

(19) (KR)
(12) (A)

(51) 。 Int. Cl.⁷
A61K 31/59 (11)
C07C 401/00 (43) 10-2004-0101530
2004 12 02

(21) 10-2004-7016745
(22) 2004 10 18
2004 10 18
(86) PCT/US2003/012013 (87) WO 2003/088976
(86) 2003 04 17 (87) 2003 10 30

(30) 10/127,005 2002 04 19 (US)
(71) 53562 , 1600
(72) 53705 3534
53711 4917
53726 24
(74) :

(54)

D /
(ARVDD)
가 ARVDD :
, (1) 1 D , (2) 1,25-(OH)₂D₃ (3) 1,25-(OH)₂D₃ .
D , 1 , 1,25-(OH)₂D₃ , 1,25-(O
H)₂D₃

, 1997 8 8 08/907,659(, 5,869,473) 1998
5 29 09/086,969 2000 2 9 09/501,093

1995 4 3 08/415,488 (, 5,602,116)
 1997 2 11 08/798,958 (, 5,707,980)
 1997 8 8 08/907,660 .

D (ARVDD)
 . ARVDD
 : (1) 1 D , (2) 1,25-(OH)₂D₃ (3)
 1,25-(OH)₂D₃ . ARVDD
 ARVDD
 , 가 가 가
 (PTH) PTH 가(30 80
 50%) D 가
 [: Lau, K.-H. W. and Baylink, D. J., Calcif. Tissue Int. 65: 295-306 (1999); Pat
 tanaungkul, S., et al., J. Clinical Endocrinol. amp; Metab. 85:11 4023-4027 (2000)].
 D [: Grady, D
 . et al., J. Clin. Endocrinol. amp; Metab. 73:1111-1117 (1991); Bischoff, H.A. et al., Arch. Phys. Med Rehabil.
 80:54-58 (1999); Theiler, R. et al., Arch. Phys. Med. Rehabil. 80:485-489 (1999); Bischoff, H.A. et al., Histo
 chem. J. 33:19-24 (2001); Glerup, H. 'Investigations on the role of vitamin D in muscle function,' Ph.D. Thesi
 s, Aarhus Bone and Mineral Research Group, University of Asrhus, Denmark (1999); Gulbrahdsen, C.E. and
 Moss, R.L., 1994 9 27 5,350,745].

ARVDD D 3가
 1,25- D₃
 D (1) 1 D , 1,25- D₃
 D / 25- D₃ ; (2) 1,25- D₃
 , 1,25- D₃ (3) 1,25- D₃ ,
 1,25- D₃ [: Lau, K.-H. W. and Bayli
 nk, D. J., Calcif. Tissue Int. 65:295-306 (1999); Pattanaungkul, S et al., J. Clinical Endocrinol. amp; Metab. 8
 5:11 4023-4027 (2000)].

1 D 1,25- D₃ , D / 2
 5- D₃ D UV-B 가
 [: Heikinehimo, R et al., (1992) Calcif Tissue Int 51:105-110]
 D [: Toss, G et al., Acta Med Scand 208:87-89 (1980)] 1 D
 D 25- 25- D
 3 , 25- 1,25-
 D₃ 25- D-1 -
 D₃ D 25- D₃
 , 1,25- D₃ 1,25- D₃ ,
 D [: Ooms, ME et al., J. Bone Miner Res. 10:1177-1184 (1995)].
 25- D₃ 1 D . 1 D
 , 2 , 가 (bone turnover),
 [: Id.; Khaw, K.T. et al., Br. Med. J. 305-273-277 (1992)] 가 [: Eastell, R a
 nd Roggs, B.L., 'Vitamin D and Osteoporosis', Vitamin D, Feldman D, Glorieux FH, Pike JW (eds) Academic P
 ress, San Diego, CA pp. 695-711 (1997); Chapuy, M.C. and Meunier, P.J., 'Vitamin D insufficaency in adults
 and the elderly', Vitamin D, Feldman D, Glorieux FH, Pike JW (eds) Academic Press, San Diego, CA pp. 679-
 693 (1997); Lau, K.-H. W. and Baylink, D.J., supra]

1 D , 1,25-(OH)₂D₃ , D / 25-

D₃, 1,25-D₃, PTH, D₃
D₃, 1,25-D₃, D₃
1,25-D₃, (renal insufficiency, renal failure)
D₃, 1,25-D₃, D₃
[: Lau, K.-H. W. and Baylink, D.J., supra].
1,25(OH)₂D₃, D₃, 1,25-D₃, 1,25-D₃
D₃, 1,25-D₃, 1,25-D₃, D₃, 1,25-D₃, D₃
D₃, 1,25-D₃, 가 () 1,25-D₃
D₃, 가 1,25-D₃, 2, 가
25-D₃, 가 1,25-D₃, 가
[: Lau K.-H. and Baylink, D.J., supra].
PTH, 가, 2.

