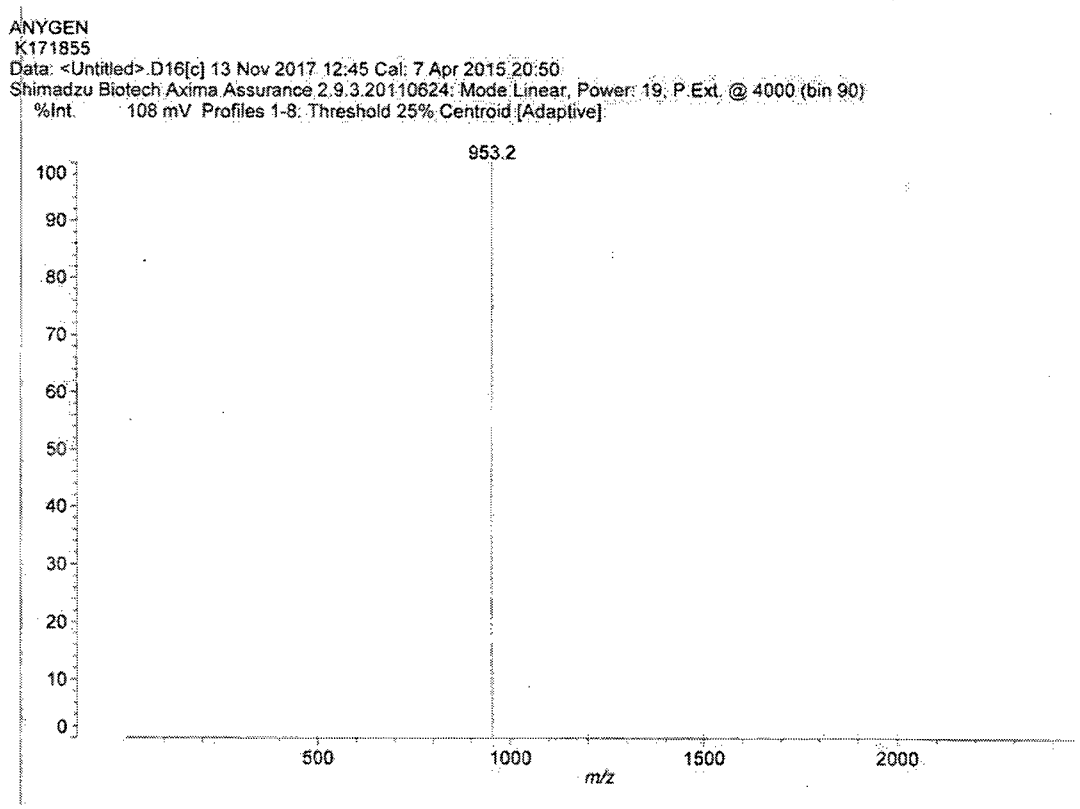
도 118


ANYGEN
K171853
Data: <Untitled>.B16[c] 13 Nov 2017 12:44 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 19, P.Ext. @ 4000 (bin 90)
%Int. 189 mV Profiles 1-19: Threshold 25% Centroid [Adaptive]
967.3
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

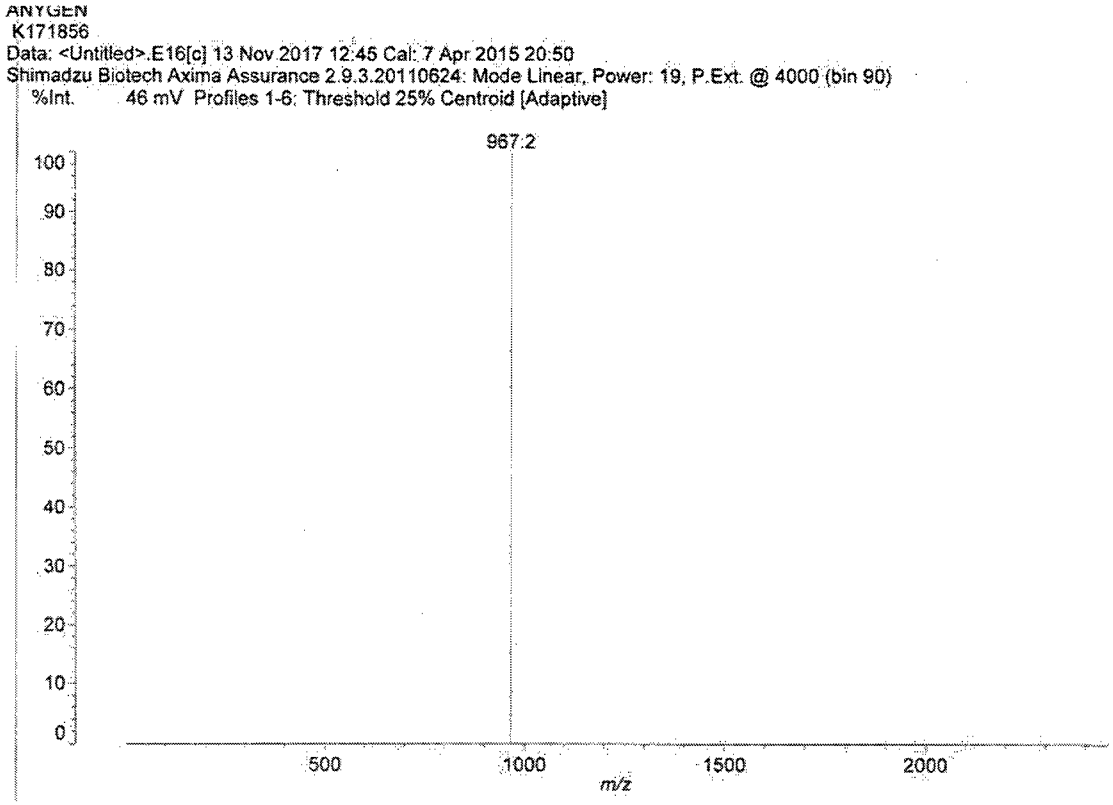
도 119


ANYGEN
K171854
Data: <Untitled>.C16[c] 13 Nov 2017 12:44 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 19, P.Ext. @ 4000 (bin 90)
%Int. 580 mV Profiles 1-17: Threshold 25% Centroid [Adaptive]
911.2
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

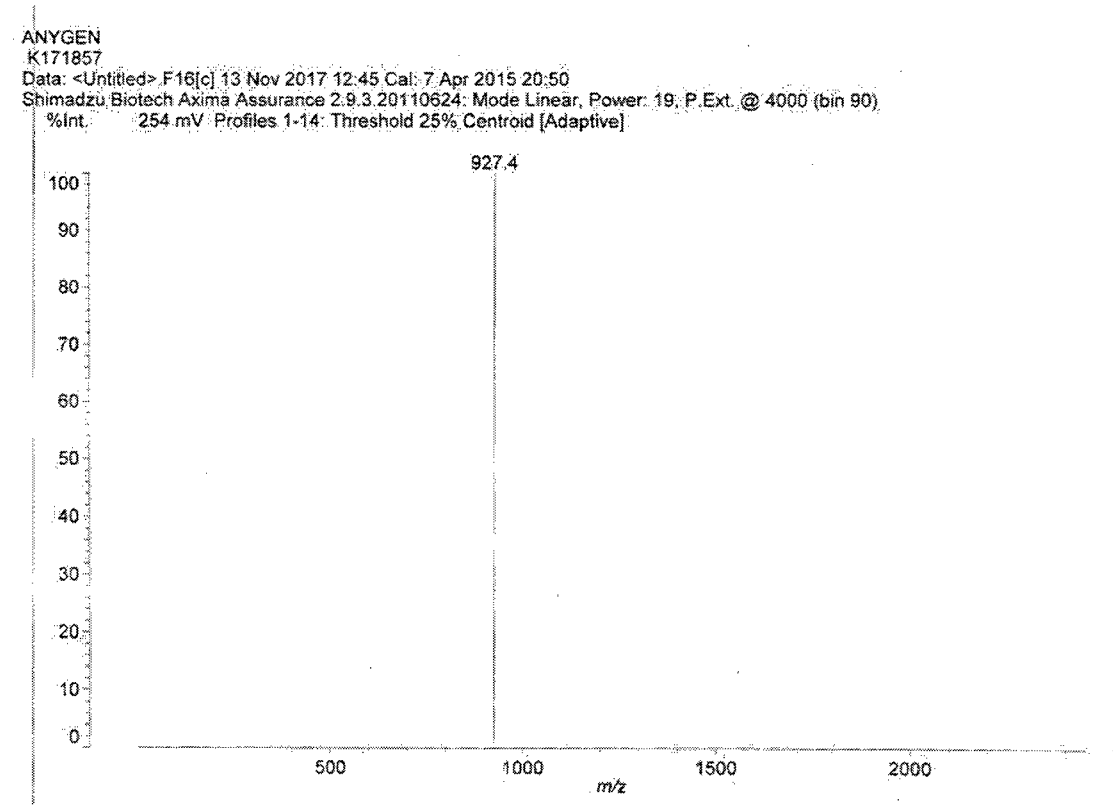
도 120


ANYGEN
K171855
Data: <Untitled>.D16[c] 13 Nov 2017 12:45 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 19, P.Ext. @ 4000 (bin 90)
%Int. 108 mV Profiles 1-8: Threshold 25% Centroid [Adaptive]
953.2
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

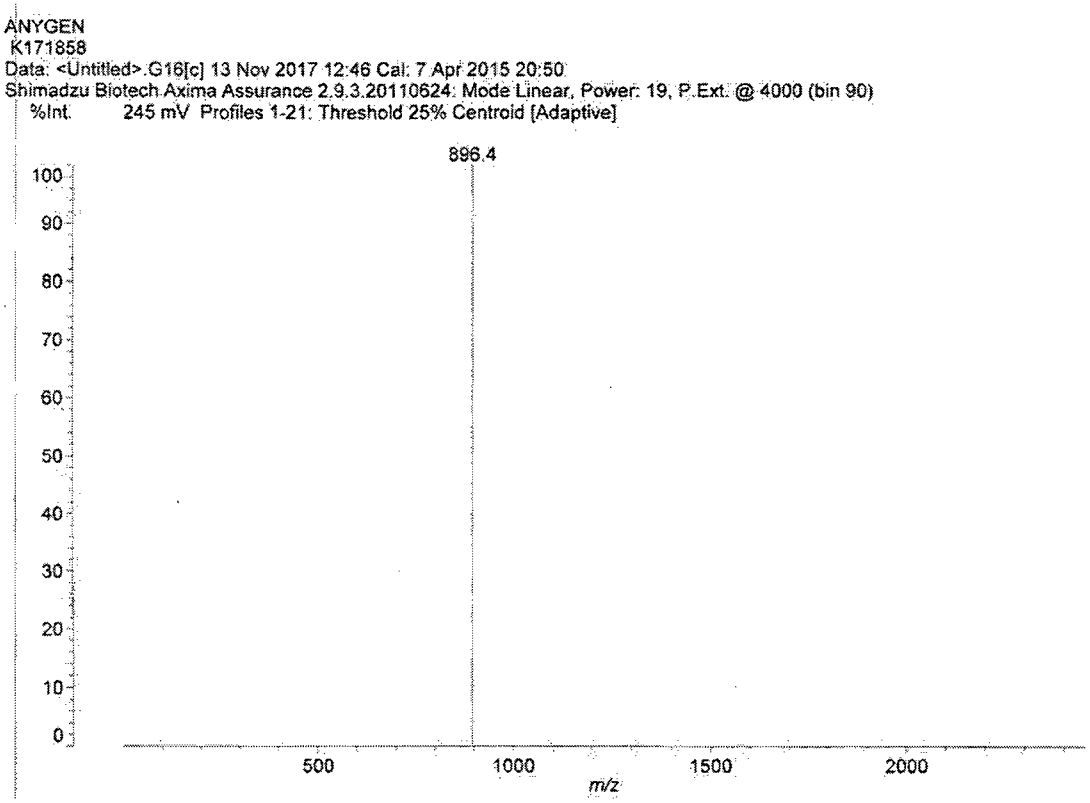
도 121


ANYGEN
K171856
Data: <Untitled>.E16[c] 13 Nov 2017 12:45 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 19, P.Ext. @ 4000 (bin 90)
%Int. 46 mV Profiles 1-6: Threshold 25% Centroid [Adaptive]
967.2
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

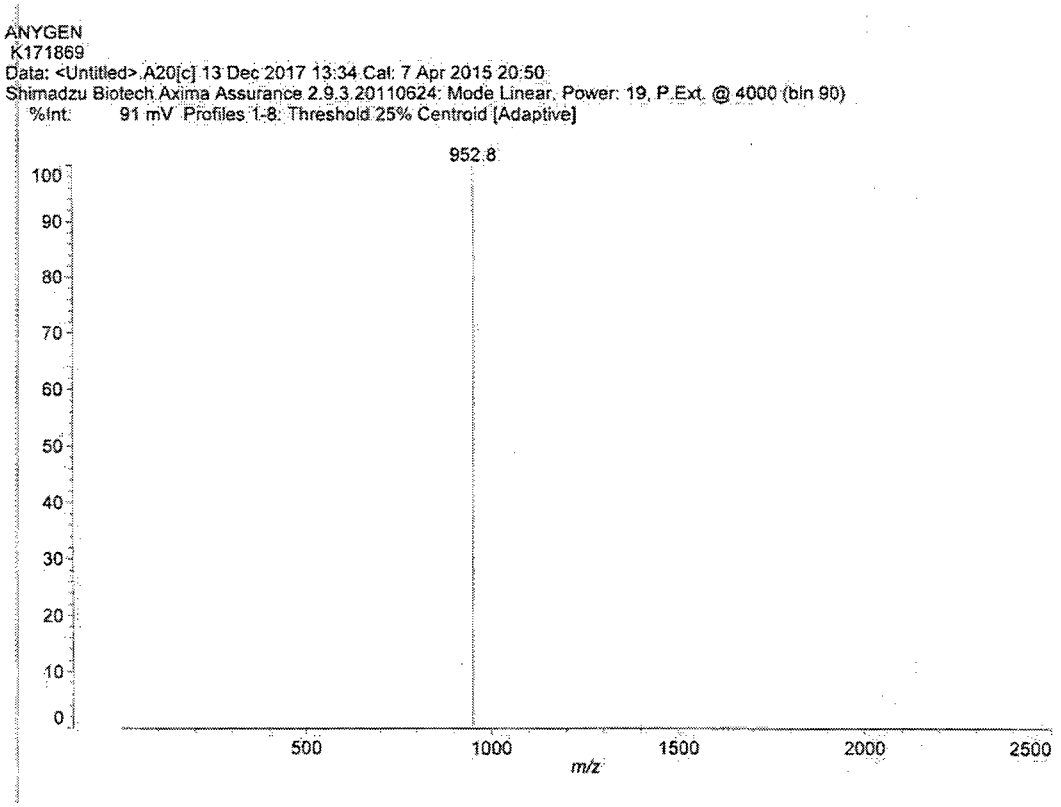
도 122


ANYGEN
K171857
Data: <Untitled> F16[c] 13 Nov 2017 12:45 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 19, P.Ext. @ 4000 (bin 90)
%Int. 254 mV Profiles 1-14: Threshold 25% Centroid [Adaptive]
927.4
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

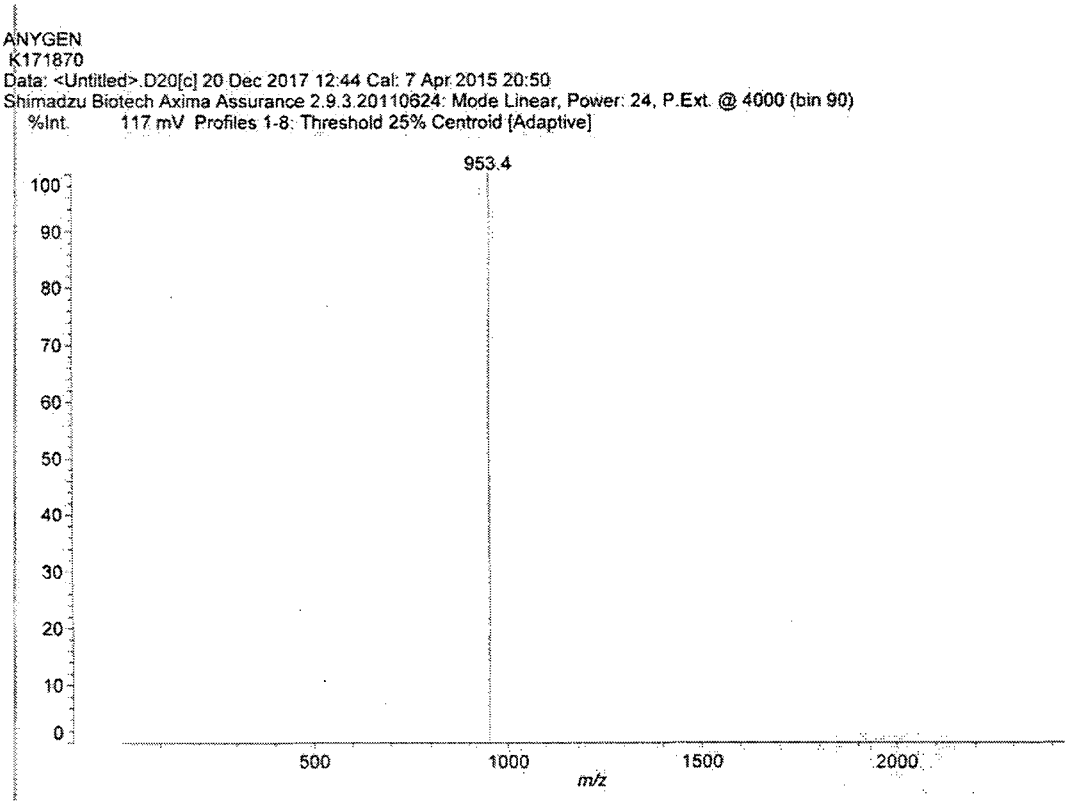
도 123


ANYGEN
K171858
Data: <Untitled>.G16[c] 13 Nov 2017 12:46 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 19, P.Ext. @ 4000 (bin 90)
%Int. 245 mV Profiles 1-21: Threshold 25% Centroid [Adaptive]
896.4
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

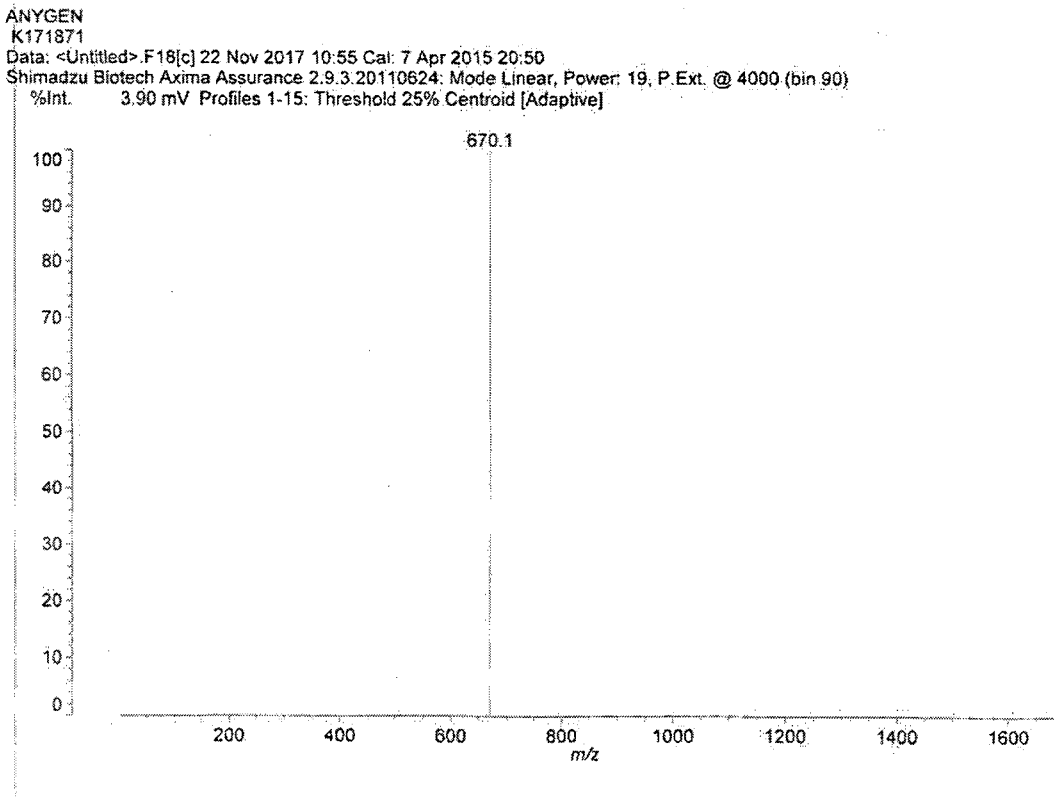
도 124


ANYGEN
K171869
Data: <Untitled>.A20[c] 13 Dec 2017 13:34 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 19, P.Ext. @ 4000 (bin 90)
%Int. 91 mV Profiles 1-8: Threshold 25% Centroid [Adaptive]
952.8
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
2500
m/z

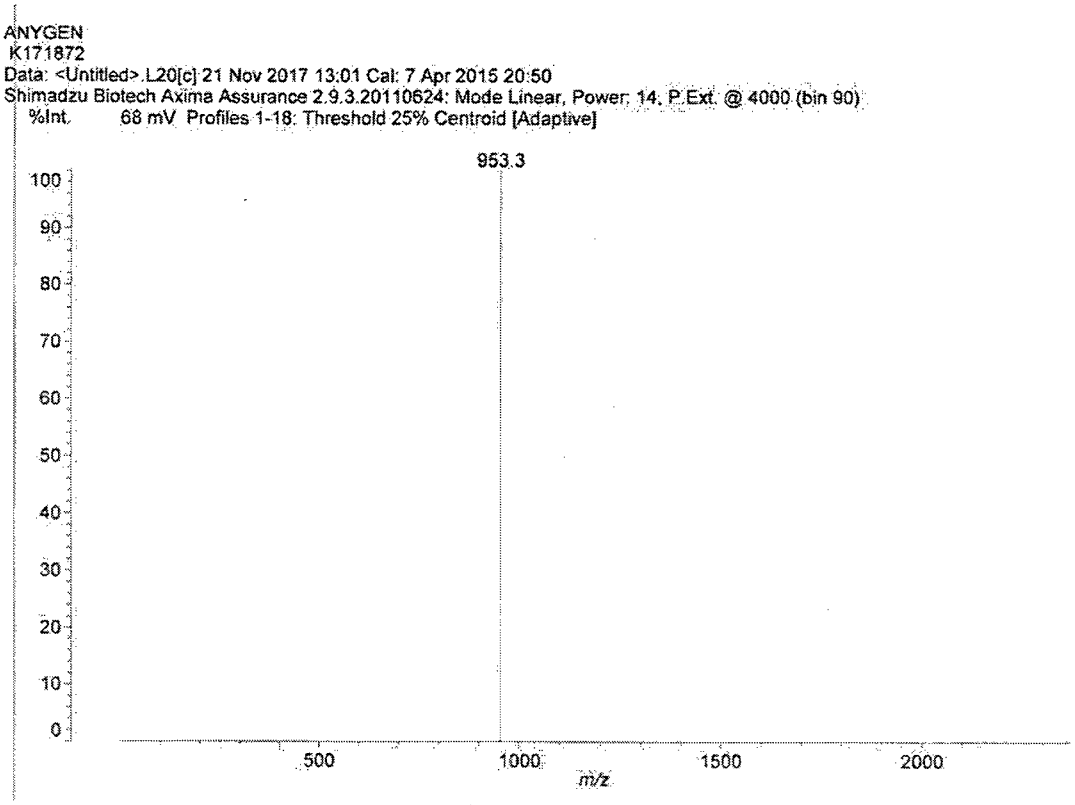
도 125


ANYGEN
K171870
Data: <Untitled>.D20[c] 20 Dec 2017 12:44 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 24, P.Ext. @ 4000 (bin 90)
%Int. 117 mV Profiles 1-8: Threshold 25% Centroid [Adaptive]
953.4
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

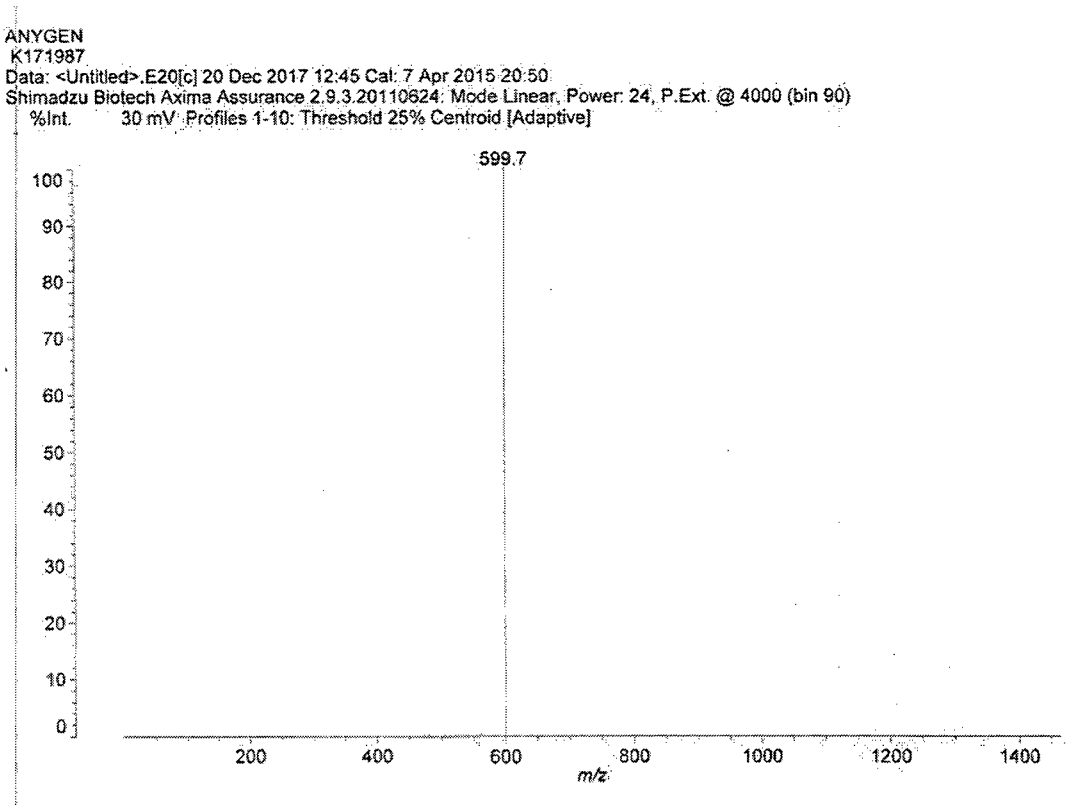
도 126


ANYGEN
K171871
Data: <Untitled>.F18[c] 22 Nov 2017 10:55 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 19, P.Ext. @ 4000 (bin 90)
%Int. 3.90 mV Profiles 1-15: Threshold 25% Centroid [Adaptive]
670.1
100
90
80
70
60
50
40
30
20
10
0
200
400
600
800
1000
1200
1400
1600
m/z

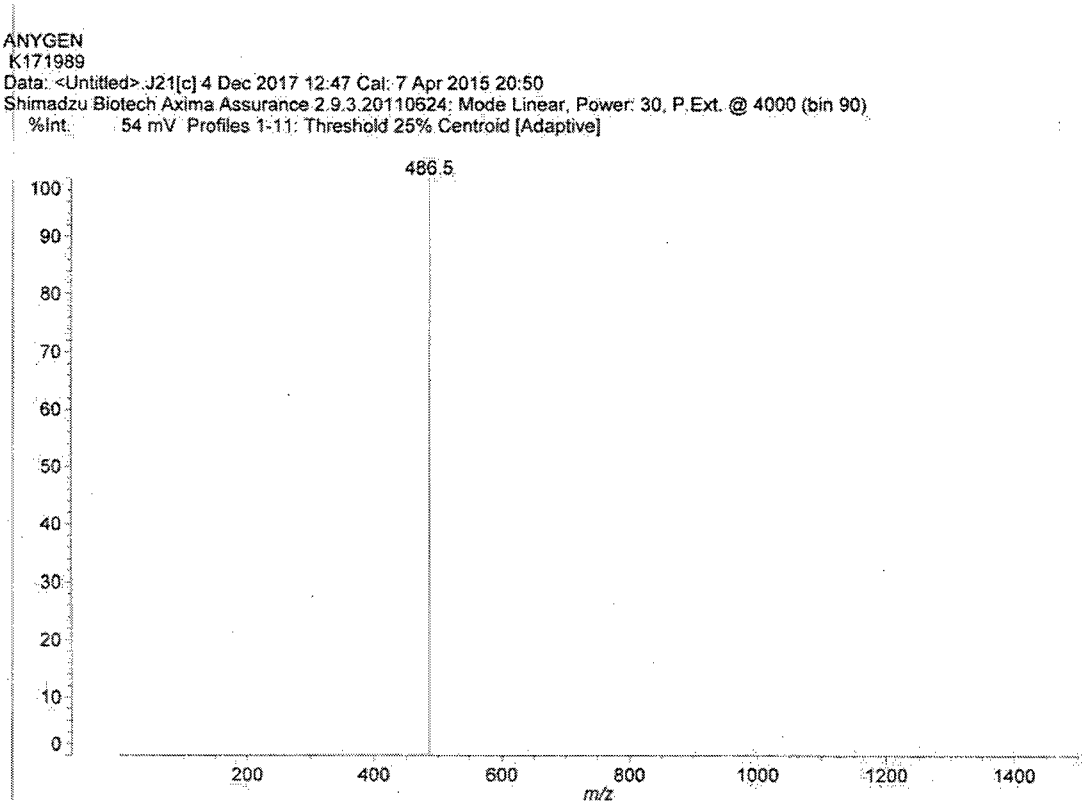
도 127


ANYGEN
K171872
Data: <Untitled>.L20[c] 21 Nov 2017 13:01 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 14, P.Ext. @ 4000 (bin 90)
%Int. 68 mV Profiles 1-18: Threshold 25% Centroid [Adaptive]
953.3
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
m/z

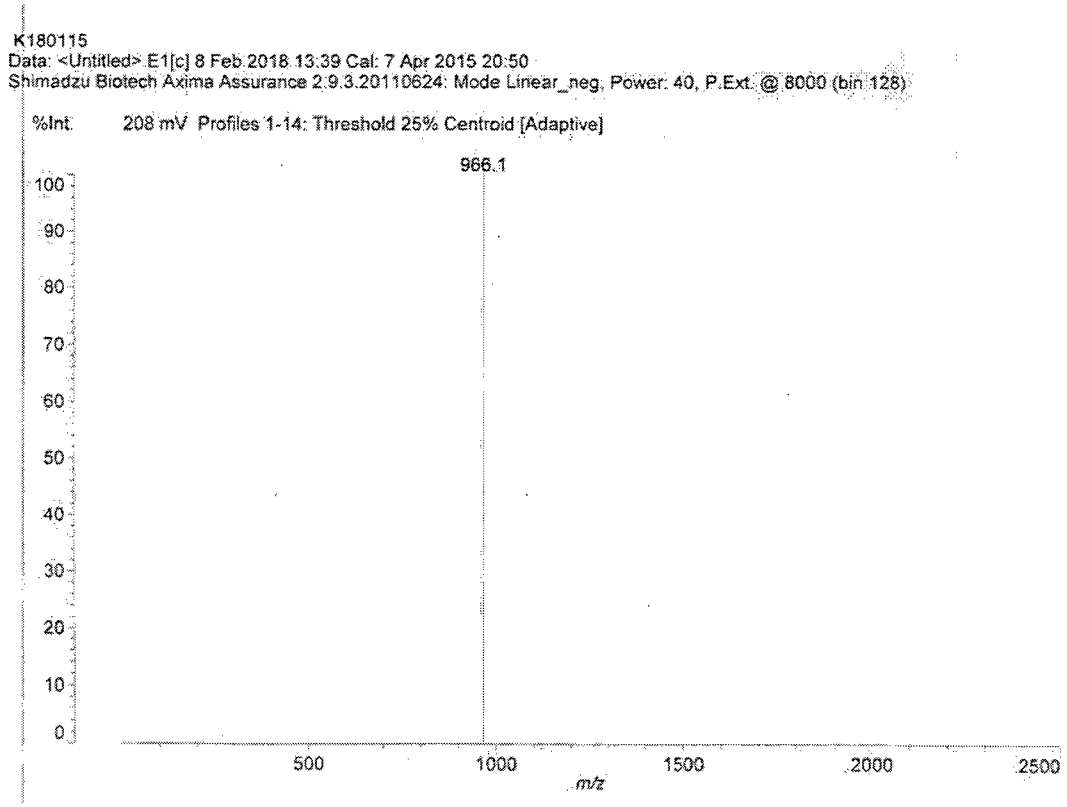
도 128


ANYGEN
K171987
Data: <Untitled>.E20[c] 20 Dec 2017 12:45 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 24, P.Ext. @ 4000 (bin 90)
%Int. 30 mV Profiles 1-10: Threshold 25% Centroid [Adaptive]
599.7
100
90
80
70
60
50
40
30
20
10
0
200
400
600
800
1000
1200
1400
m/z

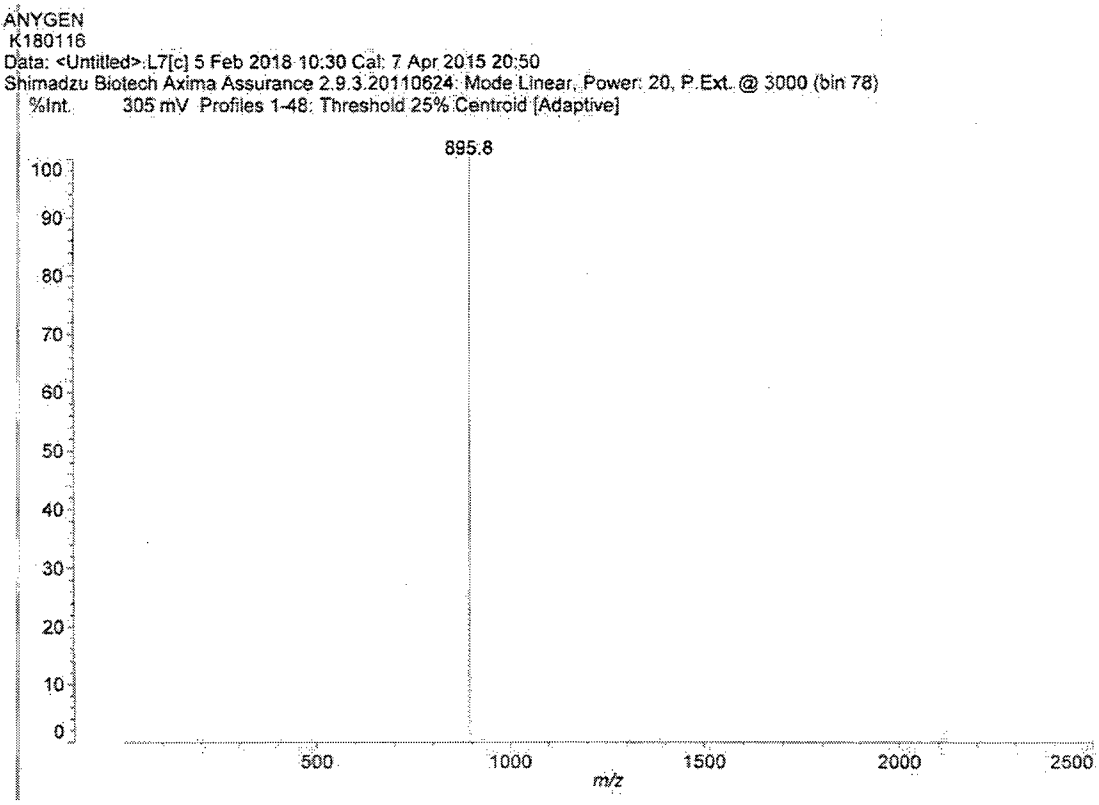
도 129


ANYGEN
K171989
Data: <Untitled> J21[c] 4 Dec 2017 12:47 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 30, P.Ext. @ 4000 (bin 90)
%Int. 54 mV Profiles 1-11: Threshold 25% Centroid [Adaptive]
486.5
100
90
80
70
60
50
40
30
20
10
0
200
400
600
800
1000
1200
1400
m/z

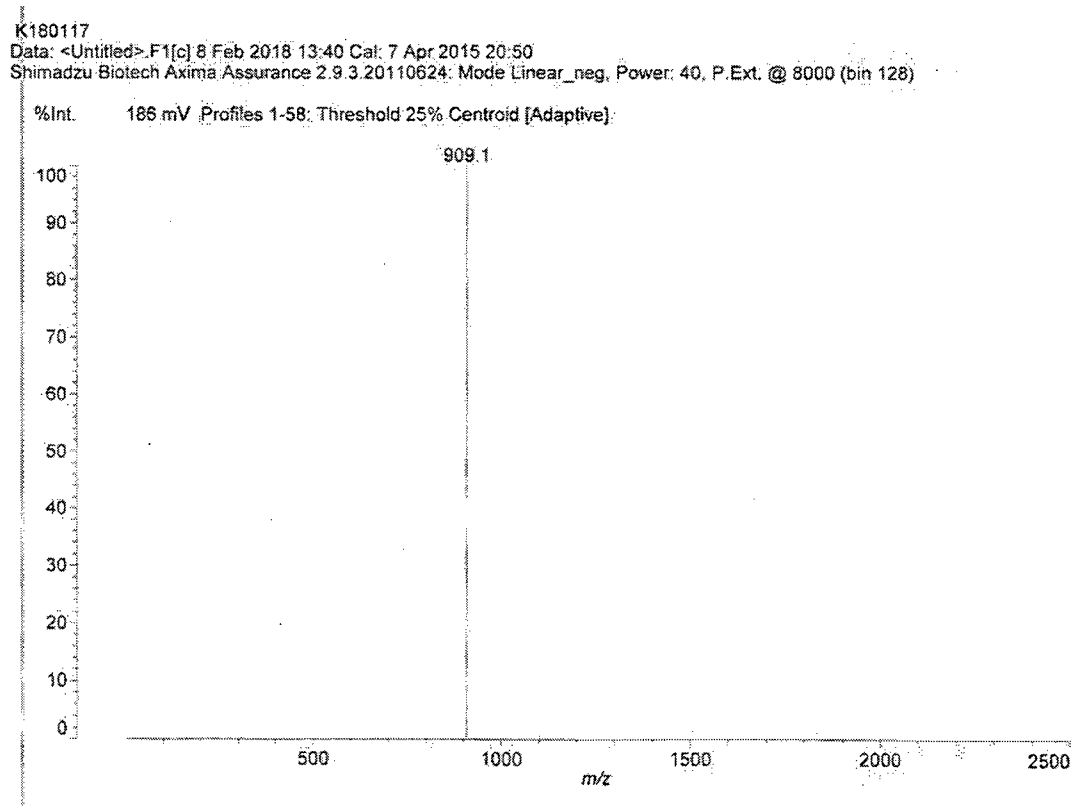
도 130


K180115
Data: <Untitled> E1[c] 8 Feb 2018 13:39 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear_neg, Power: 40, P.Ext. @ 8000 (bin 128)
%Int. 208 mV Profiles 1-14: Threshold 25% Centroid [Adaptive]
966.1
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
2500
m/z

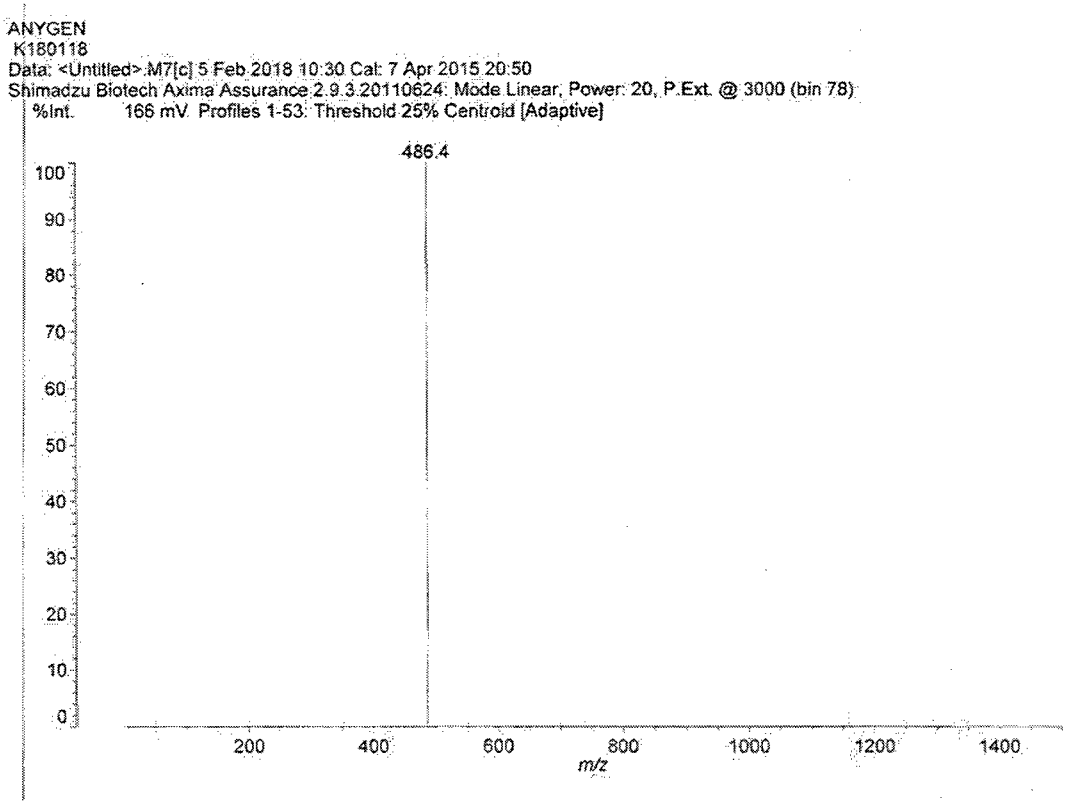
도 131


ANYGEN
K180116
Data: <Untitled>.L7[c] 5 Feb 2018 10:30 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 20, P.Ext. @ 3000 (bin 78)
%Int. 305 mV Profiles 1-48: Threshold 25% Centroid [Adaptive]
895.8
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
2500
m/z

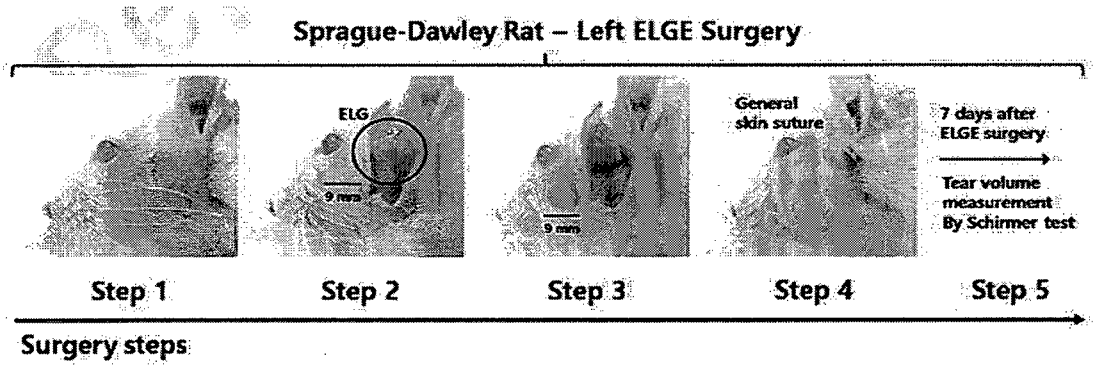
도 132


K180117
Data: <Untitled>.F1[c] 8 Feb 2018 13:40 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear_neg, Power: 40, P.Ext. @ 8000 (bin 128)
%Int. 186 mV Profiles 1-58: Threshold 25% Centroid [Adaptive]
909.1
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
2500
m/z

도 133


ANYGEN
K180118
Data: <Untitled> M7[c] 5 Feb 2018 10:30 Cal: 7 Apr 2015 20:50
Shimadzu Biotech Axima Assurance 2.9.3.20110624: Mode Linear, Power: 20, P.Ext. @ 3000 (bin 78)
%Int. 166 mV Profiles 1-53 Threshold 25% Centroid [Adaptive]
486.4
100
90
80
70
60
50
40
30
20
10
0
200
400
600
800
1000
1200
1400
m/z

도 134


Sprague-Dawley Rat – Left ELGE Surgery
ELG
9 mm
9 mm
General skin suture
7 days after ELGE surgery
Tear volume measurement By Schirmer test
Step 1
Step 2
Step 3
Step 4
Step 5
Surgery steps

도 135

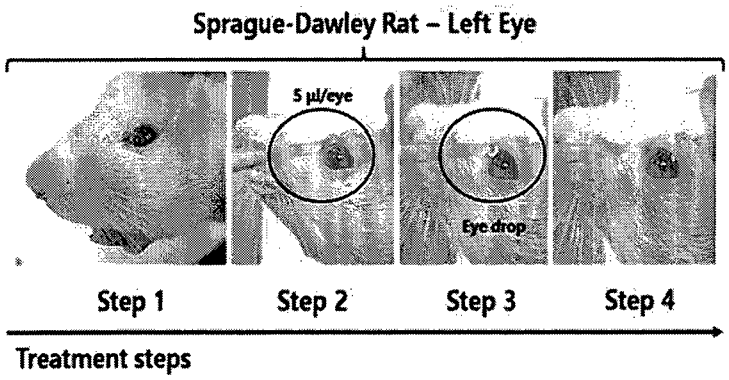
Items / Groups	Body weights at ELGE surgery*	First test material topical eye drop [A]	24 hrs after last treatment [B]*	Body weight gains [B-A]
Control				
Sham	213.63±21.04	305.50±33.53	340.50±38.46	35.00±11.19
ELGE	215.50±16.10	302.63±20.42	339.13±20.01	36.50±9.97
Reference				
DS	220.50±8.70	304.50±13.11	340.63±10.20	36.13±5.38
Test materials (0.3% solutions)				
YY-102	211.88±12.89	302.00±20.70	337.75±25.95	35.75±6.84
YDE-01	212.63±11.30	302.25±24.57	341.00±24.98	38.75±9.50
YDE-02	210.38±10.89	302.00±15.96	338.00±22.39	36.00±12.29
YDE-03	212.50±14.84	301.00±20.63	339.38±22.93	38.38±7.74
YDE-04	217.50±16.25	302.50±19.66	338.50±21.44	36.00±10.97
YDE-05	212.50±16.75	303.50±17.77	341.50±17.53	38.00±3.12
YDE-06	212.38±19.00	306.38±25.21	345.13±21.06	38.75±6.14
YDE-07	219.13±4.73	310.50±9.99	349.88±12.28	39.38±4.53
YDE-08	213.38±13.99	307.00±13.73	345.63±17.87	38.63±7.01
YDE-09	215.63±13.69	304.25±18.58	341.38±25.47	37.13±10.34
YDE-10	216.00±12.99	305.25±13.82	343.63±16.36	38.38±6.44
YDE-11	219.88±13.42	309.13±20.36	347.00±27.91	37.88±13.66
YDE-12	222.13±9.98	311.00±15.57	349.88±21.70	38.88±9.08
YDE-13	217.63±4.69	305.13±7.66	343.25±11.44	38.13±7.20
YDE-14	216.75±15.53	301.25±20.11	339.75±26.99	38.50±9.94
YDE-15	214.88±14.74	302.13±16.57	340.00±16.44	37.88±12.69
YDE-16	213.50±18.31	299.50±16.42	337.38±20.50	37.88±7.57
YDE-17	214.63±11.81	306.63±17.54	346.25±19.26	39.63±10.51
YDE-18	213.88±13.24	307.88±13.27	347.38±23.02	39.50±14.68
YDE-19	218.88±11.29	307.25±12.85	345.38±21.71	38.13±9.83
YDE-20	217.88±9.61	300.75±16.79	339.25±15.68	38.50±5.71
YDE-21	216.38±15.31	301.38±20.89	340.13±21.53	38.75±8.14
YDE-22	219.38±10.85	304.13±14.56	343.50±21.37	39.38±9.30
YDE-23	219.00±12.54	308.25±15.64	346.00±15.26	37.75±6.94
YDE-24	212.13±18.41	298.38±25.85	334.00±31.75	35.63±10.29
YDE-25	213.13±13.39	303.63±21.87	342.50±19.82	38.88±5.84
YDE-26	213.63±14.71	305.75±23.07	343.25±29.09	37.50±9.38
YDE-27	214.75±13.73	306.63±25.44	345.38±26.40	38.75±10.02
YDE-28	212.75±13.36	297.63±21.12	336.38±22.02	38.75±7.63

Revised Sheet (Rule 26)