1, 2, 3 . 1 가 ,
D, 1,25-D₃ / 2, 가
. 2 , , . 3
2 가 , D 가

D가 . 1970
D [: Holick, M. F. et al., Proc. Natl. Acad. Sci. USA 68, 803-804 (1971); Jones, G. et al., Biochemistry 14, 1250-1256 (1975)] D [: Holick, M. F. et al., Science 180, 190, 191 (1973); Lam, H. Y. et al., Science 186, 1038-1040 (1974)]

D 가
(PTH) D₃
) . 1, 25-D₃ 1 - D₃ 1 - D₃
가
[: Ott, S. M. and Chesnut, C. H., Annals of Int. Med.; 110: 267-274 (1989); Gallagher, J. C. et al., Annals of Int. Med.; 113:649-655 (1990); Aloia, J. et al., Amer. J.Med. 84: 401-08 (1988); and Shiraki, M. et al.,Endocrinol. Japan 32, 305-315 (1985)].
가
가 . 1, 25-D₃ 0.5μg/
0.5μg/
[: Jensen, G. F. et al., Clin. Endocrinol. 16, 515-524 (1982); Christiansen, C.

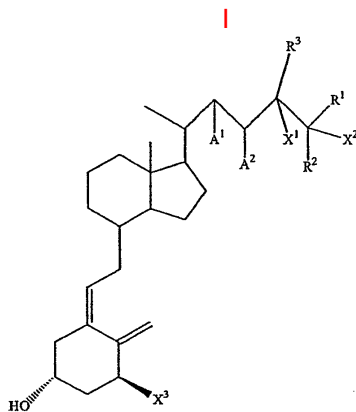
et al., Eur. J. Clin. Invest. 11, 305-309(1981)]. 1 - D_3 (1 - (OH) D_3) 2 μ g/가 [: Sorensen, O. H. et al., Clin. Endocrinol. 7, 169S-175S (1977)]. 가 1 - D_3 1 μ g/ [: Shiraki, M. et al., Endocrinol. Japan. 32: 305-315 (1985); Orimo, H. et al, Bone and Mineral 3, 47-52 (1987)]. , 2 μ g/ , 1 - D_3 67% , 1 μ g/ 20 % . , 1- D_3 . 가, (Aloia) [: Aloia, J. et al., Amer. J. Med. 84:401-408 (1988)]. 1 - D_3 1 ,25- D_3 , 1 - D_3 1 ,25- D_3 [: Gillespie, et al., Abstract, The Cochrane Library, issue 2, 2001; DeChant, K.L. and Goa, K.L., Drugs amp; Aging, 5(4):300-317 (1994); Ikeda, K Ogata, E., Mechanisms of Ag ing amp; Development 116:103-111 (2000); Tanizawa, T., Osteoporos. Int. 9:163-170 (1999); Civitelli, R., C alcif. Tissue 57:409-414 (1995); Parfitt, A.M., Drugs 36: 513-520 (1988); Thompson, S.P. et al., Brit. Edit. Soc. Bone Joint Surgery, 72:1053-1056 (1990); Sairanen, S. et al., Calcif. Tissue Int. 67:122-127 (2000); Ha as, H.G., Horm. Metab. Res. 11:168-171(1979); Tilyard, M.W. et al., New England J. Med. 326:357-362 (199 2); Aloia, J.F. et al., Am. J. Med. 84:401-408 (1988); Avioli, L., Calcif. Tissue Int. 65: 2392-294 (1999); Ori mi, H. et al., Calcif. Tissue Int. 54: 370-376 (1994); Sorensen, O.H. et al., Clinical Endocrinol. 7(Suppl.): 16 9S-175S (1997)]. 1 - D_3 1 ,25- D_3 D가 , , , D 가 . D , 1 ,25- D_3 , 1 ,25- PTH 1 ,25- D_3 [: Zerwekh, J.E. et al., J. Clin. Endocrinol Metab. 56: 410-413 (1983); Nordin, B.E.C. et al., Calcif. Tissue Int. 65:307-310 (1999); Morris, H.A. et al., Calcif. Tissue Int. 49:240-243 (1991) ; Shiraishi, A. et al., Calcif. Tissue Int. 65:311-316 (1999); Silverberg, S.J. et al., New England J. Med. 320(5):277-281 (1989), Francis, R.M., Calcif. Tissue Int. 60: 111-114 (1997); Francis, R.M. et al., Osteoporosis In t. 6:284-290 (1996); Theiler, R. et al., Int. J. Vit. Nur. Res. 68: 36-41 (1998)]. , , 2 , 300,000 , 25- D_3 25- D_2 D ('1 ,25-(OH) $_2$ D') 1 25- D-1 - , 1 ,25-(OH) $_2$ D . 1 ,25-(OH) $_2$ D PTH 가 가 (Mockerberg's sclerosis) . 1 ,25-(OH) $_2$ D (가) . D , 2 , 1 ,25-(OH) $_2$ D $_3$ 1 -(OH) D_3 1 ,25-(OH) $_2$ D 1 -(OH) D_3 , 1 ,25-(OH) $_2$ D $_3$, 0 .5 μ g () 0.5 1.0 μ g/ 3 0.5 3.0 μ g , D 1.0 μ g/ 1 -(OH) 0.25 0.10 μ g/ , 1.