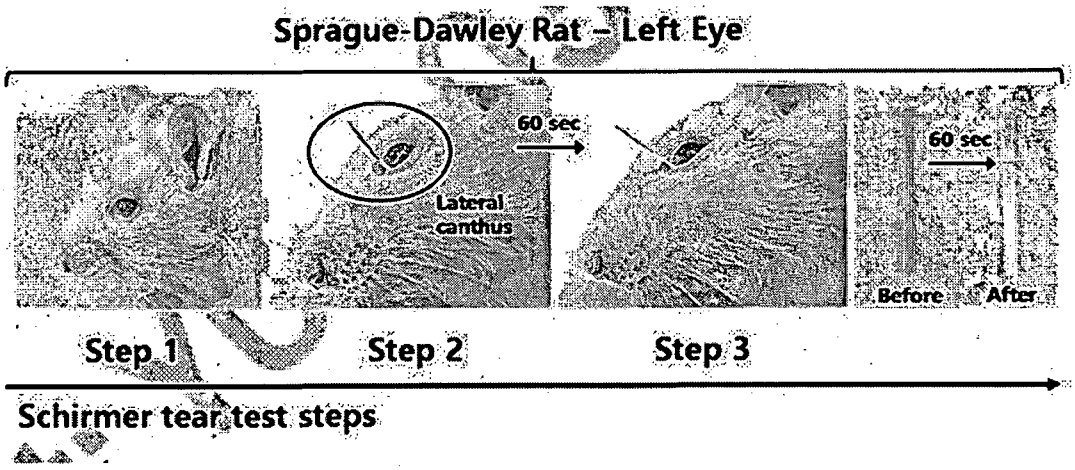
도 136

Items / Groups	Body weights at ELGE surgery*	First test material topical eye drop [A]	24 hrs after last treatment [B]*	Body weight gains [B-A]
Control				
Sham	242.38±7.73	320.25±9.91	363.38±27.21	43.13±19.71
ELGE	243.88±3.83	329.25±18.90	367.50±19.89	38.25±11.40
Reference				
DS	246.63±15.68	330.50±23.33	369.63±37.46	39.13±25.56
YY-101	241.25±4.37	318.88±10.91	356.25±18.16	37.38±7.82
YY-102	242.38±11.46	318.75±15.20	361.25±23.56	42.50±9.41
Test materials (0.3% solutions)				
YDE-029	242.25±16.63	327.38±18.75	373.75±28.50	46.38±12.49
YDE-030	243.25±10.26	315.88±14.96	355.50±29.68	39.63±16.61
YDE-031	241.00±15.82	316.75±27.58	359.00±39.87	42.25±14.96
YDE-032	242.75±9.32	324.25±14.59	365.38±16.16	41.13±10.12
YDE-033	243.50±11.96	327.50±17.57	377.13±26.59	49.63±16.27
YDE-034	243.88±8.68	322.63±17.15	361.63±19.08	39.00±4.99
YDE-035	240.88±11.29	321.00±22.17	358.50±29.18	37.50±20.36
YDE-036	242.25±14.01	329.38±21.07	378.38±24.20	49.00±10.81
YDE-037	244.50±10.94	324.88±17.36	369.13±21.43	44.25±8.83
YDE-039	242.88±7.14	325.25±15.51	363.25±28.35	38.00±15.41
YDE-040	241.13±13.39	319.25±14.10	357.00±27.93	37.75±19.37
YDE-041	244.75±14.49	322.88±22.47	366.13±37.43	43.25±16.97
YDE-042	239.13±8.29	323.38±8.28	372.38±19.46	49.00±13.54
YDE-043	246.25±7.92	324.00±14.31	361.25±19.20	37.25±13.63

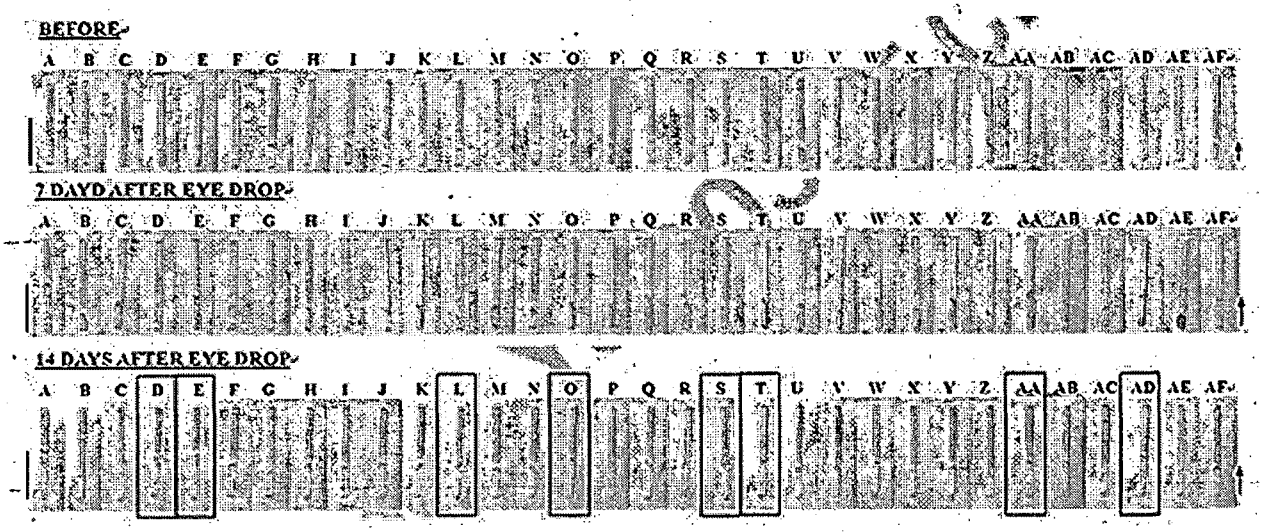
도 137



도 138


Sprague-Dawley Rat – Left Eye
60 sec
Lateral canthus
60 sec
Before
After
Step 1
Step 2
Step 3
Schirmer tear test steps

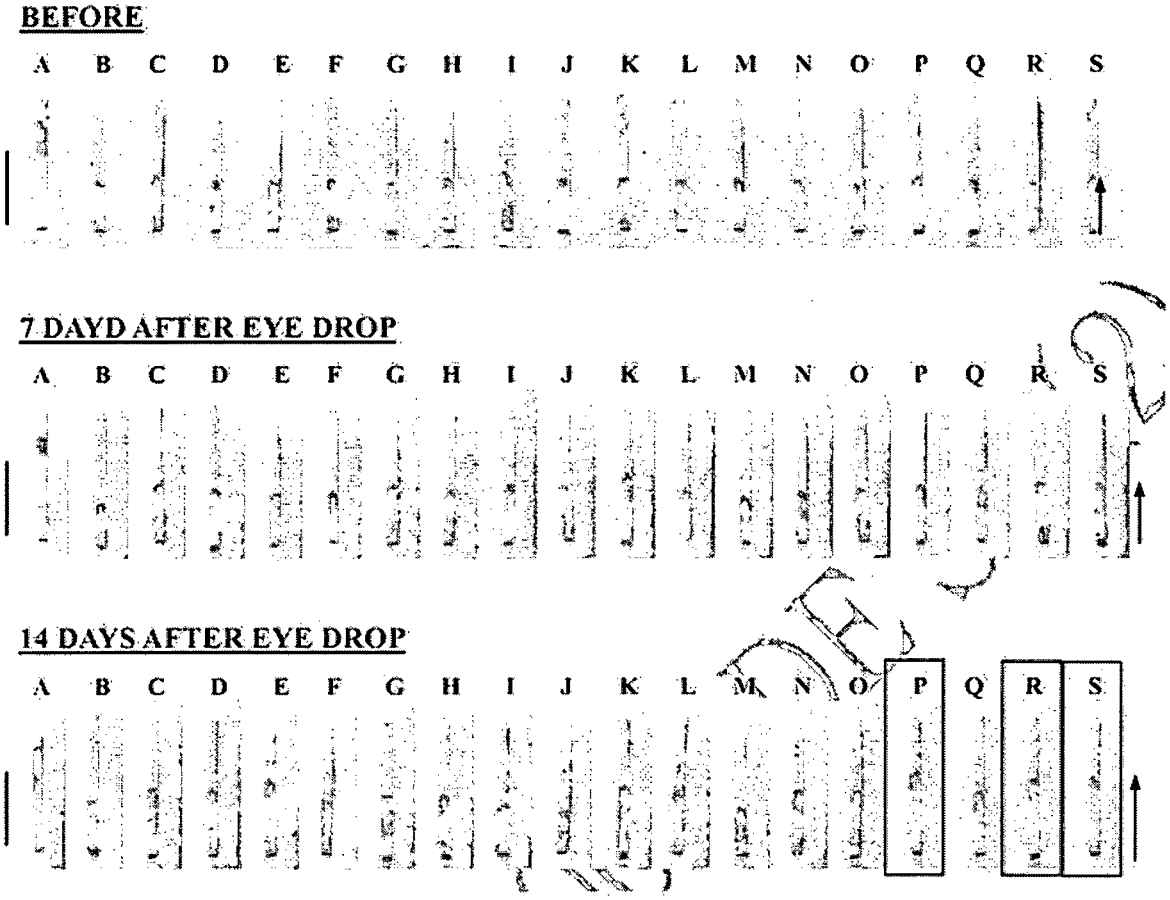
도 139


BEFORE
A B C D E F G H I J K L M N O P Q R S T U V W X Y Z AA AB AC AD AE AF
7 DAYD AFTER EYE DROP
A B C D E F G H I J K L M N O P Q R S T U V W X Y Z AA AB AC AD AE AF
14 DAYS AFTER EYE DROP
A B C D E F G H I J K L M N O P Q R S T U V W X Y Z AA AB AC AD AE AF

도 140

Items / Groups	Tear volumes (mm) after test material topical eye drop		
	-1 day	7 days	14 days
Control			
Sham	8.34±0.73	8.56±0.76	8.63±0.93
ELGE	3.54±0.78[a]	2.65±0.85[a]	3.27±1.06[a]
Reference			
DS	3.53±0.66[a]	4.10±1.07[ad]	4.80±0.94[ad]
Test materials (0.3% solutions)			
YY-102	3.58±0.93[a]	4.59±1.43[ac]	5.77±1.99[ac]
YDE-01	3.55±0.93[a]	4.88±1.62[ac]	5.92±2.19[ac]
YDE-02	3.59±0.75[a]	3.84±1.16[a]	5.01±1.67[ad]
YDE-03	3.56±0.74[a]	4.13±1.76[ad]	4.88±1.57[ad]
YDE-04	3.57±0.55[a]	3.42±1.06[a]	5.19±1.84[ad]
YDE-05	3.56±0.86[a]	3.85±0.93[a]	5.08±1.91[ad]
YDE-06	3.56±0.65[a]	3.44±1.69[a]	5.35±1.68[ad]
YDE-07	3.53±0.68[a]	3.91±1.28[a]	5.45±1.26[ad]
YDE-08	3.54±0.82[a]	4.57±1.25[ac]	6.10±2.36[ac]
YDE-09	3.56±0.78[a]	3.76±1.21[a]	4.54±1.11[a]
YDE-10	3.52±0.61[a]	3.42±1.31[a]	4.35±1.36[a]
YDE-11	3.56±0.88[a]	4.22±1.45[ad]	6.16±2.16[ac]
YDE-12	3.55±0.71[a]	3.68±0.99[a]	5.67±1.86[ac]
YDE-13	3.55±0.49[a]	5.27±1.50[ac]	5.49±1.92[ac]
YDE-14	3.55±0.66[a]	3.81±1.21[a]	5.62±1.85[ac]
YDE-15	3.54±0.73[a]	4.03±2.19[ad]	6.65±2.13[bc]
YDE-16	3.56±0.93[a]	4.59±1.13[ac]	5.98±2.27[ac]
YDE-17	3.54±0.91[a]	4.00±1.22[ad]	4.89±1.50[a]
YDE-18	3.58±0.68[a]	3.75±1.54[a]	4.99±1.60[ad]
YDE-19	3.58±0.63[a]	4.84±1.39[ac]	4.52±1.07[a]
YDE-20	3.56±0.86[a]	3.41±1.47[a]	4.20±1.35[a]
YDE-21	3.55±0.72[a]	4.08±1.33[ad]	4.90±1.13[a]
YDE-22	3.50±0.75[a]	3.19±0.67[a]	4.10±0.95[a]
YDE-23	3.51±0.72[a]	5.32±2.30[ac]	5.78±2.23[ac]
YDE-24	3.53±0.63[a]	3.85±1.30[a]	5.72±1.36[ac]
YDE-25	3.56±0.75[a]	3.21±0.72[a]	4.72±2.19[a]
YDE-26	3.57±0.57[a]	4.32±1.47[ad]	6.01±1.83[ac]
YDE-27	3.57±0.64[a]	2.82±0.86[a]	3.95±1.52[a]
YDE-28	3.56±0.91[a]	4.04±0.99[ad]	4.73±1.18[a]

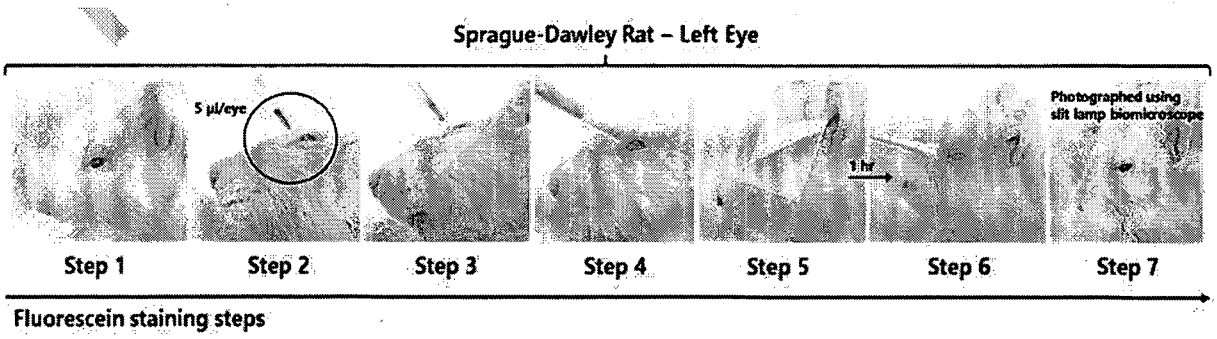
도 141


BEFORE
A B C D E F G H I J K L M N O P Q R S
7 DAYD AFTER EYE DROP
A B C D E F G H I J K L M N O P Q R S
14 DAYS AFTER EYE DROP
A B C D E F G H I J K L M N O P Q R S

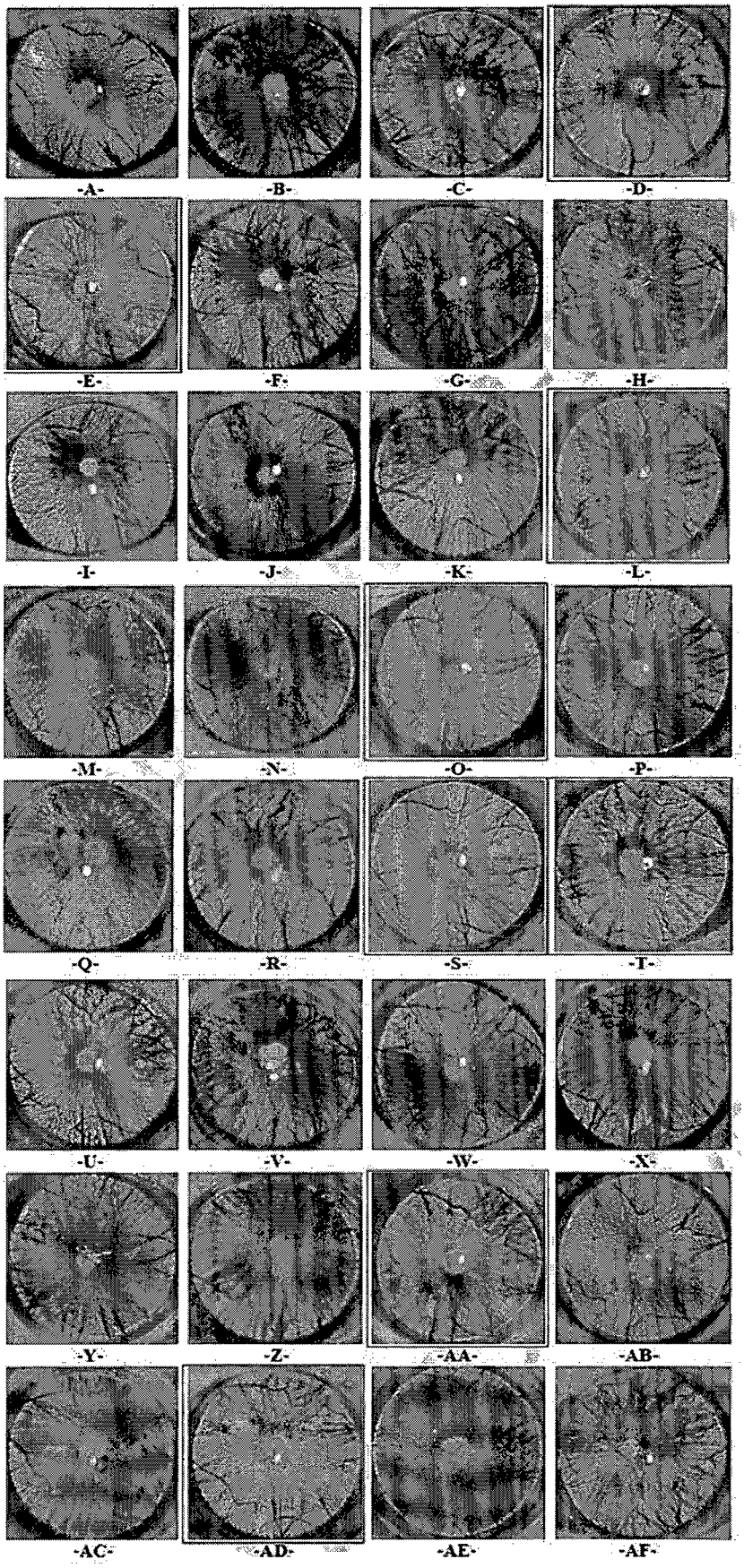
도 142

Items	Tear volumes (mm) after test material topical eye drop		
Groups	-1 day	7 days	14 days
Control			
Sham	10.90±1.69	10.38±1.08	10.28±0.69
ELGE	4.81±1.09[a]	4.37±0.83[b]	4.70±0.65[b]
Reference			
DS	4.74±1.30[a]	5.72±1.28[be]	6.56±1.15[bd]
YY-101	4.86±1.08[a]	5.36±0.68[be]	6.25±0.68[bd]
YY-102	4.94±0.71[a]	5.77±1.01[be]	6.60±0.64[bd]
Test materials (0.3% solutions)			
YDE-029	4.72±1.05[a]	5.33±1.43[b]	6.03±1.71[b]
YDE-030	4.93±1.15[a]	5.69±1.79[b]	6.65±2.17[b]
YDE-031	4.70±0.69[a]	5.63±1.97[b]	5.91±0.85[be]
YDE-032	4.94±1.04[a]	5.58±0.80[be]	5.03±0.93[b]
YDE-033	4.77±1.32[a]	4.99±1.20[b]	4.54±1.16[b]
YDE-034	4.88±1.07[a]	6.16±1.01[bd]	6.43±1.86[b]
YDE-035	4.92±1.18[a]	4.96±0.96[b]	6.25±0.79[bd]
YDE-036	4.83±1.07[a]	4.95±1.05[b]	5.13±1.03[b]
YDE-037	4.68±0.83[a]	4.98±0.66[b]	5.80±0.96[be]
YDE-039	4.81±1.27[a]	6.04±1.01[bd]	6.44±1.96[be]
YDE-040	4.77±0.91[a]	5.77±1.05[be]	8.63±1.53[cd]
YDE-041	4.87±1.19[a]	5.01±1.26[b]	6.25±2.15[b]
YDE-042	4.83±0.84[a]	6.30±1.08[bd]	7.97±1.48[bd]
YDE-043	4.86±0.81[a]	5.90±1.06[bd]	8.16±1.42[bd]

도 143



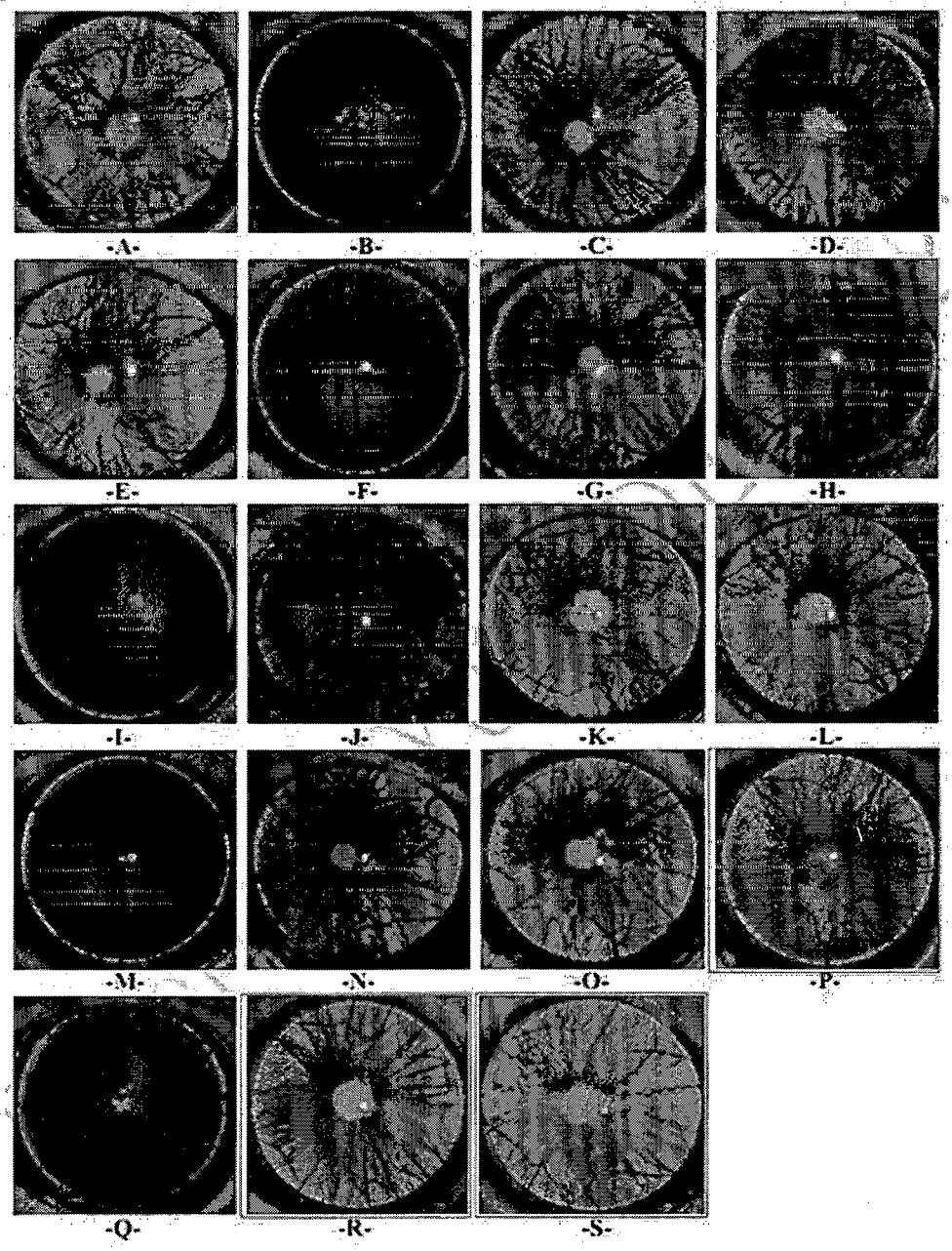
도 144



도 145

Groups	Items Fluorescent stained cornea areas (%)
Control	
Sham	2.62±1.71
ELGE	57.34±12.83[a]
Reference	
DS	35.40±13.32[a]
Test materials (0.3% solutions)	
YY-102	27.48±14.37[ac]
YDE-01	25.49±11.62[ac]
YDE-02	38.26±11.25[ac]
YDE-03	40.45±6.46[ac]
YDE-04	35.05±11.74[ac]
YDE-05	37.98±11.53[ac]
YDE-06	33.23±13.26[ac]
YDE-07	32.79±10.77[ac]
YDE-08	20.32±11.87[ac]
YDE-09	41.50±7.86[ac]
YDE-10	49.29±12.06[a]
YDE-11	18.11±11.61[ac]
YDE-12	31.01±11.38[ac]
YDE-13	32.24±7.84[ac]
YDE-14	31.15±10.87[ac]
YDE-15	15.95±6.48[bc]
YDE-16	24.57±10.34[ac]
YDE-17	39.76±7.42[ac]
YDE-18	38.19±10.96[ac]
YDE-19	40.39±12.57[ac]
YDE-20	47.84±13.47[a]
YDE-21	37.00±10.49[ac]
YDE-22	47.82±10.01[a]
YDE-23	26.51±8.18[ac]
YDE-24	30.63±10.41[ac]
YDE-25	47.10±11.45[a]
YDE-26	22.63±11.23[ac]
YDE-27	50.24±11.94[a]
YDE-28	41.17±10.25[ac]

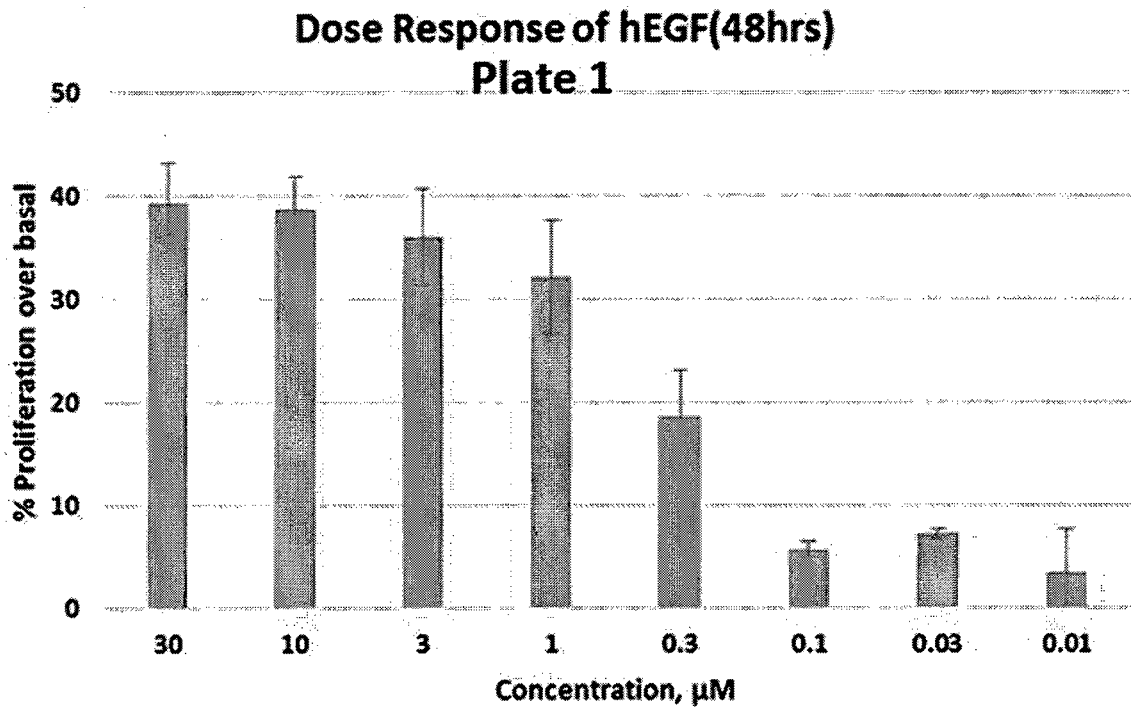
도 146



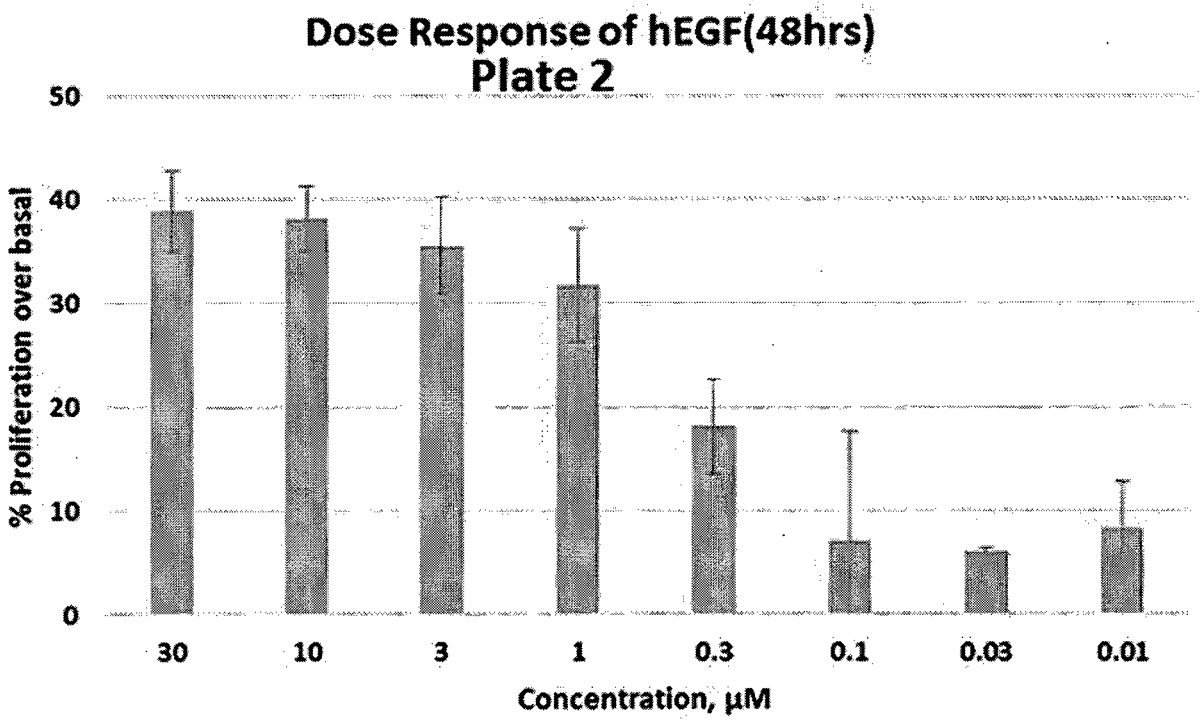
도 147

Groups	Items Fluorescent stained cornea areas (%)
Control	
Sham	1.53±0.65
ELGE	66.71±10.02[b]
Reference	
DS	30.03±10.97[bd]
YY-101	33.80±11.11[bd]
YY-102	27.89±7.10[bd]
Test materials (0.3% solutions)	
YDE-029	63.45±11.57[b]
YDE-030	30.60±13.61[bd]
YDE-031	33.35±11.01[bd]
YDE-032	58.90±19.81[b]
YDE-033	60.55±21.22[b]
YDE-034	32.17±12.94[bd]
YDE-035	27.62±6.51[bd]
YDE-036	57.87±22.91[b]
YDE-037	36.30±9.75[bd]
YDE-039	29.94±11.40[bd]
YDE-040	18.33±9.41[bd]
YDE-041	46.38±26.65[b]
YDE-042	20.72±11.37[bd]
YDE-043	19.04±7.36[bd]

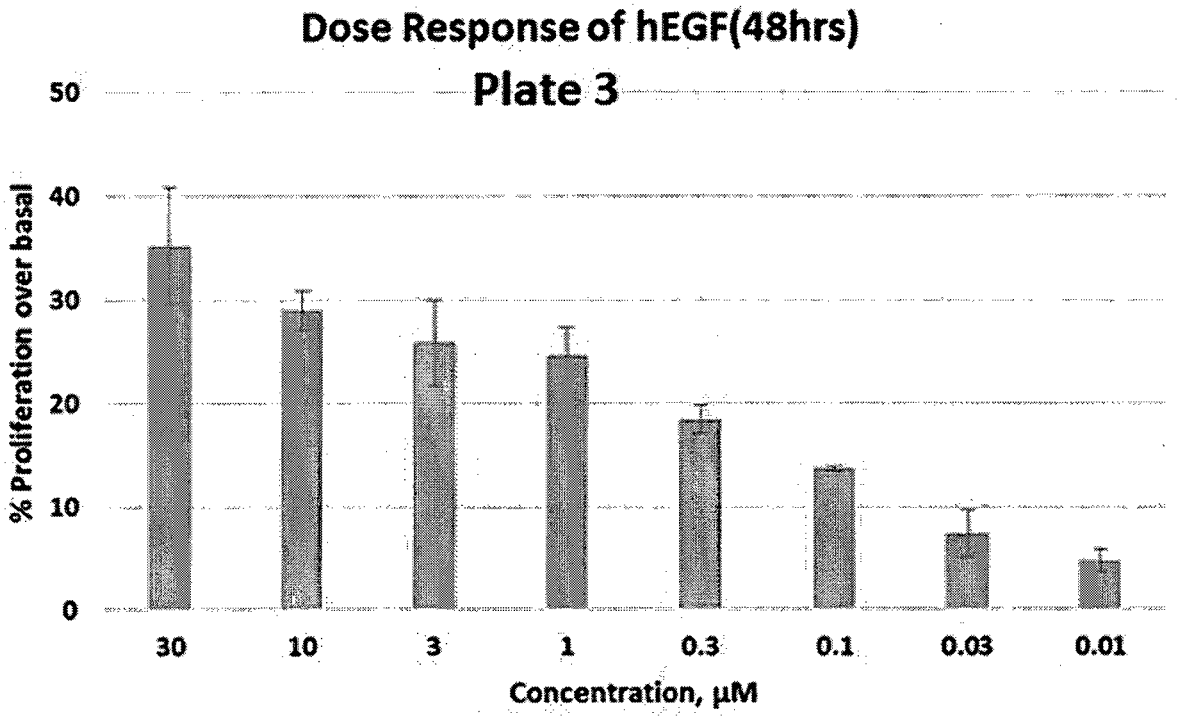
도 148


Dose Response of hEGF(48hrs)
Plate 1
% Proliferation over basal
50
40
30
20
10
0
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

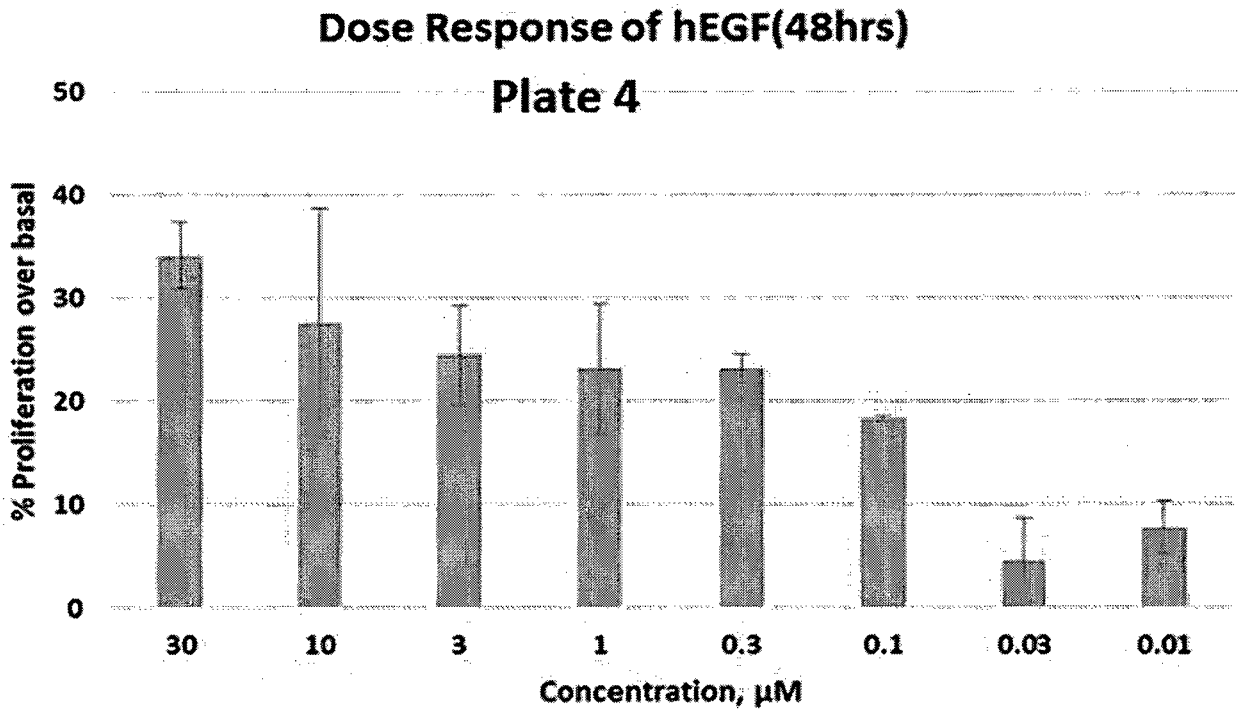
도 149


Dose Response of hEGF(48hrs)
Plate 2
% Proliferation over basal
50
40
30
20
10
0
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

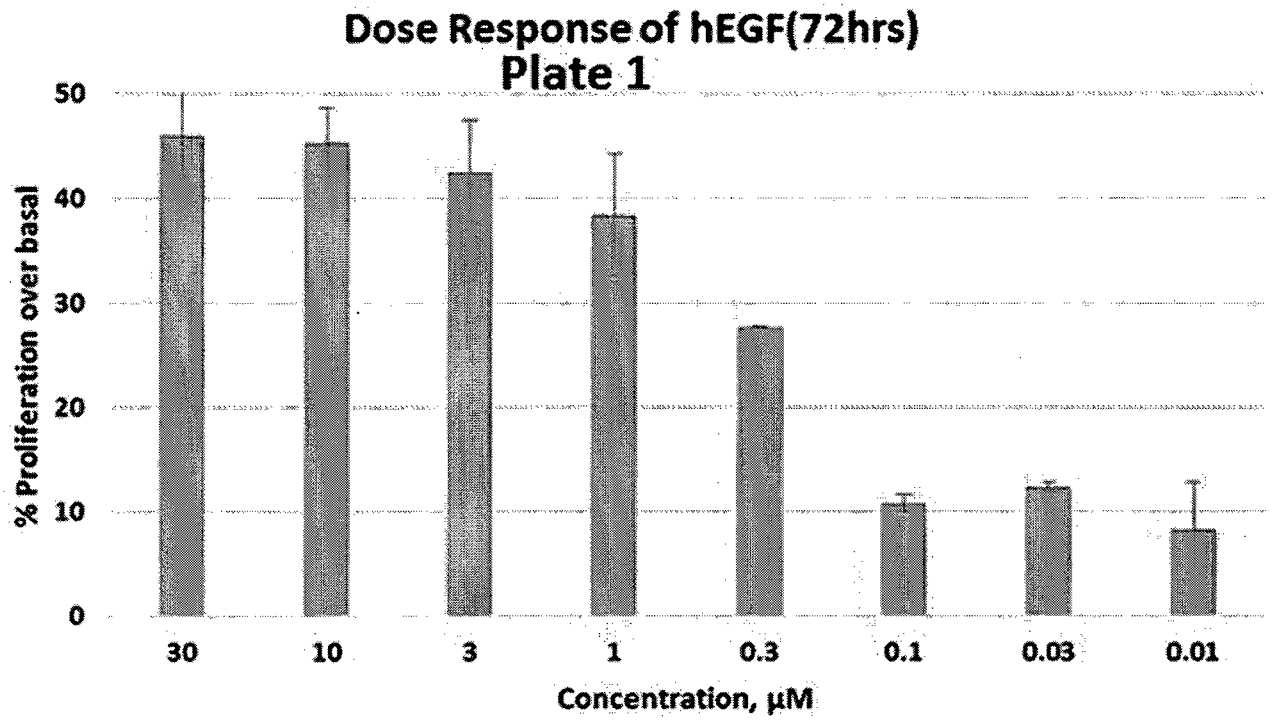
도 150


Dose Response of hEGF(48hrs)
Plate 3
% Proliferation over basal
50
40
30
20
10
0
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

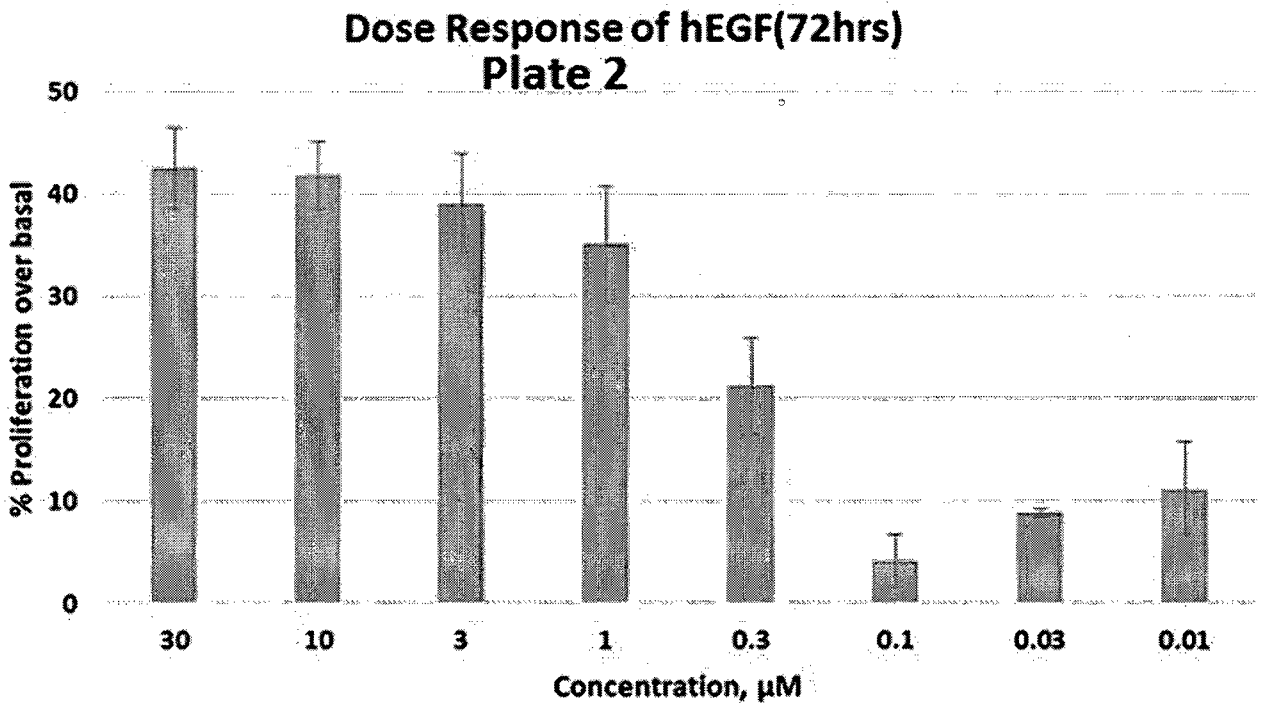
도 151


Dose Response of hEGF(48hrs)
Plate 4
% Proliferation over basal
50
40
30
20
10
0
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

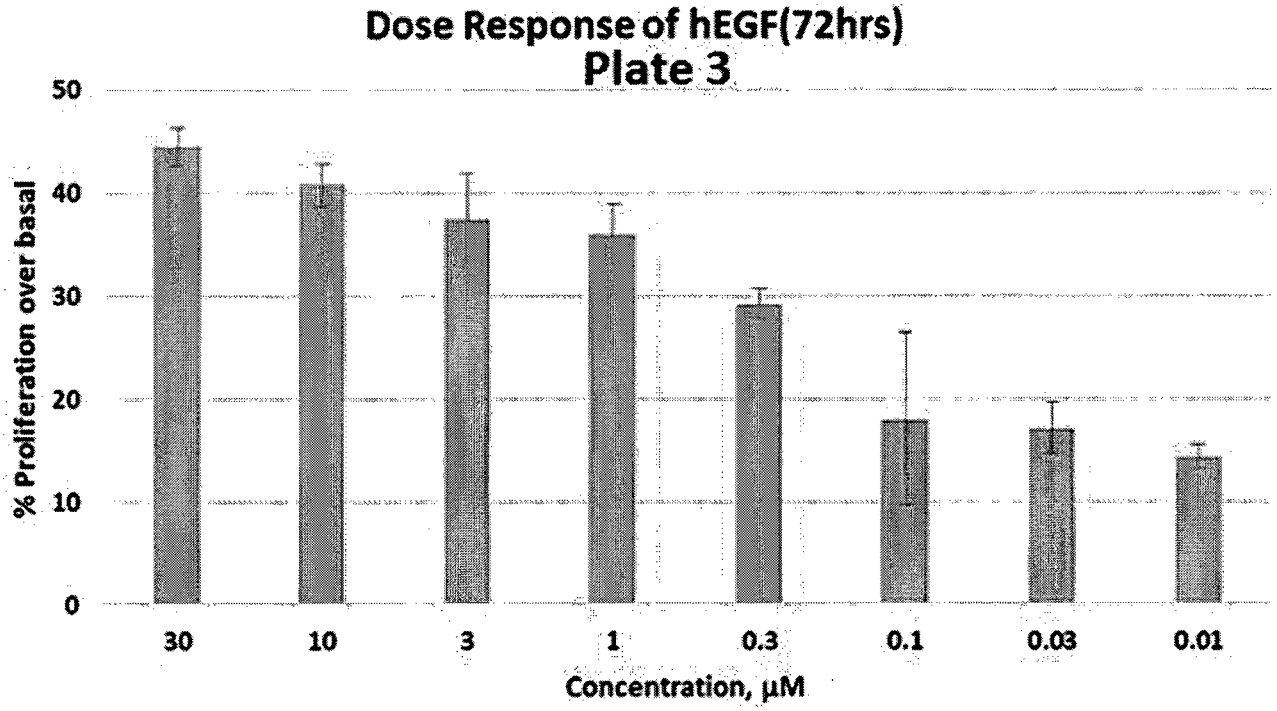
도 152


Dose Response of hEGF(72hrs)
Plate 1
% Proliferation over basal
50
40
30
20
10
0
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

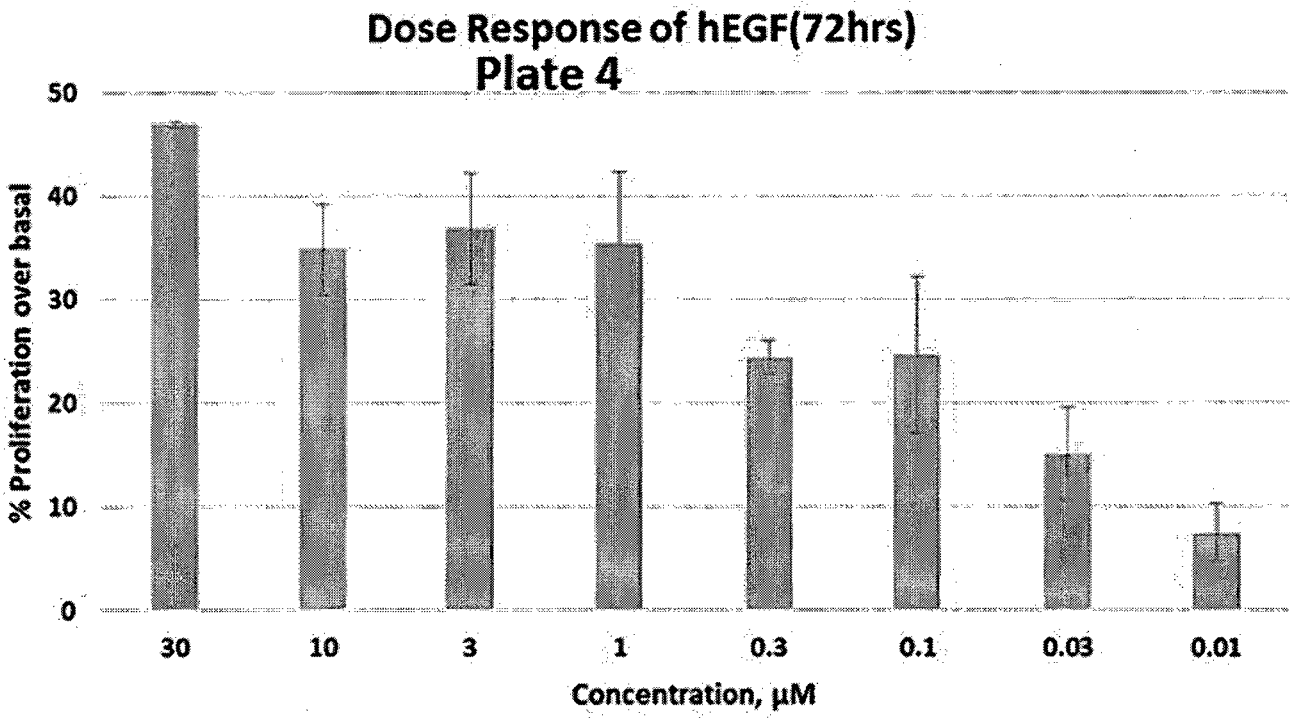
도 153


Dose Response of hEGF(72hrs)
Plate 2
% Proliferation over basal
50
40
30
20
10
0
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