0 μ g/ , 가 1,25-(OH) $_2$ D $_3$ 1-(OH)D $_3$ D $_3$ 가 1.25mM 가 PTH 가 , 2 가 D 가 , 2 , 1-(OH)-D $_3$ 가 D [: Shiraishi, A et al., Calcif. Tissue Int. 65:292-294 (1999)]. , D $_3$ 가 가

D , 가 D $_3$, (PTH) , (PTH) D (ARVDD) D , ARVD D 1 , D , 1,25-(OH) $_2$ D $_3$ 1,25-(OH) $_2$ D $_3$, ARVD 가 D (episodic) D 가 D 가

D (ARVDD) D / , ARVD D 25-(OH) $_2$ D $_3$: (1) 1 D , (2) 1,25-(OH) $_2$ D $_3$ (3) 1, ARVDD 가 , , (PTH) / / ARV DD , PTH 1,25-(OH) $_2$ D $_3$ 가 , 1,25-(OH) $_2$ D $_3$ D / ARVDD

[illegible]



I ,

A^1 A^2 - C-22 C-23 ;

R^1 R^2 , O- , O- , O- , O- [, R^1 , R^2 , C₃-C₈ ;

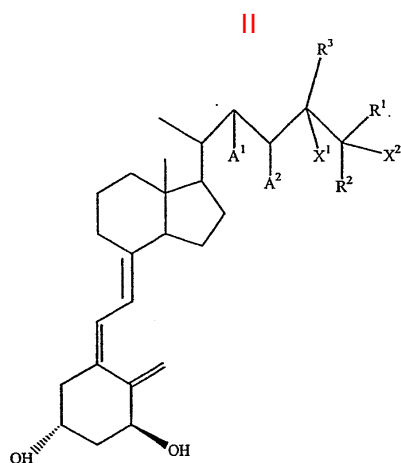
R^3 , O- , O- , O- ;

X^1 ;

X^2 , R^1 R^2 ;

X^3 , X^1 , X^2 X^3 .

1 - D II .



II ,

A^1 A^2 - C-22 C-23 ;

R^1 R^2 , O- , O- , O- , O- [, R^1 , R^2 ,

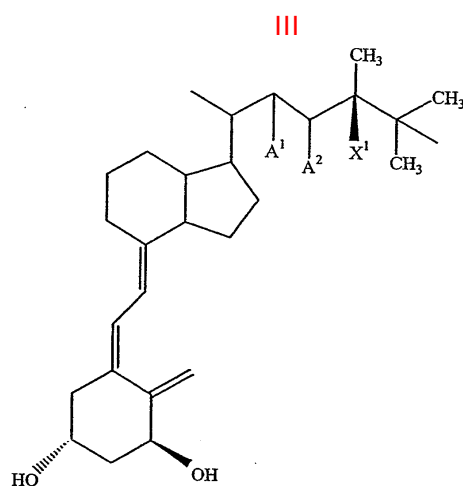
] , R¹ R² C₃-C₈ ;

R³ , O- , O- , O- ;

X¹ ;

X² , R¹ R² .

R¹, R² R³ X²가 , 1 - D
III .

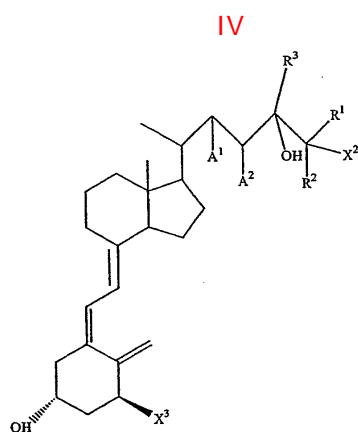


III ,

A¹ A² - ;

X¹ .

24- D IV .



IV ,

A^1 A^2 - C-22 C-23 ;
 R^1 R^2 , O- , O- , O- , O- [, R^1 , R^2 ,
] , R^1 R^2 C₃-C₈ ;
 R^3 , O- , O- , O- ;
 X^3 ;
 X^2 , R^1 R^2 .
 I IV 24- D , 25- D
 1 - D I IV
 , 1 , 24- D₂ , 1 , 24- D₄ , 1 , 25- D₄ , 1
 , 25- D₂ , 1 , 24, 25- D₂ , 1 , 25- D₃ 1 ,
 24, 25- D₃ , 1 - D₂ , 1 - D₂ , 24- D₄ , 25- D₂ 25- D₄
 - D₂ , 24- D₄ , 25- D₂ 25- D₄
 .
 D 1 , 25- D_3 D_3
 D 1 , 25- D_3 D_3
 , 1 , 25- D_3 1 , 25- D_3 0.001 0.5 .
 , 1 , 25- D_3
 1 . D
 .
 가 , C-24 I IV , (, R S)
 가 , 가 , 1 , 24(S)- D_2 (
 R) , 1 , 24(R)- D_4 (S) (
 .
 I IV D D
 C_1 , C_{24} C_{25} D ,
 D III D_3 , III ,
 D_3 가 ,
 1 μ g 150 μ g , 10 μ g/ 200 μ g/
 .
 ARVDD
 D ,
 D , D_2 , D_3 D_4 () .
 D ,
 , ARVDD 1
 , 25- D_3 () 1 - (OH)- D_3 () ,
 , 10 μ g , 20 μ g 100 μ g , 300 μ g ,
 D , D 1
 .

12 1 , 3 1 . , 0.2 μ g 4.
5 μ g .

[illegible]

DD
가
I IV
D
가
2
가
(
)
, 2
가
(
가
, 1
가
D
D
가
1

[1]

			가
가 (mg/)	0.3 - 5.0	0.4 - 2.4	0.6 - 1.2
(mg/)	5 - 150	30 - 75	40 - 60
(IU/)	5 - 800	25 - 500	50 - 200
(mg/)	50 - 2000	100 - 1500	500 - 1000
(mg/)	250 - 2500	500 - 1500	750 - 1000
(µg/)	5 - 200	20 - 100	30 - 50
(mg/)	0.1 - 2000	10 - 1500	100 - 1000
(mg/)	0.10 - 3000	1 - 250	2 - 100

, , , , ,
.
D
D
/
ARVDD
D
D [: 3,907, 843 ; 4,195,027 ; 4,20
2,829 ; 4,234,495 ; 4,260,549 ; 4,555,364 ; 4,554,106 ; 4,670,190 ; 5,488,120 ; WO
94/05630, Strugnell et al., 310 Biochem. J. 233-241 (1995);]

가 , .

1 -OH- D₂ 1 -OH- D₃

1 -(OH)D₃ 1 -(OH)D₂ . 1 -(OH)D₂ [: G. Sjoden et al., J. Nutr . 114, 2043-2946 (1984)]. , 1 -OH-D₂ 1 -OH-D₃ 5 15

[: G. Sjoden et al., Proc. Soc. Exp. Biol. Med. 178, 432-436 (1985)]. , 2 3

1 -OH-D₂
μg

1 (OH)D₂ 1 ,24-(OH₂)D₄가

PTH

1 ,25-(OH)₂D₃ 1 -(OH)D₃

가 1 -(OH)D₂ 1 ,24-(OH)₂D₄

, 1 ,24(S)-(OH)₂D₄가

. , 1 ,24(S)-(OH)₂D₂ 1 ,24(R)-(OH)₂D₃
D₃

1:

1 -(OH)D₂ 15 [: J. Bone Min. Res. ; 9: 607-614 (1994)]. 55 75 LUNAR - ('BMD') (0.7 1.05g/cm² L2-L3 0.85±0.17g/cm² 15 85).

, 400 600mg

24

1 , 5 7 1

1 -(OH)D₂ 0.5μg/ 1.0, 2.0, 4.0, 5.0, 8.0 10.0μg/

가 ,

1

24

1 -(OH)D₂가

가 ,

1 -(OH)D₂

가

, 24

가

2:

1 -(OH)D₂ 60 가 60 70 x- (DEXA) 0.7 1.05g/cm² L2-L3 BMD .