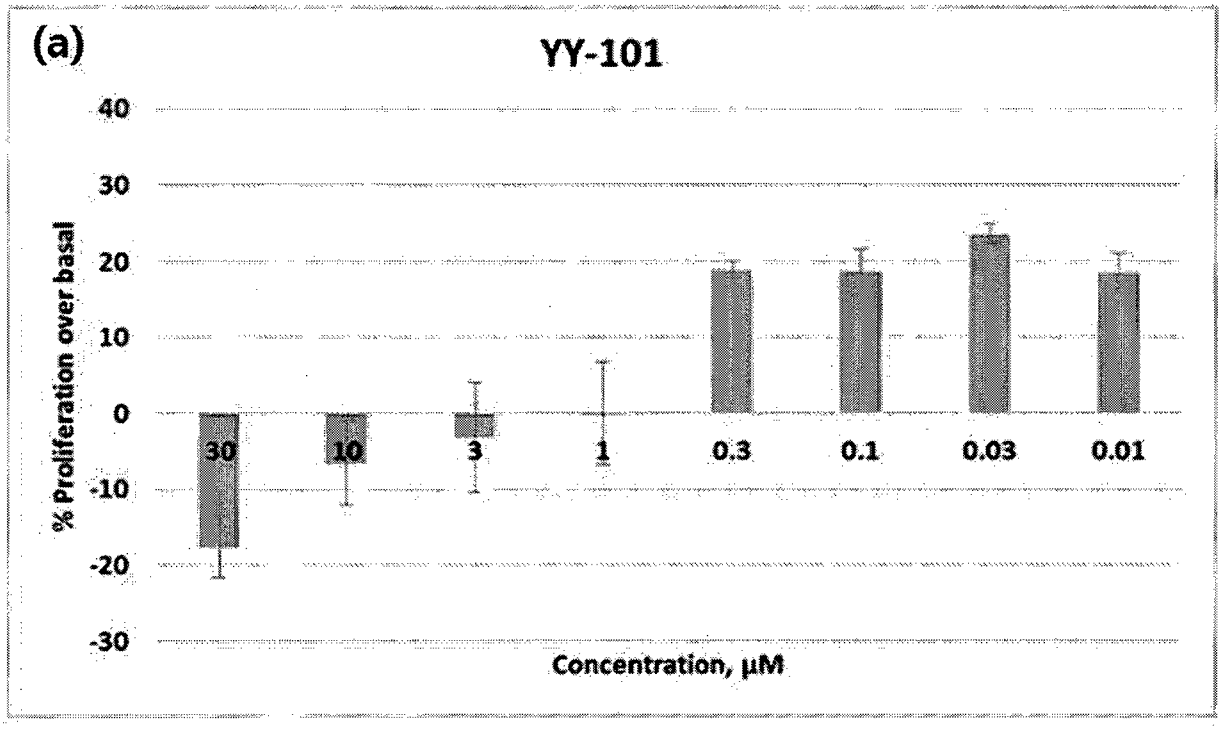
도 154

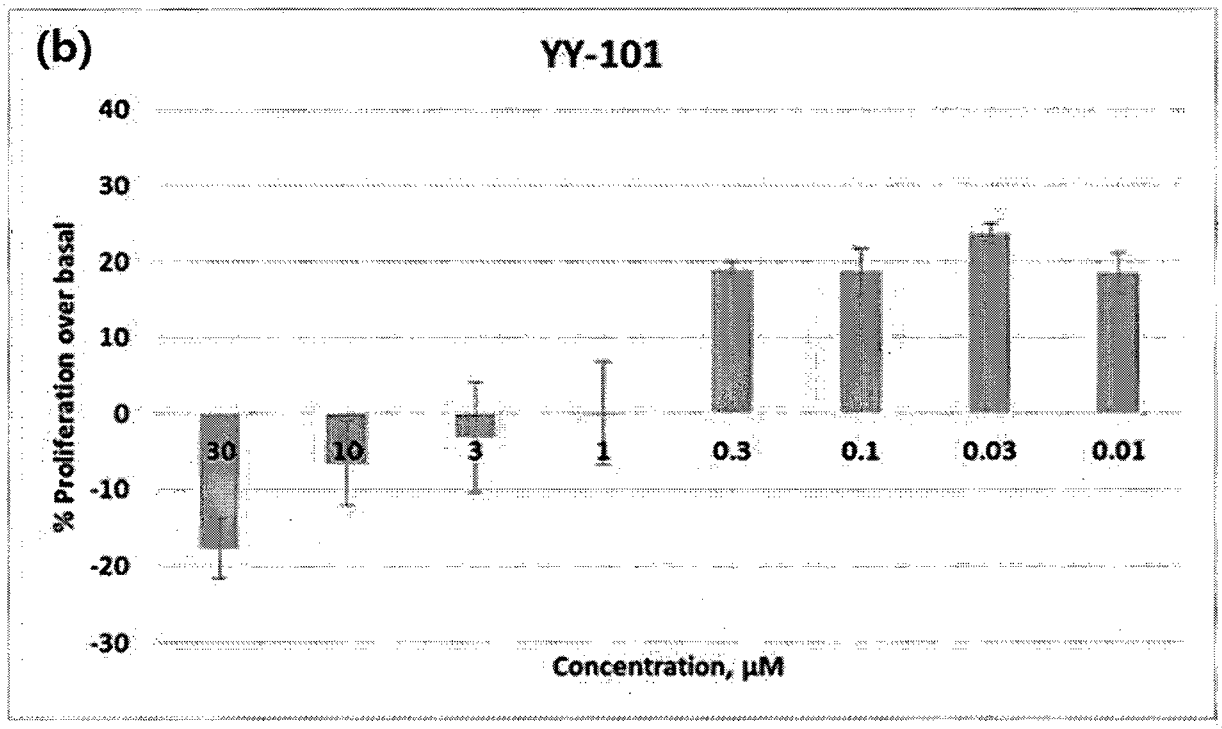

Dose Response of hEGF(72hrs)
Plate 3
% Proliferation over basal
50
40
30
20
10
0
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

도 155

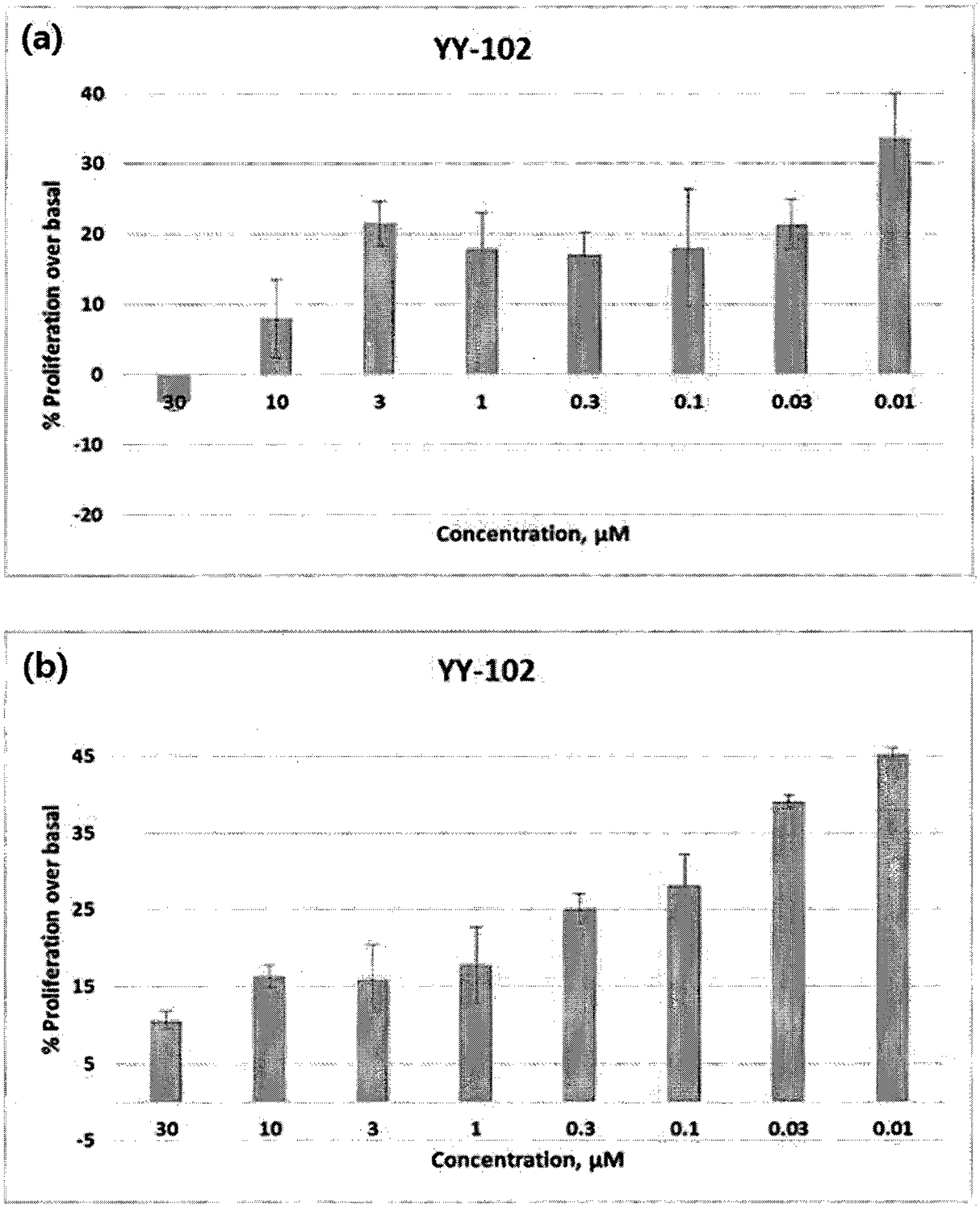

Dose Response of hEGF(72hrs)
Plate 4
% Proliferation over basal
50
40
30
20
10
0
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

도 156

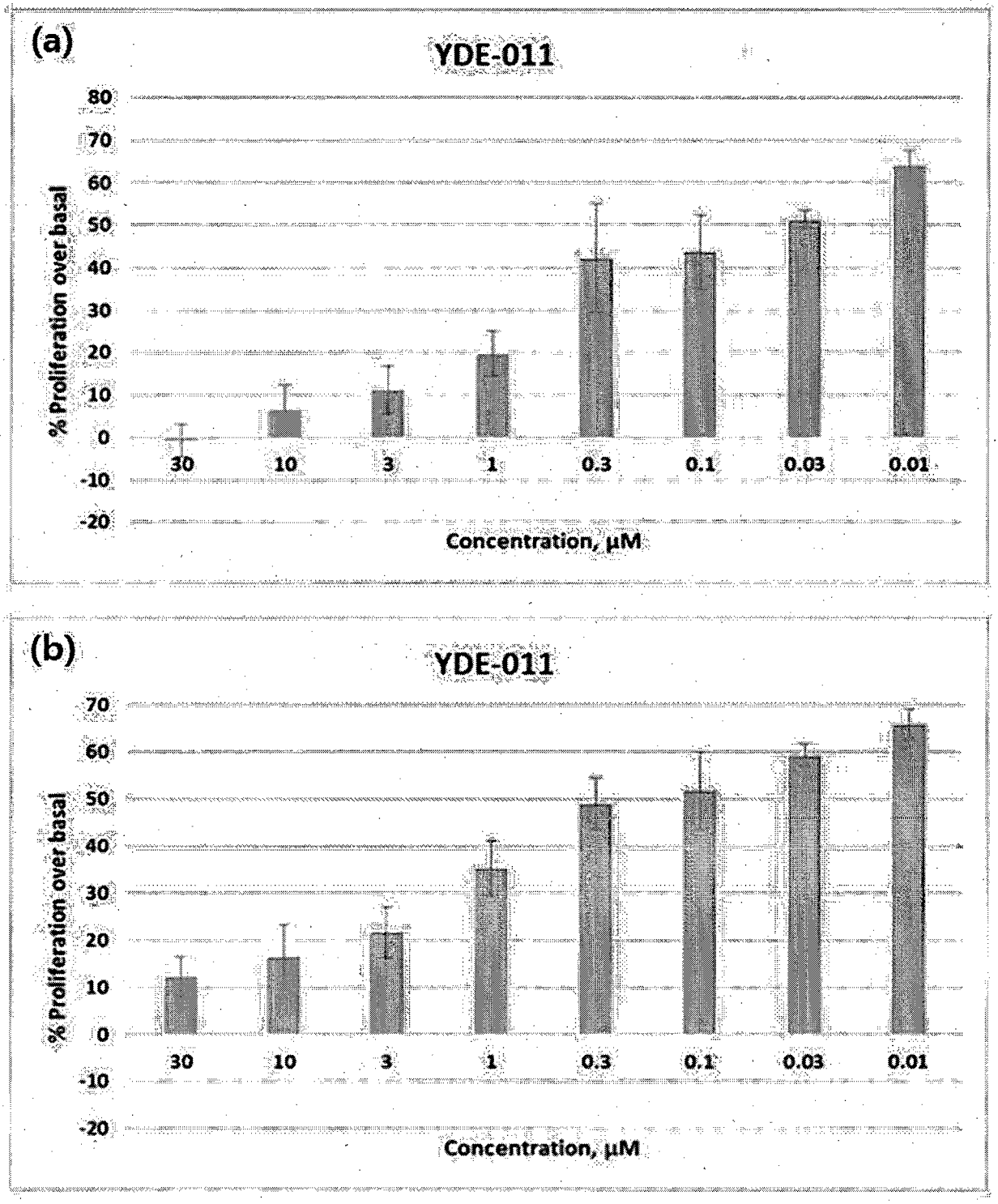

(a)
YY-101
40
30
20
10
0
-10
-20
-30
% Proliferation over basal
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM


(b)
YY-101
40
30
20
10
0
-10
-20
-30
% Proliferation over basal
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

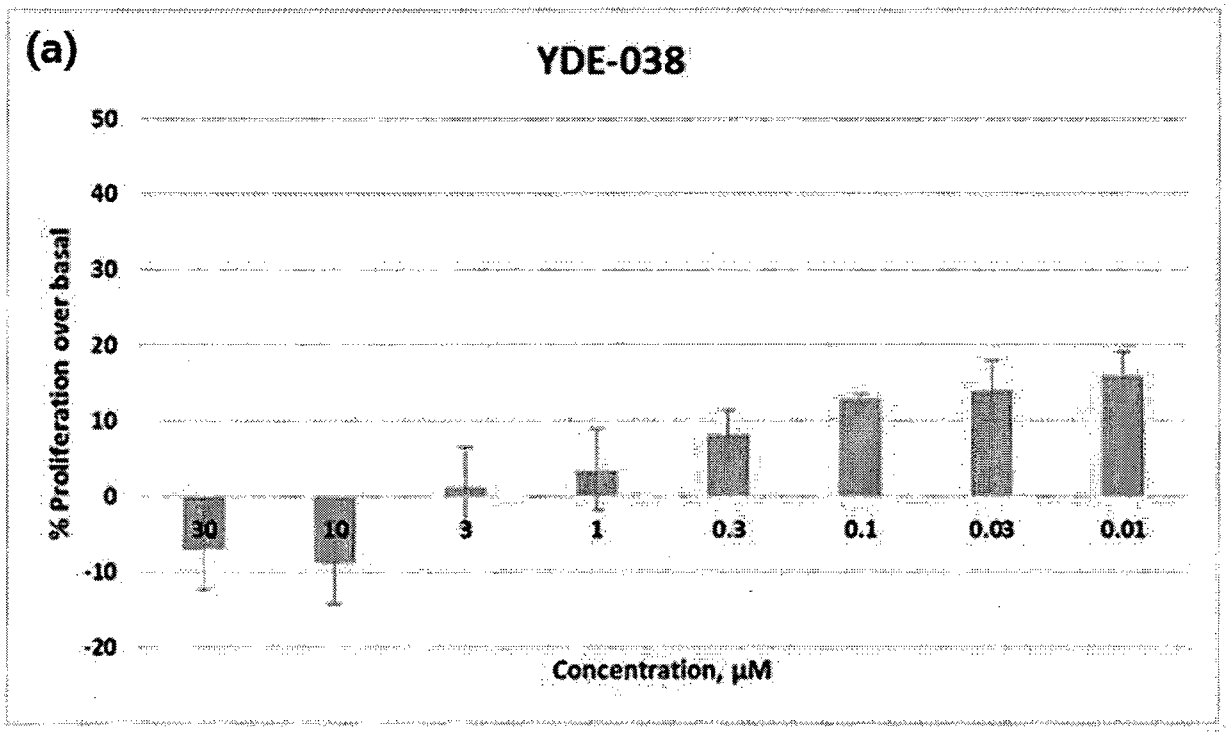
도 157

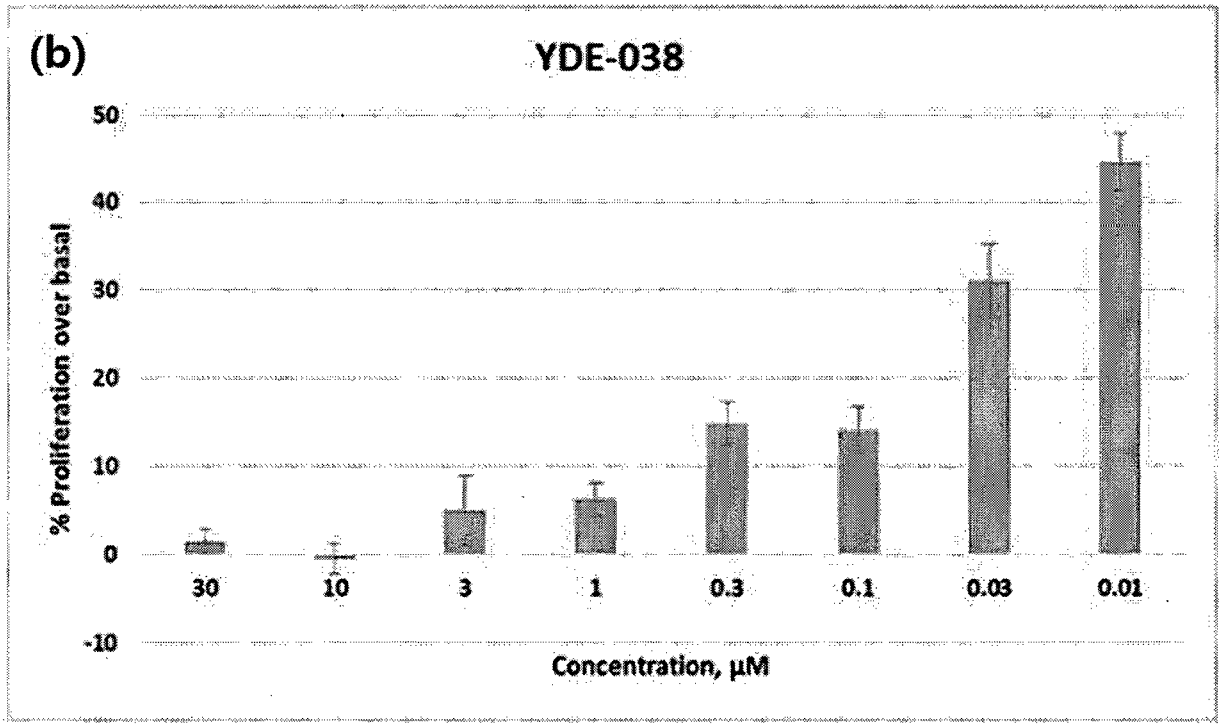

(a)
YY-102
% Proliferation over basal
40
30
20
10
0
-10
-20
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM
(b)
YY-102
% Proliferation over basal
45
35
25
15
5
-5
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

도 158

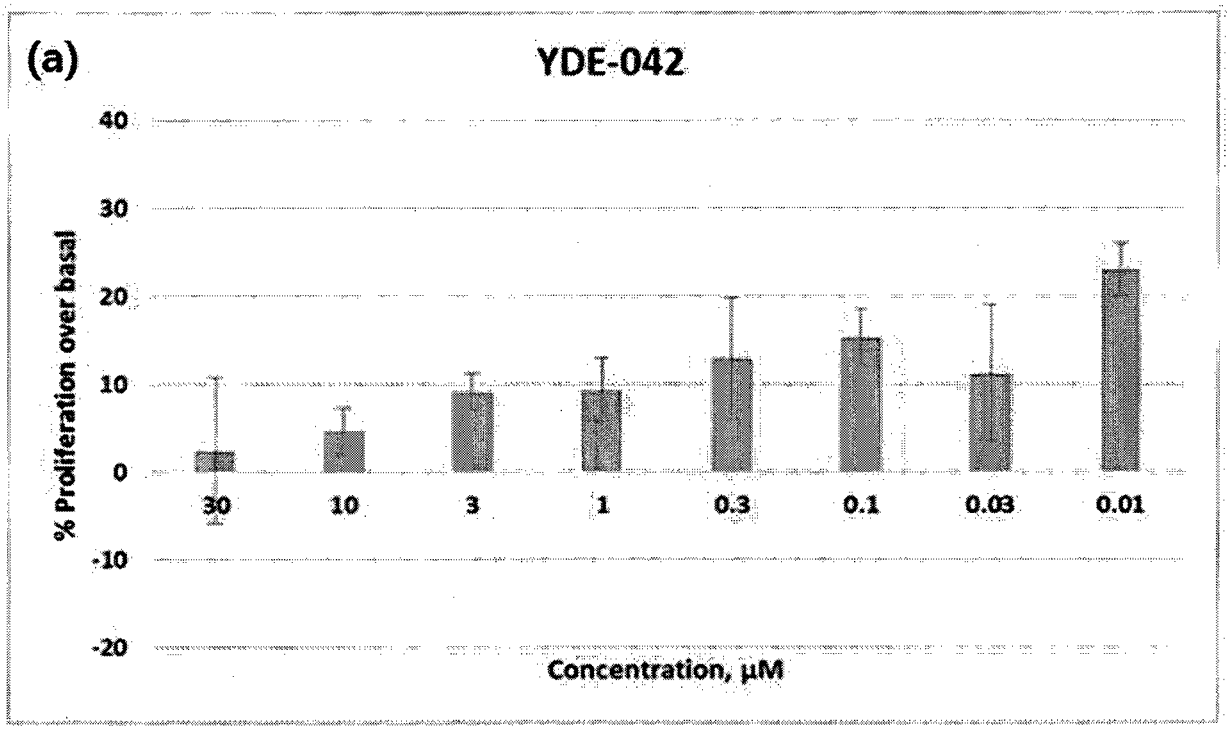

(a)
YDE-011
% Proliferation over basal
80
70
60
50
40
30
20
10
0
-10
-20
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM
(b)
YDE-011
% Proliferation over basal
70
60
50
40
30
20
10
0
-10
-20
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

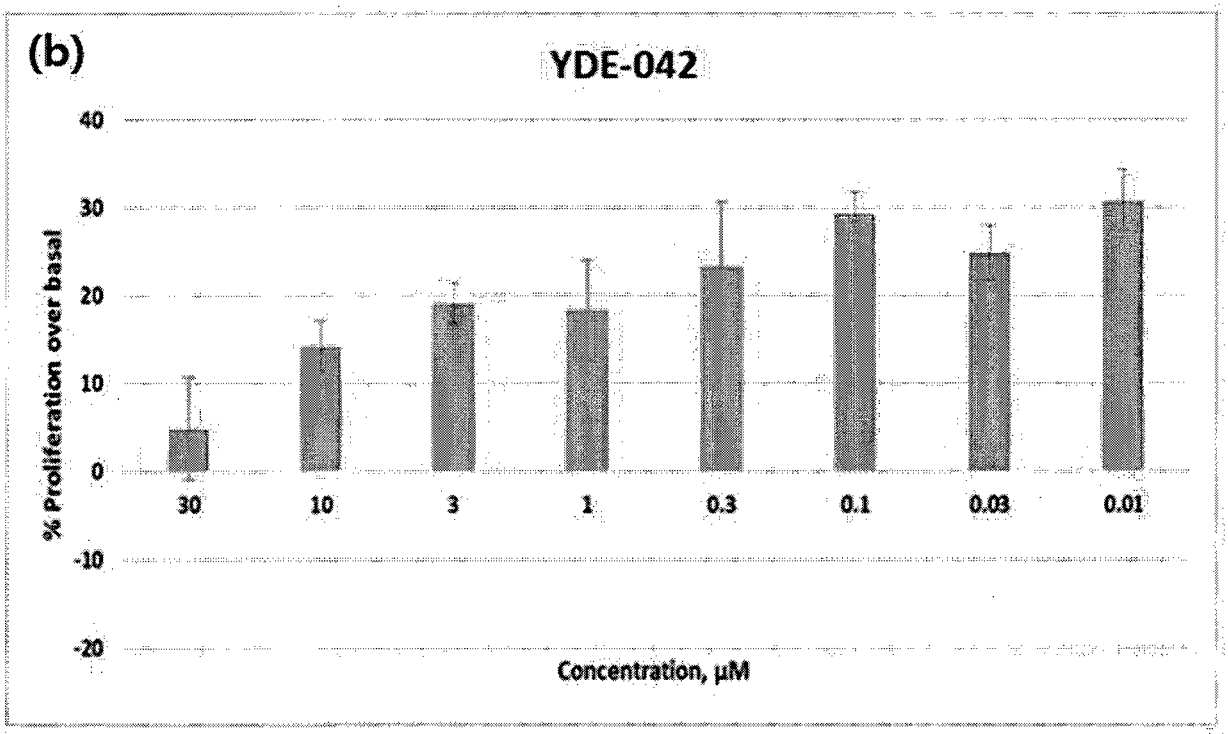
도 159


(a)
YDE-038
% Proliferation over basal
50
40
30
20
10
0
-10
-20
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

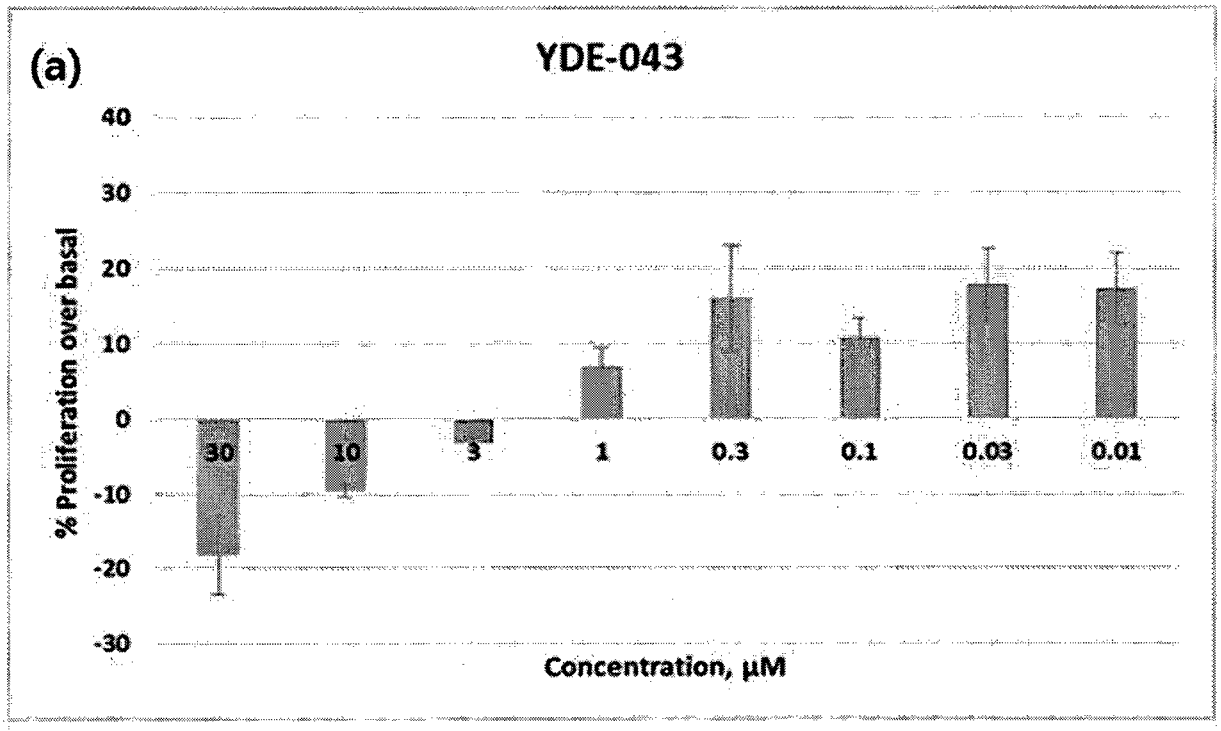

(b)
YDE-038
% Proliferation over basal
50
40
30
20
10
0
-10
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

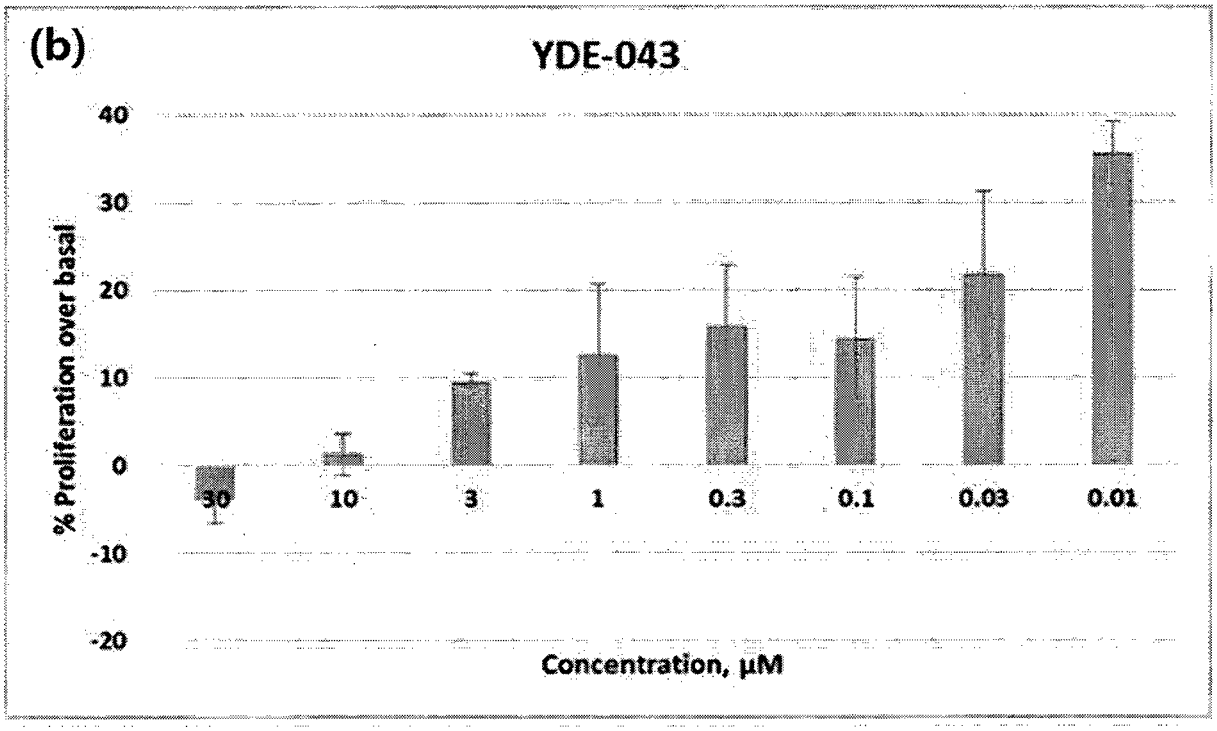
도 160


(a)
YDE-042
40
30
20
10
0
-10
-20
% Proliferation over basal
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

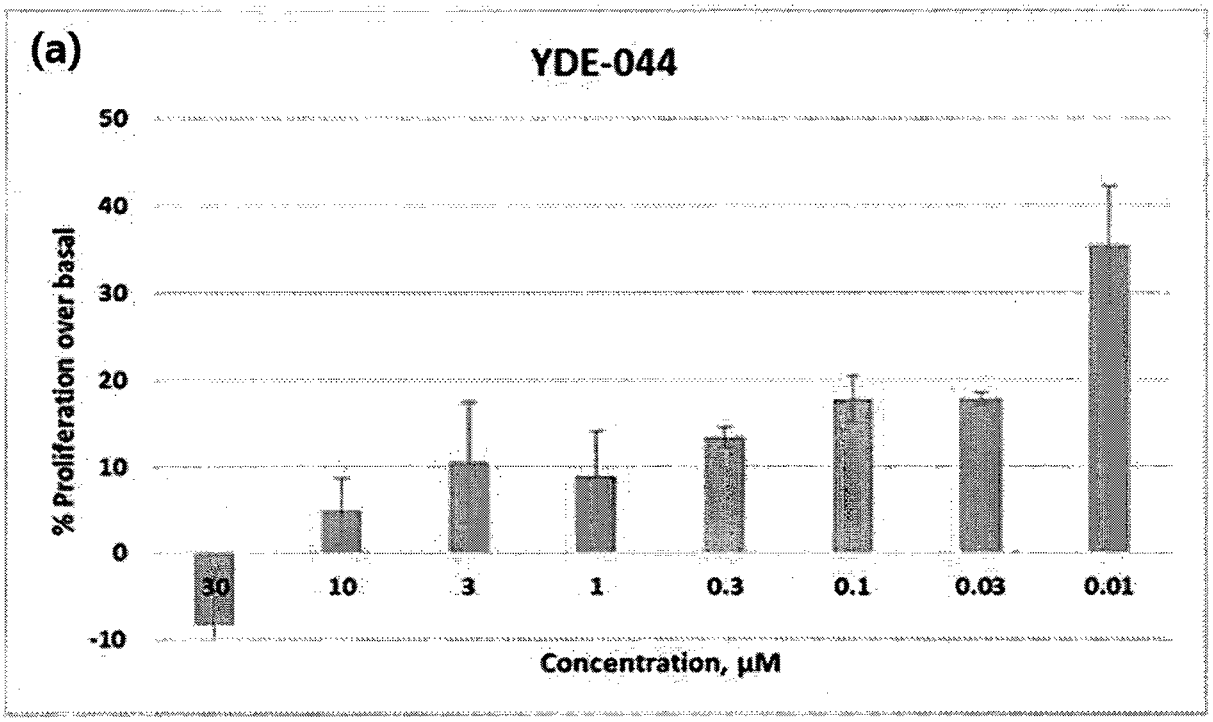

(b)
YDE-042
40
30
20
10
0
-10
-20
% Proliferation over basal
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

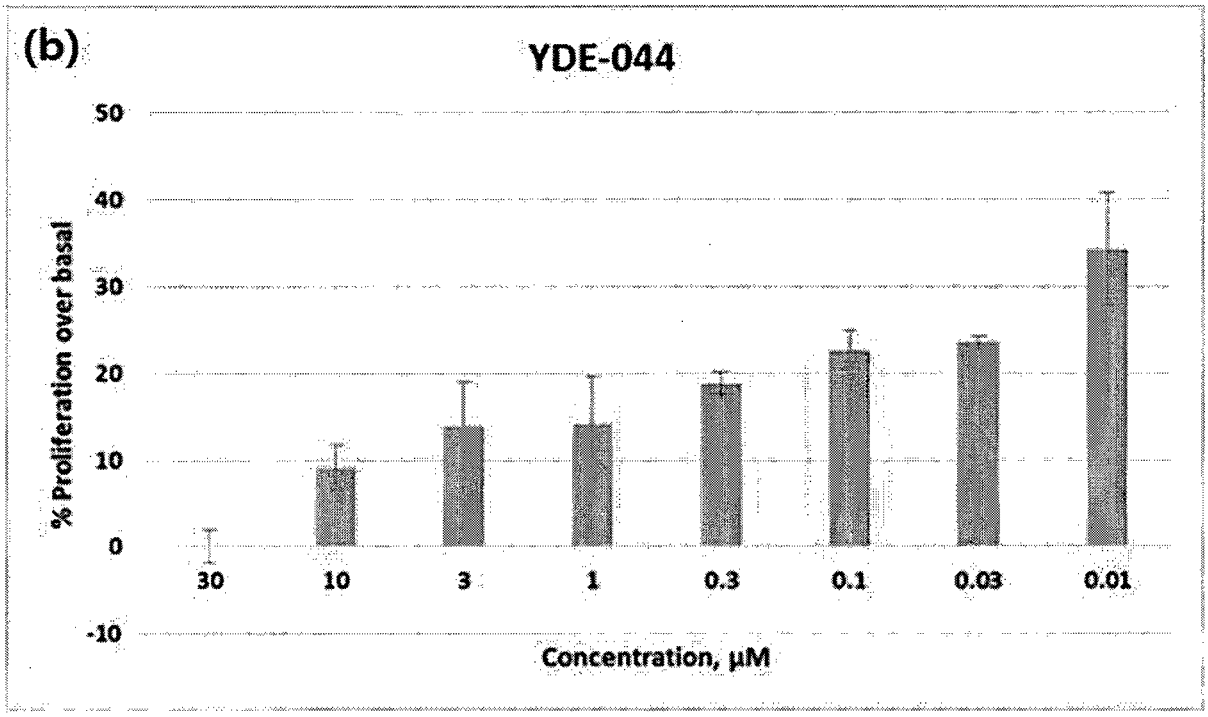
도 161


(a)
YDE-043
% Proliferation over basal
40
30
20
10
0
-10
-20
-30
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

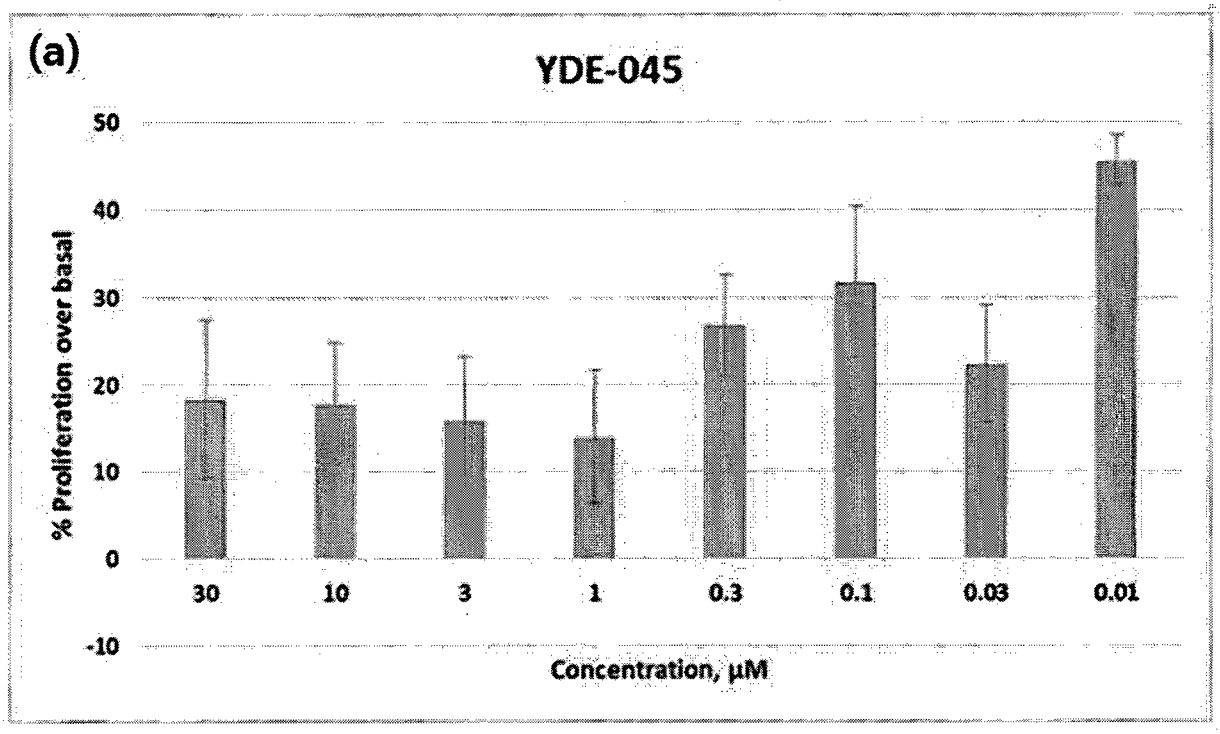

(b)
YDE-043
% Proliferation over basal
40
30
20
10
0
-10
-20
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

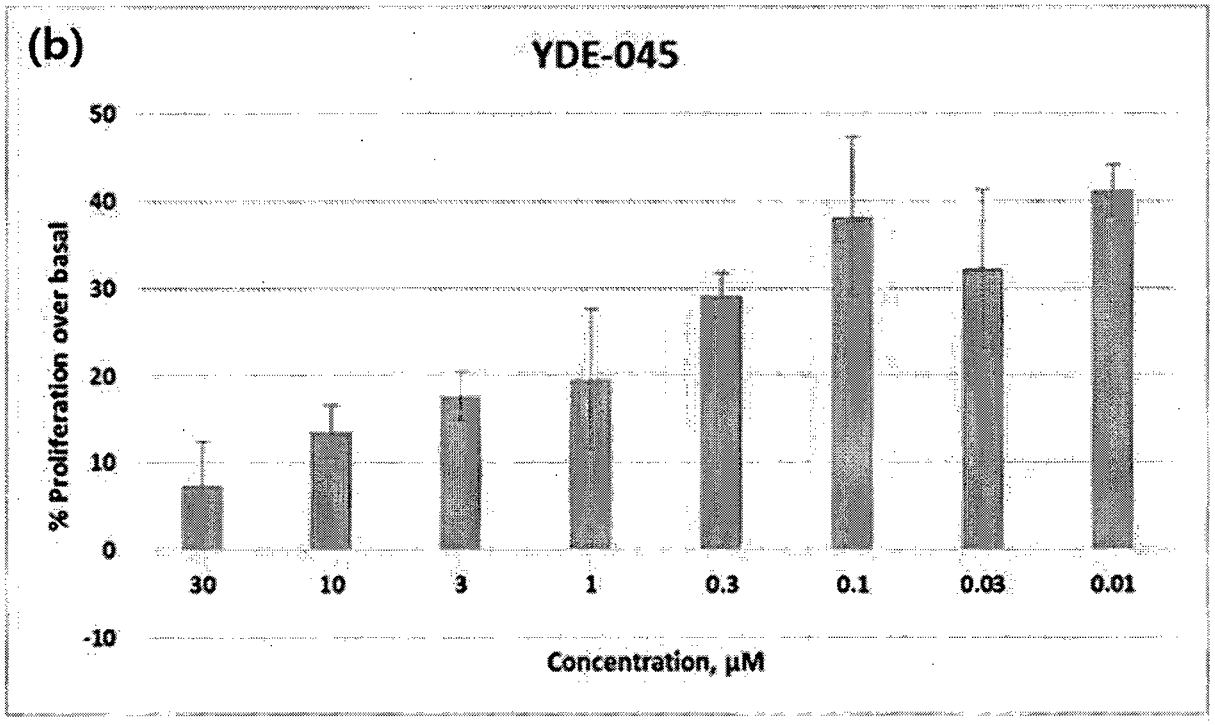
도 162


(a)
YDE-044
% Proliferation over basal
50
40
30
20
10
0
-10
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

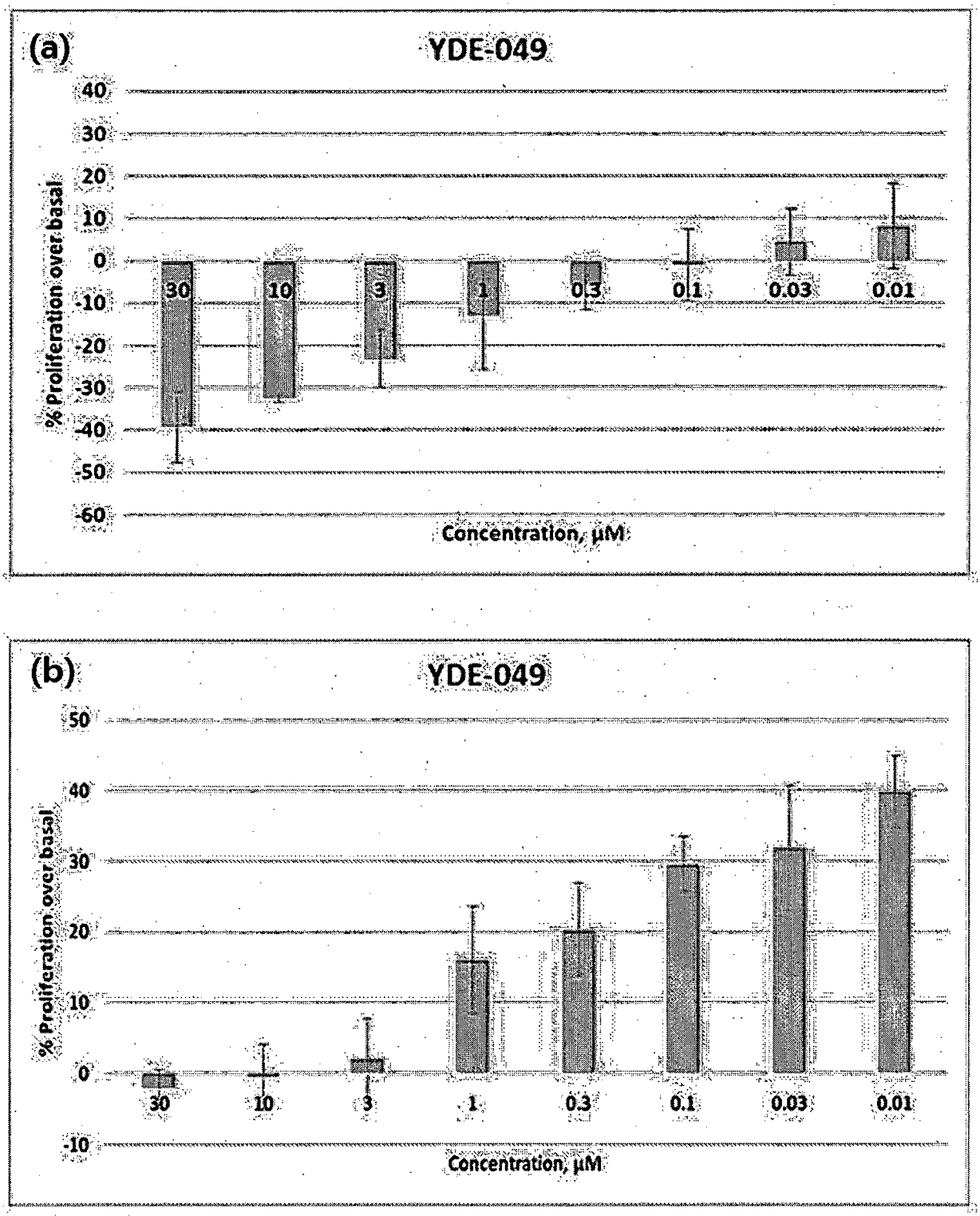

(b)
YDE-044
% Proliferation over basal
50
40
30
20
10
0
-10
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

도 163

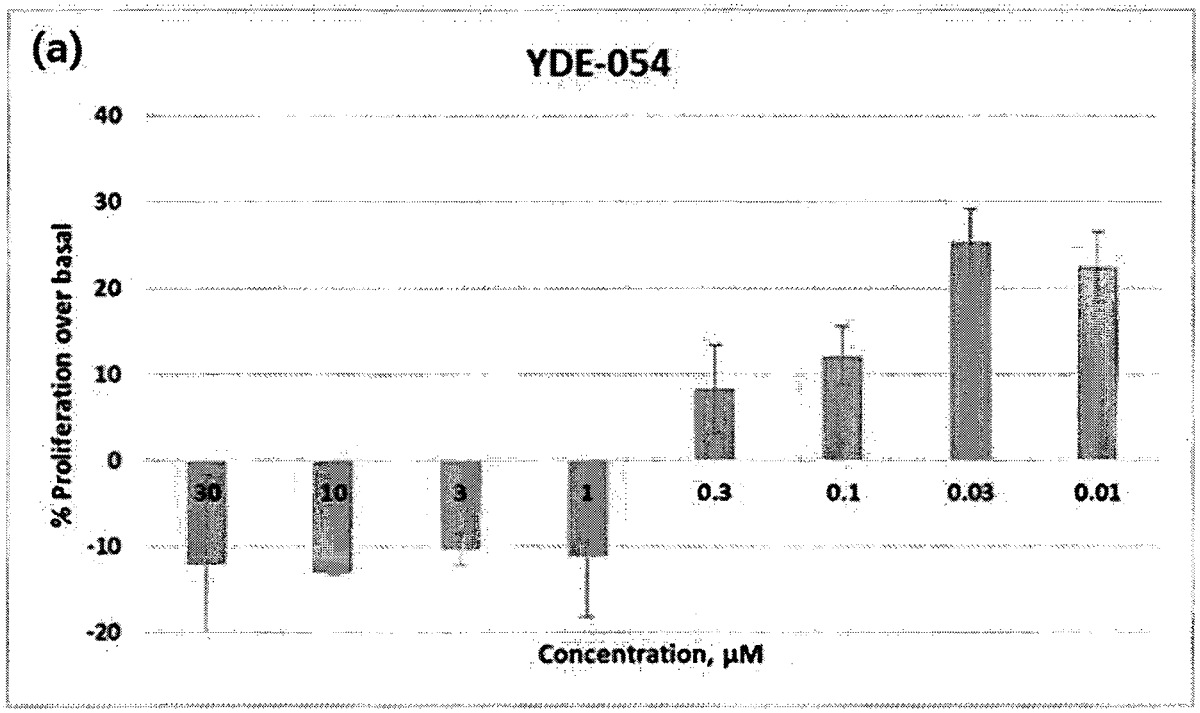

(a)
YDE-045
% Proliferation over basal
50
40
30
20
10
0
-10
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

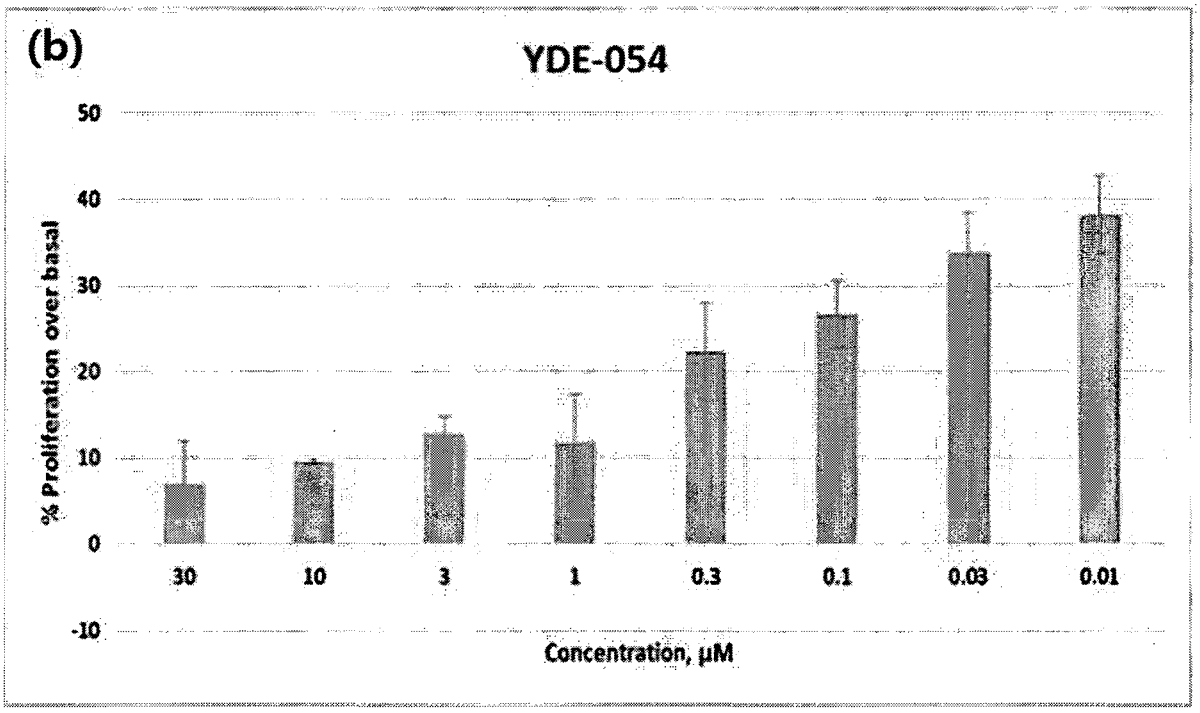

(b)
YDE-045
% Proliferation over basal
50
40
30
20
10
0
-10
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

도 164

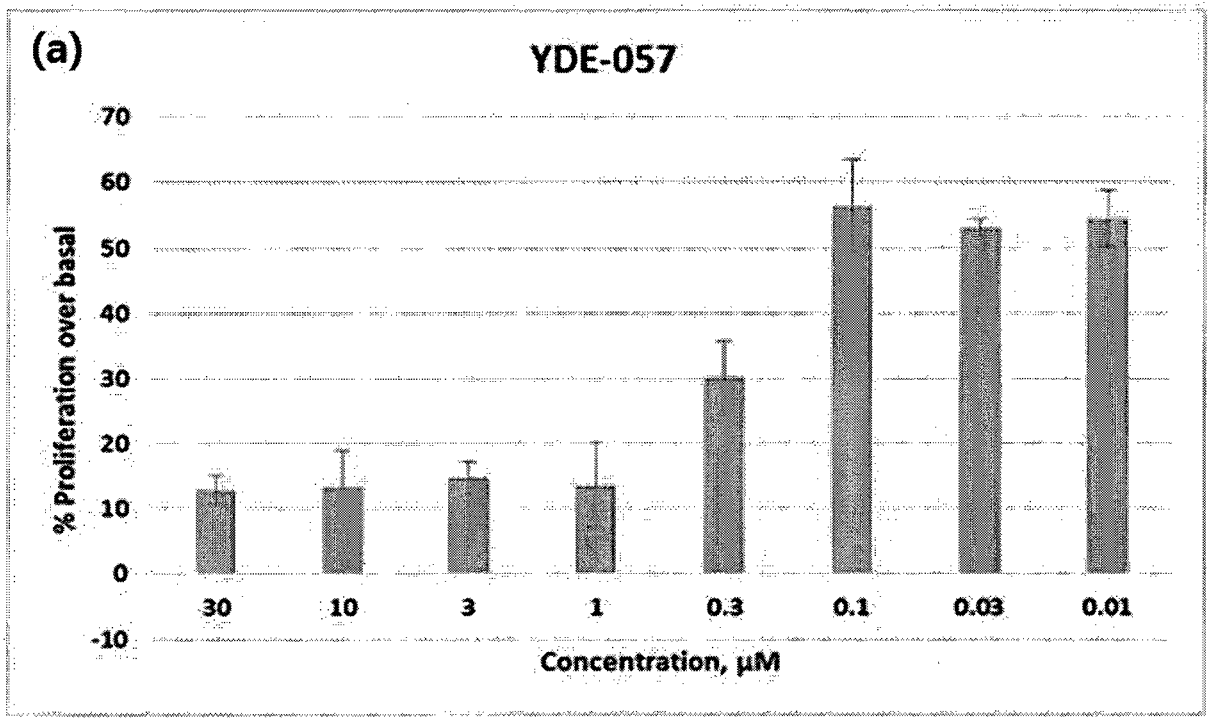

(a)
YDE-049
% Proliferation over basal
40
30
20
10
0
-10
-20
-30
-40
-50
-60
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM
(b)
YDE-049
% Proliferation over basal
50
40
30
20
10
0
-10
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

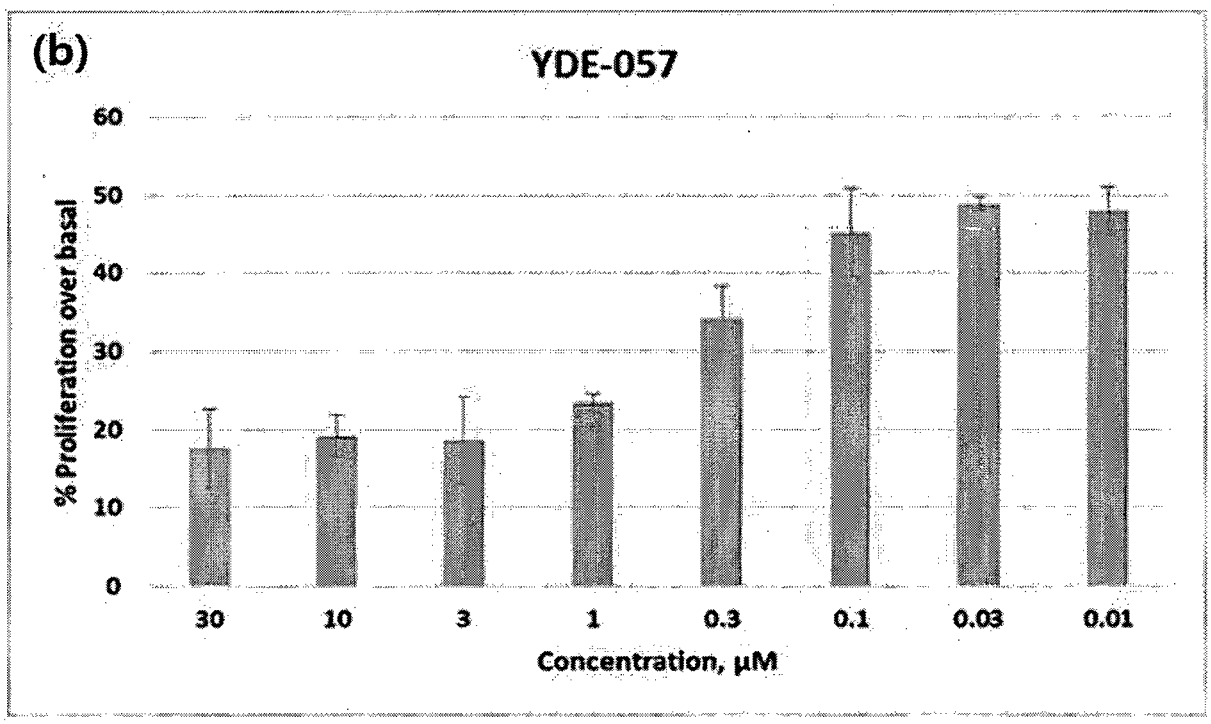
도 165


(a)
YDE-054
% Proliferation over basal
40
30
20
10
0
-10
-20
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

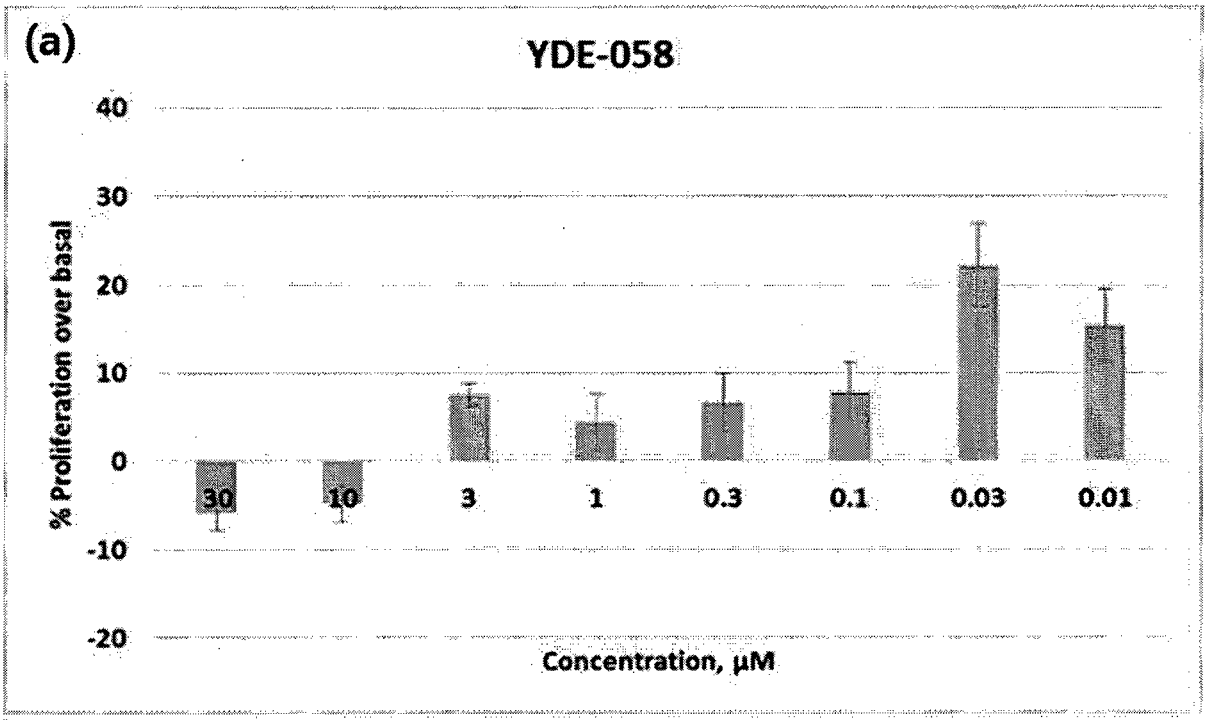

(b)
YDE-054
% Proliferation over basal
50
40
30
20
10
0
-10
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

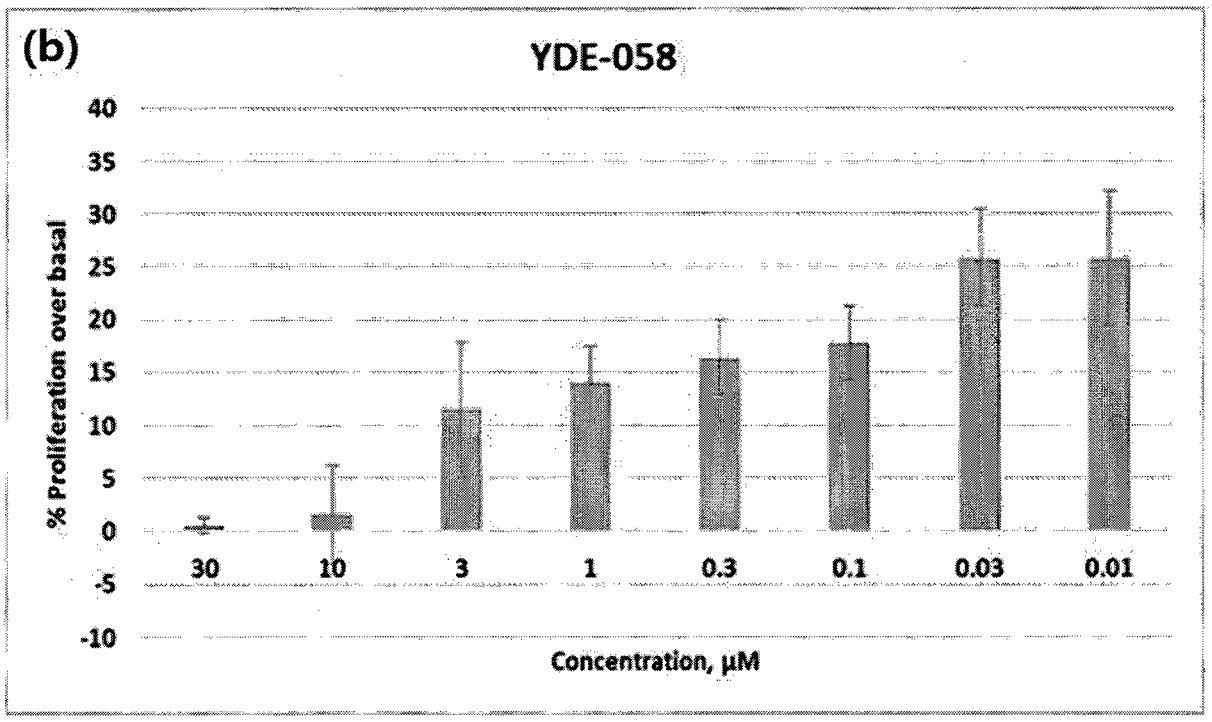
도 166


(a)
YDE-057
% Proliferation over basal
70
60
50
40
30
20
10
0
-10
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

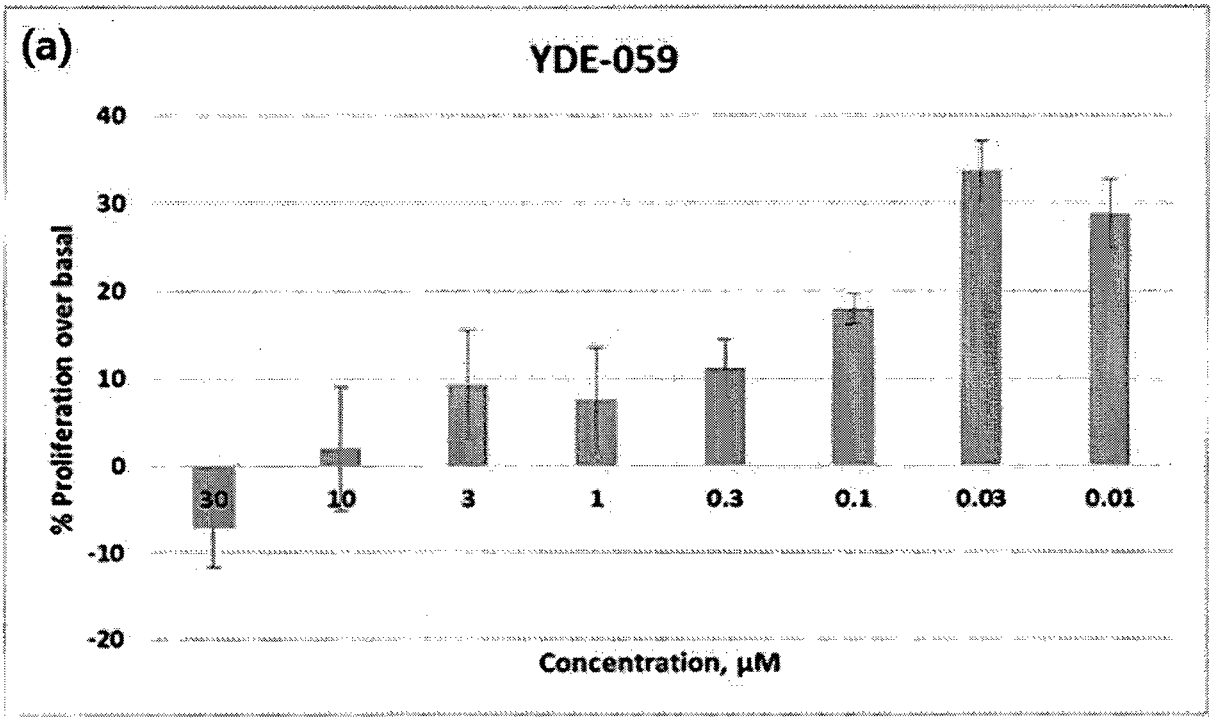

(b)
YDE-057
% Proliferation over basal
60
50
40
30
20
10
0
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

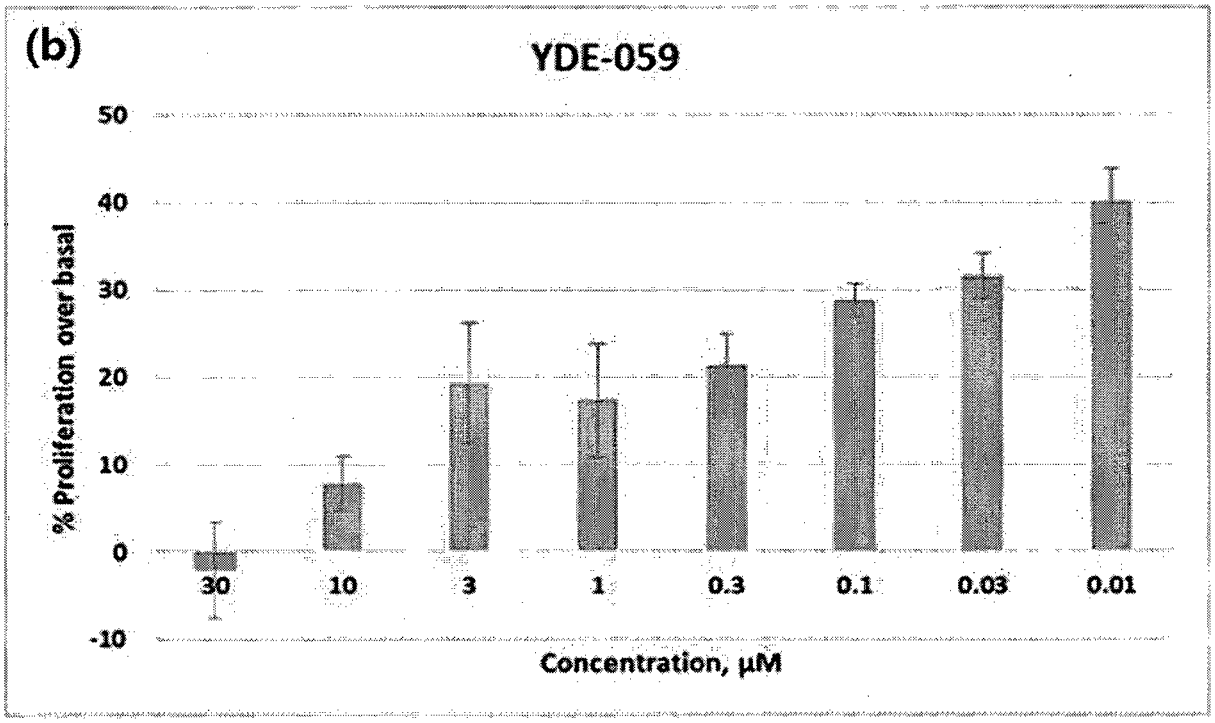
도 167


(a)
YDE-058
% Proliferation over basal
40
30
20
10
0
-10
-20
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

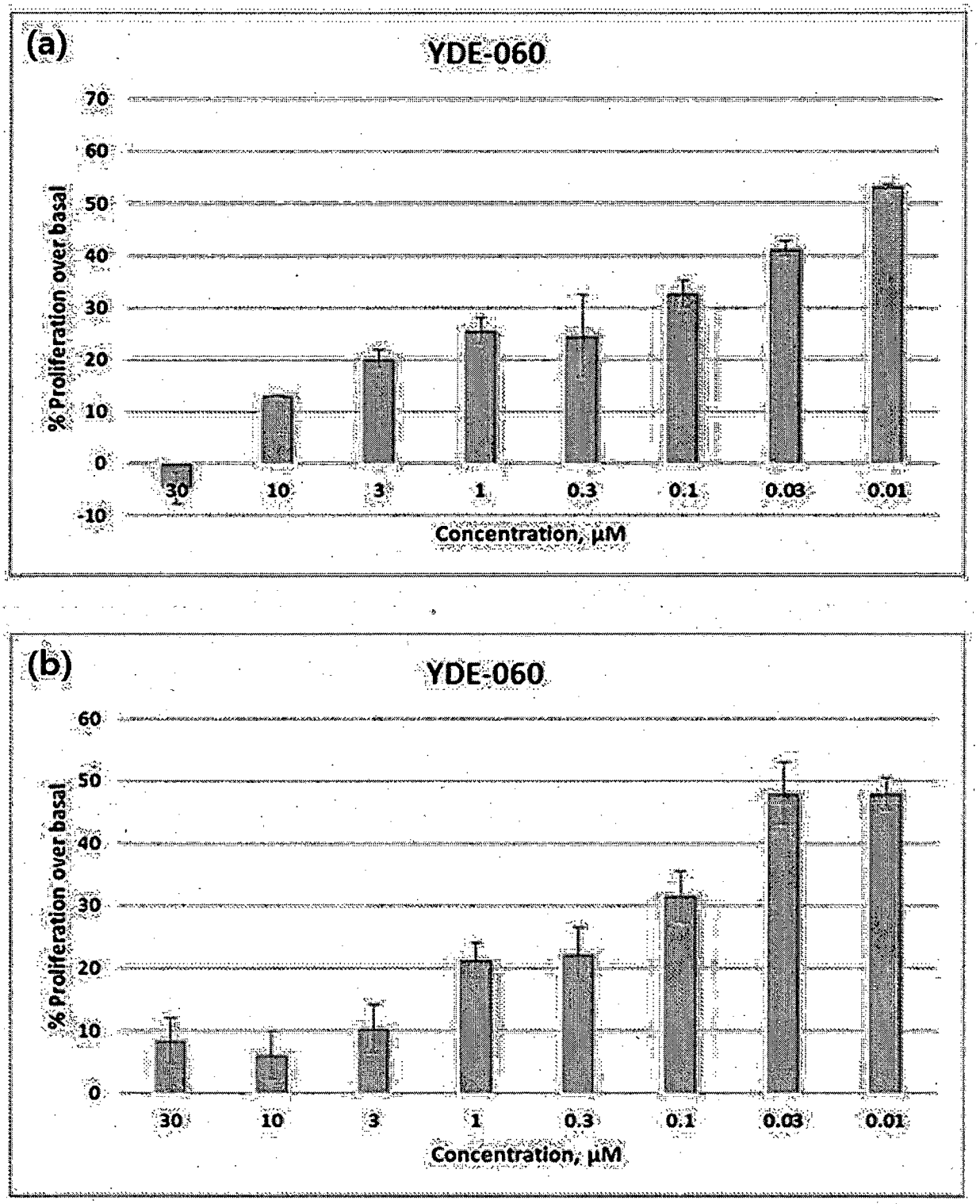

(b)
YDE-058
% Proliferation over basal
40
35
30
25
20
15
10
5
0
-5
-10
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

도 168

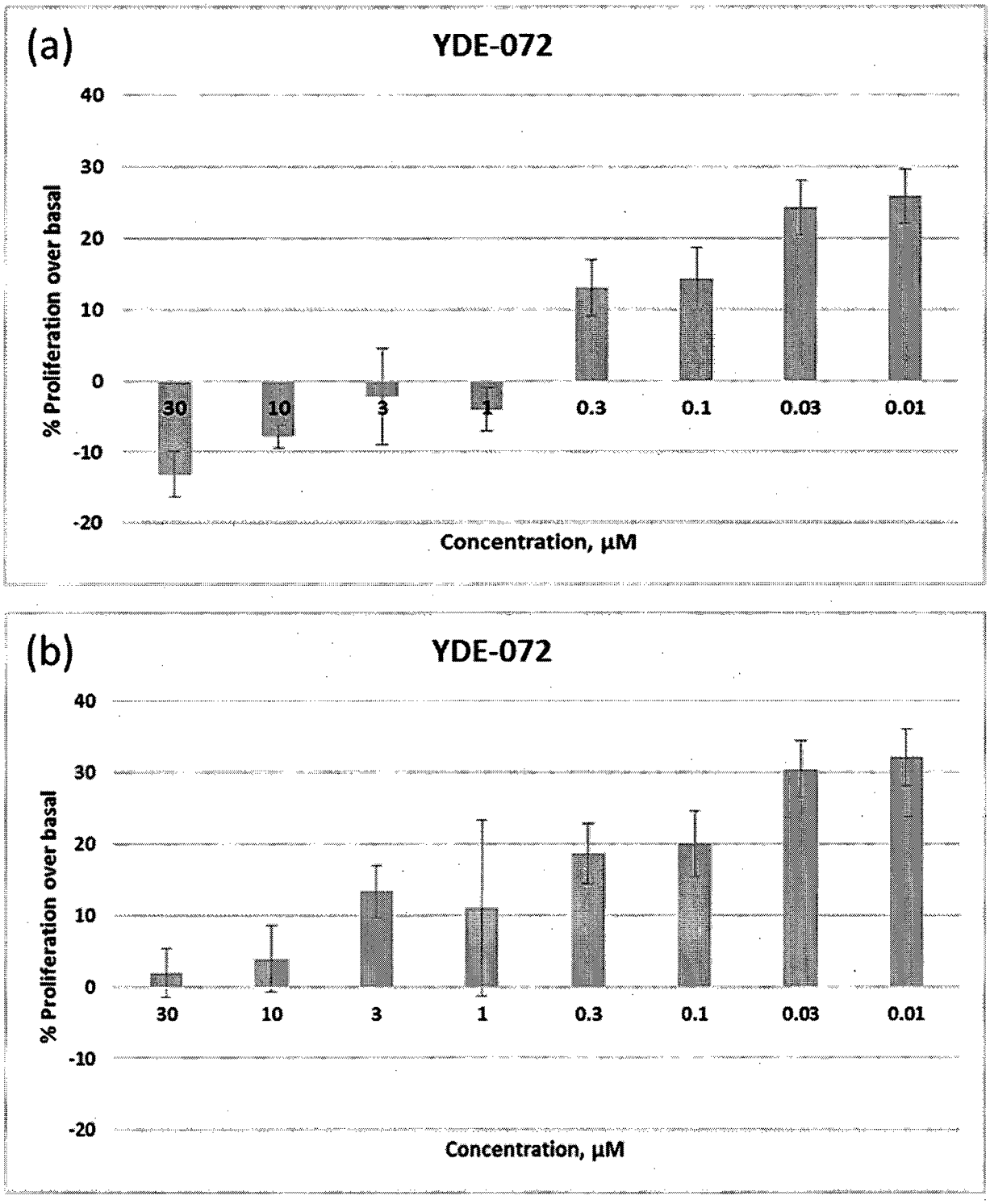

(a)
YDE-059
% Proliferation over basal
40
30
20
10
0
-10
-20
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM


(b)
YDE-059
% Proliferation over basal
50
40
30
20
10
0
-10
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

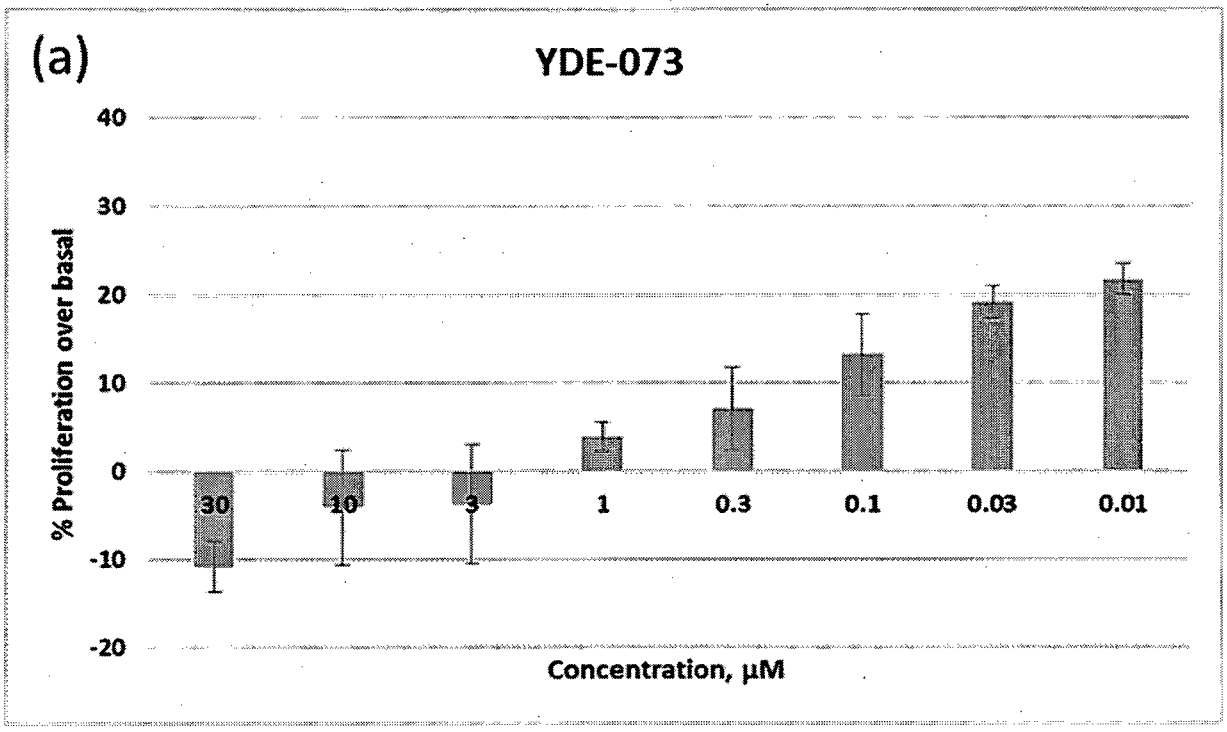
도 169

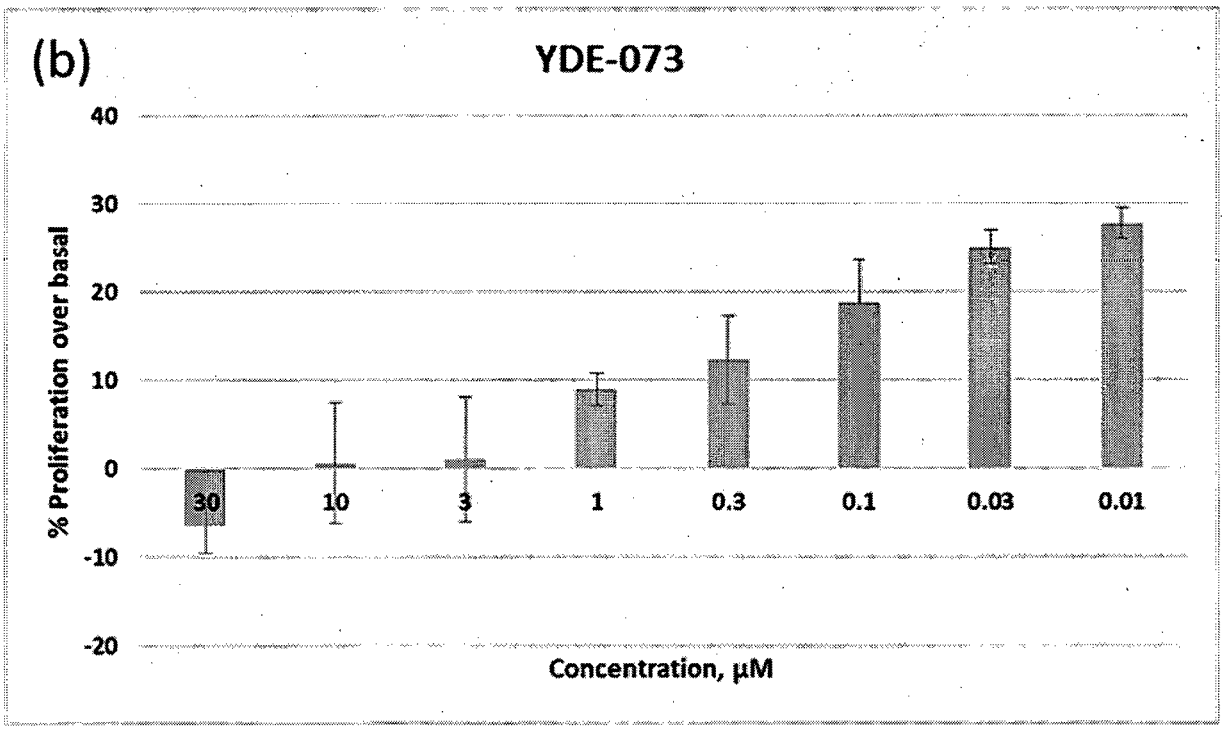

(a)
YDE-060
% Proliferation over basal
70
60
50
40
30
20
10
0
-10
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM
(b)
YDE-060
% Proliferation over basal
60
50
40
30
20
10
0
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

도 170

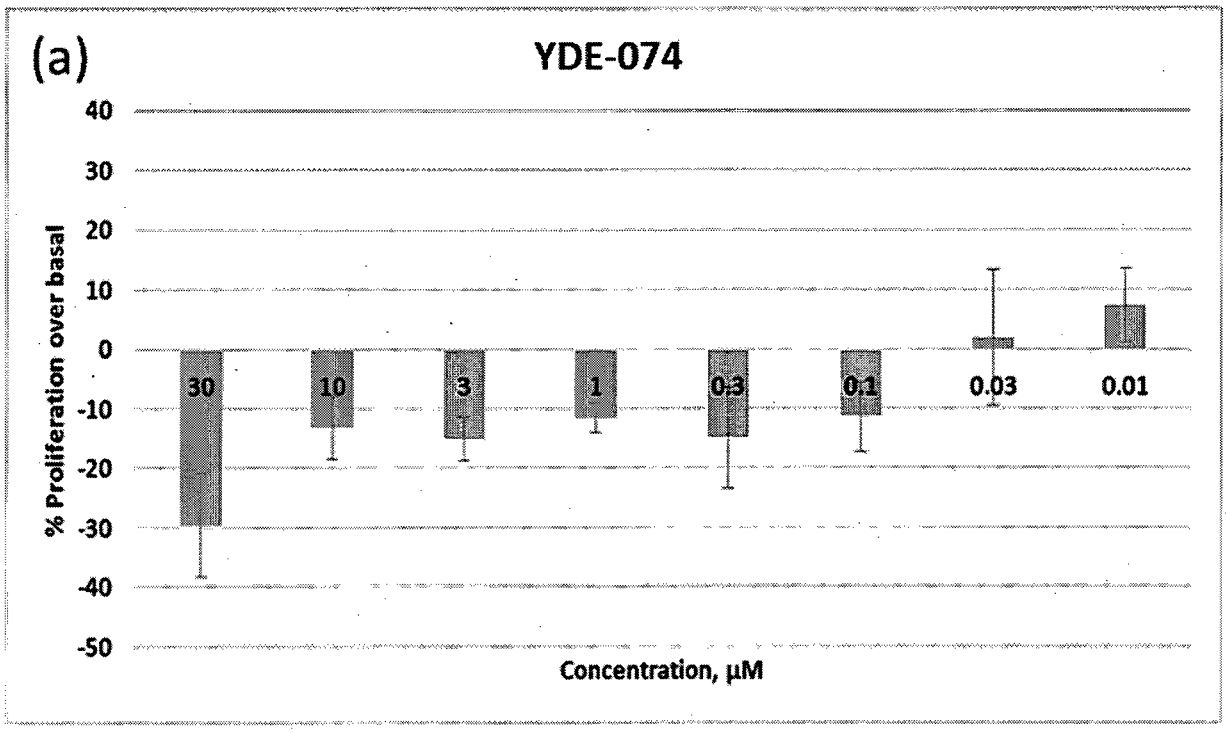

(a)
YDE-072
40
30
20
10
0
-10
-20
% Proliferation over basal
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM
(b)
YDE-072
40
30
20
10
0
-10
-20
% Proliferation over basal
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

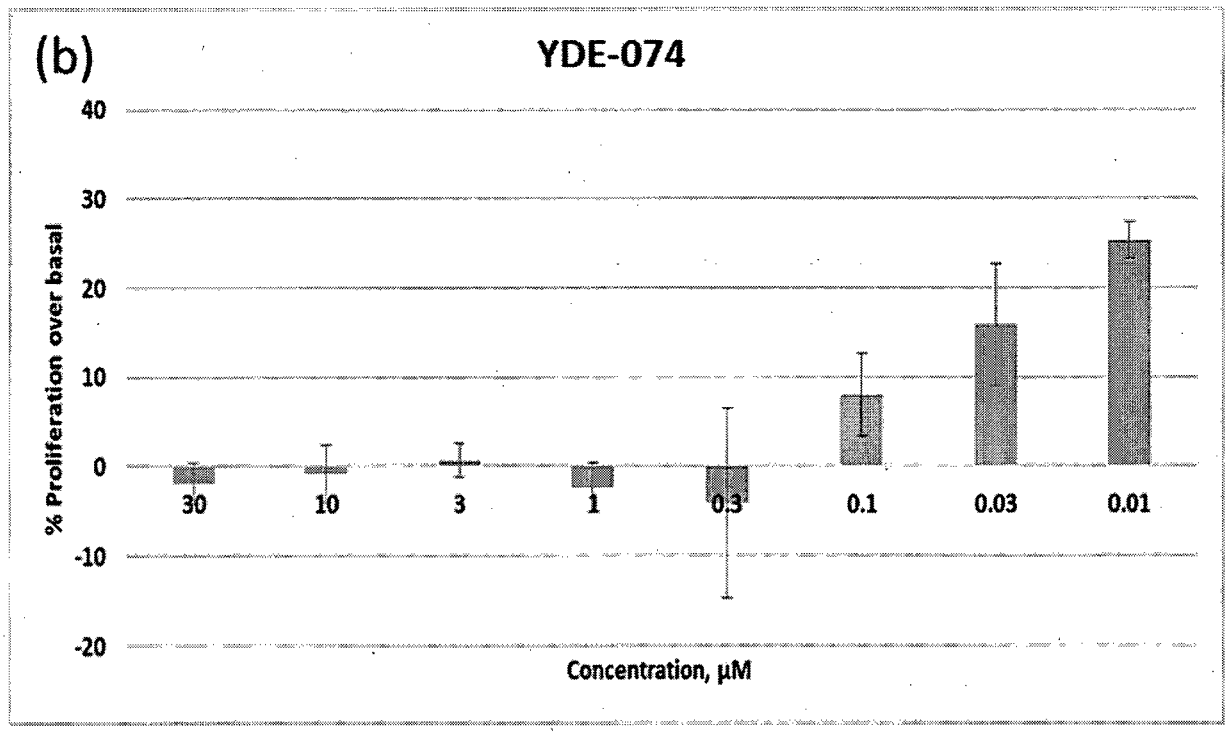
도 171


(a)
YDE-073
% Proliferation over basal
40
30
20
10
0
-10
-20
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

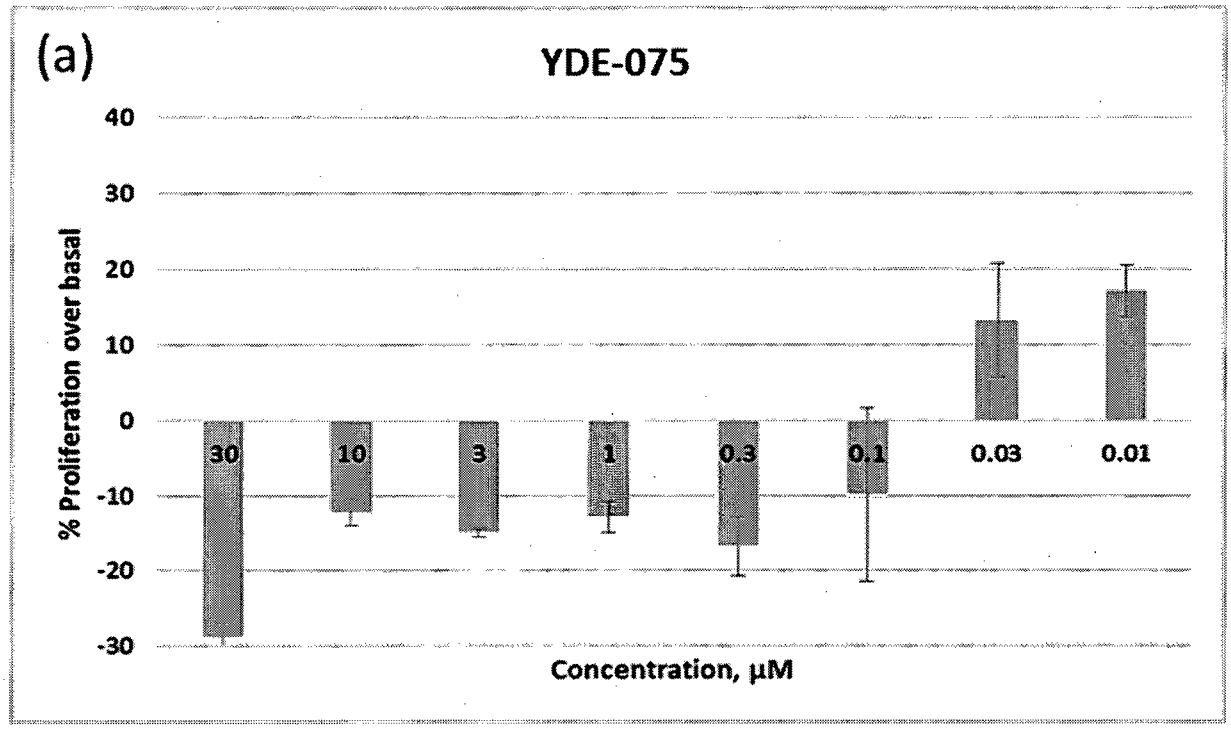

(b)
YDE-073
% Proliferation over basal
40
30
20
10
0
-10
-20
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

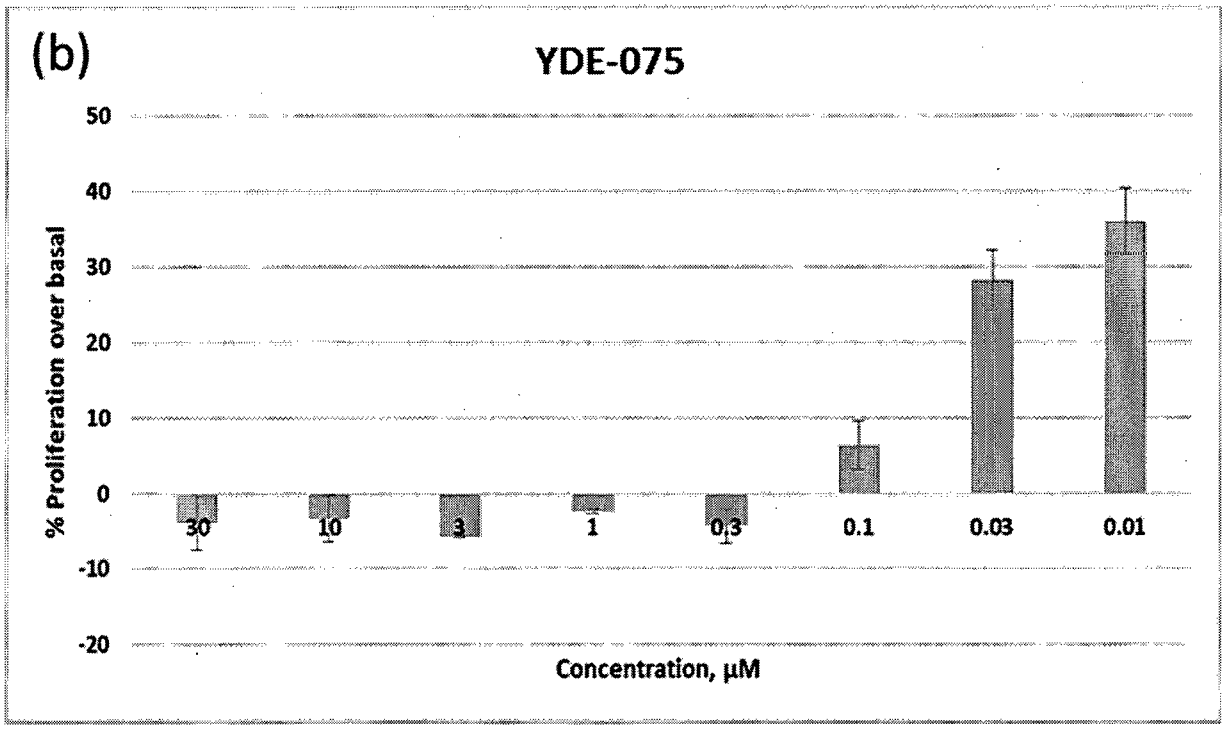
도 172


(a)
YDE-074
40
30
20
10
0
-10
-20
-30
-40
-50
% Proliferation over basal
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM


(b)
YDE-074
40
30
20
10
0
-10
-20
% Proliferation over basal
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

도 173


(a)
YDE-075
40
30
20
10
0
-10
-20
-30
% Proliferation over basal
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM


(b)
YDE-075
50
40
30
20
10
0
-10
-20
% Proliferation over basal
30
10
3
1
0.3
0.1
0.03
0.01
Concentration, μM

<110> Yuyu Pharma, Inc.

<120> NOVEL PEPTIDES AND PHARMACEUTICAL COMPOSITION FOR TREATING OCULAR DISEASES COMPRISING SAME

<130> PCB804042YUY

<150> KR 10-2017-0061250
<151> 2017-05-17

<160> 63

<170> KoPatentIn 3.0

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<400> 1
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1 5 10

<210> 2
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<220>
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Pro Gly Gln Asn Gly Leu Ala Gly Pro Lys
1 5 10

<210> 3
<211> 10
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<213> Artificial Sequence

<220>
<223> Amino acid sequence for YDE-003

<220>
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<223> 4Hyp

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<220>
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<223> 4Hyp

<400> 4
Pro Gly Gln His Gly Leu Ala Gly Pro Lys
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<220>
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<223> 4Hyp

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Pro Gly Gln Lys Gly Leu Ala Gly Pro Lys
1 5 10

<210> 6
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<400> 6
Pro Gly Gln Ser Gly Leu Ala Gly Pro Lys
1 5 10

<210> 7
<211> 10

<212> PRT
<213> Artificial Sequence

<220>
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1 5 10

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<220>
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<220>

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<223> 4Hyp

<400> 10
Pro Gly Gln Ile Gly Leu Ala Gly Pro Lys
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Pro Gly Gln Leu Gly Leu Ala Gly Pro Lys
1 5 10

<210> 12
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<220>
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Pro Gly Gln Tyr Gly Leu Ala Gly Pro Lys
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<223> 4Hyp

<220>
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<223> METHYLATION, Asp(Me)

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<223> 4Hyp

<220>
<221> MOD_RES
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<220>
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<220>
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<223> D-4Hyp(2R, 4S)

<400> 18
Pro Gly Gln Leu Gly Leu Ala Gly Pro Lys
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<220>
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<223> D-4Hyp(2R, 4S)

<220>

<221> MOD_RES
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<220>
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<220>
<221> MOD_RES
<222> (9)
<223> D-Pro

<220>
<221> MOD_RES
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<223> D-Lys

<400> 19
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1 5 10

<210> 20
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<213> Artificial Sequence

<220>
<223> Amino acid sequence for YDE-060

<220>
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<220>
<221> MOD_RES
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<223> D-Gln

<220>
<221> MOD_RES
<222> (4)
<223> D-Leu

<220>

<221> MOD_RES
<222> (6)
<223> D-Leu

<220>
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<222> (7)
<223> D-Ala

<220>
<221> MOD_RES
<222> (9)
<223> D-Pro

<220>
<221> MOD_RES
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<400> 20
Pro Gly Gln Leu Gly Leu Ala Gly Pro Lys
1 5 10

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<220>
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Pro Gly Gln Asp Val Leu Ala Gly Pro Lys
1 5 10

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Pro Gly Gln Asp Ile Leu Ala Gly Pro Lys
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Pro Gly Gln Asp Leu Leu Ala Gly Pro Lys
1 5 10

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Pro Gly Gln Asp Ala Leu Ala Gly Pro Lys
1 5 10

<210> 25
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Pro Gly Gln Asp Phe Leu Ala Gly Pro Lys
1 5 10

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<211> 10
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1 5 10

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<220>
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<400> 27
Pro Gly Gln Asp Trp Leu Ala Gly Pro Lys
1 5 10

<210> 28
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<220>
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<222> (1)
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<400> 28
Pro Gly Gln Asp His Leu Ala Gly Pro Lys
1 5 10

<210> 29
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<223> 4Hyp

<400> 29

Pro Gly Gln Asp Ser Leu Ala Gly Pro Lys
1 5 10

<210> 30
<211> 10
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<400> 30
Pro Gly Gln Asp Thr Leu Ala Gly Pro Lys
1 5 10

<210> 31
<211> 10
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<400> 31
Pro Gly Gln Asp Gly Leu Ala Gly Pro Lys
1 5 10

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<220>
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<222> (1)
<223> 4Hyp

<400> 32
Pro Gly Gln Leu Ala Leu Ala Gly Pro Lys
1 5 10

<210> 33
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<400> 33
Pro Gly Gln Leu Gly Leu Ala Gly Pro Tyr
1 5 10

<210> 34
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<223> 4Hyp

<400> 34
Pro Gly Gln Leu Gly Leu Ala Gly Pro Leu
1 5 10

<210> 35
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<400> 35
Pro Gly Gln Leu Gly Leu Ala Gly Pro Glu
1 5 10

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<400> 36
Pro Gly Gln Leu Gly Leu Ala Gly Pro Gln
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<210> 37
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<220>
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<223> 4Hyp

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<220>
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<220>
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<222> (1)
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<400> 38
Pro Gly Gln Leu Gly Leu Ala Gly Pro Ala
1 5 10

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<220>
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<220>
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<222> (1)
<223> D-4Hyp(2R, 4S)

<400> 39
Pro Gly Gln Leu Gly Leu Ala Gly Pro Ala
1 5 10

<210> 40
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<220>
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<222> (1)
<223> (4-oxo)Pro

<400> 40
Pro Gly Gln Leu Gly Leu Ala Gly Pro Lys
1 5 10

<210> 41
<211> 10
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<220>
<223> Amino acid sequence for YDE-036

<220>
<221> MOD_RES
<222> (1)
<223> (5-oxo)Pro

<400> 41
Pro Gly Gln Leu Gly Leu Ala Gly Pro Lys
1 5 10

<210> 42
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
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<400> 42
Pro Gly Gln Leu Gly Leu Ala Gly Pro Lys
1 5 10

<210> 43
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<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence for YDE-038

<220>
<221> MOD_RES
<222> (1)
<223> (4-hydroxyMe)Pro

<400> 43
Pro Gly Gln Leu Gly Leu Ala Gly Pro Lys
1 5 10

<210> 44
<211> 10
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<213> Artificial Sequence

<220>
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<220>
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<222> (1)
<223> (4-Fluoro)Pro

<400> 44
Pro Gly Gln Leu Gly Leu Ala Gly Pro Lys
1 5 10

<210> 45
<211> 10
<212> PRT
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<220>
<223> Amino acid sequence for YDE-040

<220>
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<222> (1)
<223> (4-Dimethyl)Pro

<400> 45
Pro Gly Gln Leu Gly Leu Ala Gly Pro Lys
1 5 10

<210> 46
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
<222> (1)
<223> (4-Me)Pro

<400> 46

Pro Gly Gln Leu Gly Leu Ala Gly Pro Lys
1 5 10

<210> 47
<211> 10
<212> PRT
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<220>
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<220>
<221> MOD_RES
<222> (1)
<223> (5-Me)Pro

<400> 47
Pro Gly Gln Leu Gly Leu Ala Gly Pro Lys
1 5 10

<210> 48
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence for YDE-049

<220>
<221> MOD_RES
<222> (1)
<223> 4Hyp

<400> 48
Pro Gly Ala Leu Gly Leu Ala Gly Pro Lys
1 5 10

<210> 49
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence for YDE-052

<220>
<221> MOD_RES
<222> (1)
<223> 4Hyp

<400> 49
Pro Gly Gln Leu Gly Ala Ala Gly Pro Lys
1 5 10

<210> 50
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence for YDE-054

<220>
<221> MOD_RES
<222> (1)
<223> 4Hyp

<400> 50
Pro Gly Gln Leu Gly Leu Ala Ala Pro Lys
1 5 10

<210> 51
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence for YDE-048

<220>
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<222> (1)
<223> 4Hyp

<400> 51
Pro Ala Gln Leu Gly Leu Ala Gly Pro Lys
1 5 10

<210> 52
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence for YDE-074

<220>
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<223> D-4Hyp(2R, 4S)

<400> 52
Pro Ala Gln Leu Gly Leu Ala Gly Pro Lys
1 5 10

<210> 53
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence for YDE-072

<220>
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<222> (1)

<223> D-4Hyp(2R, 4S)

<400> 53
Pro Ala Gln Leu Gly Leu Ala Gly Pro Ala
1 5 10

<210> 54
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence for YDE-047

<400> 54
Ala Gly Gln Leu Gly Leu Ala Gly Pro Lys
1 5 10

<210> 55
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<222> (1)
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<400> 55
Pro Gly Gln Leu Gly Leu Ala Gly Ala Lys
1 5 10

<210> 56
<211> 7
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<220>
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<223> 4Hyp

<400> 56
Pro Gly Gln Leu Gly Leu Ala
1 5

<210> 57
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<212> PRT
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<220>

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