, 2 (1 -(OH)D₂ 104

; 900mg

700

24

, 1 - (OH)D₂ 1.0μg/ 가
 , 2.0, 3.0, 4.0μg/ 275 300mg/24 5.0μg/ 가
 , 1 - (OH)D₂ 2 가
 BMD 6 DEXA
 D 12 6
 , PTH 6
 , 12 (KUB) x -
 :
 : 52 60 가 가 60 , 55 1
 (28 ; 27) , 41 2
 : 1 - (OH)D₂ 52 52 4.2μg/ 104
 8μg/ 3.6μg/ 4.8μg/ 104 4.
 : 1 1 , 25-(OH)D₂
 PTH () 3
 . 700 900mg/
 / : 1 - (OH)D₂ (>10.8mg/dL) 5.0μg/ (10.4
 10.8mg/dL) 5.0μg/ 2 (10.
 2 10.4mg/dL) 4 , 2
 1 - (OH)D₂ 17 2
 0.1 / : 1 - (OH)D₂ (P<0.05).
 0.2mg/dL 1 - (OH)D₂ 0.05 0.10mg/dL
 : 1 - (OH)D₂ 50 130%(P<0.01) 가
 : BUN, 1 - (OH)D₂
 . KUB x -
 : L2-L4 (BMD) 2 1 - (OH)D₂ 가
 (P<0.05) 가 BMD BMD 24 가 18 (P<0.
 001) 24 (P<0.05)
 : 45 Ca 52 1 - (OH)D₂ 40%(P<
 0.001) 가 , 104 1 - (OH)D₂ 29%(P<0.5) 가
 D : 1 - (OH)D₂ 1 - (OH)D₃ 6 21
 %(P<0.05) 24 49%(P<0.01) 가 가 1 - (OH)D₂

가, 1, 25-(OH)₂D₃ 50+%

PHT 1 -(OH)D₂ 52 17% 1 4
25%

1 -(OH)D₂

-(OH)D₂ : 1 -(OH)D₂ 가, 1

1 -(OH)D₂ 가

D₃
1 -(OH)D₂ 가 2.0 3.0μg/
(D)
1 -(OH)D₂

가

가 PTH

1 -(OH)D₂ 가

2

3: 2

5 가 36 72 가 4
가 2 3.0 6.9mg/dL (

400pg/mL

PTH

가 1 -(OH)₂D₃
. 8 , 6

, 1 -(OH)D₂ 8 1 -(OH)₂D₃
4μg/ 1 -(OH)D₂ . 8

(washout period)

PTH

6.9mg/dL , 1.25mM (3)
(1 10g Ca)

: PHT - 480 ± 21pg/mL; Ca - 8 ± 0.3 mg/mL - 5.1 ± 0.2mg/
mL. 3 , PTH 2 68%, 74% 87% , PTH 4
33% , 2
4 49 ± 17% 33 ± 9% (p<0.05). 2 , 1 -OH-D₂ 2
0.4(p<0.05) 9.8 ± 0.2(NS) (NS), (mg/dL) 5.4 ± 0.5 5.5 ± 0.8 (NS). 1 -(OH)D₂ 10.2 ±
PTH가 130 3 , 1 -(OH)D₂ 2 4 PTH가
(, 10.3 11.4mg/dL) , 1 -(OH)D₂
2 . 1 -(OH)D₂ 4μg 4 6 , 5
4 가 PTH , 10.0 ± 0.2mg/dL , 5.3 ± 0.2mg
/dL . 6 1 -(OH)D₂ , PTH
(OH)D₂ 38% , 가 PTH 8 1 -
1 -(OH)D₂ 가 2

4:

12 - 35
D₃ (400IU/) 8

-(OH)D₂ (u.i.d.; 3.0µg/) , 2 : 1
 가 . 7.0mg/dL D₃ , ,
 . (a) , (b) , (c) (d)
 가 .

5: 2

(ESRD)

120 ESRD() (multicenter) , 20 7
 5 , 2 , 4 ()
) , ()
 가 , 1 -(OH)D₂ 12 1 -(OH)D₂
 , 12 1 -(OH)D₂ 12 (4µg/) 8
 1 ,25-(OH)₂D₃ 8 () 2 12
 , - , D , , , PTH
 , 1.25mM (3) , (6.9
 mg/dL) (:)
 3 4µg() . 1 -(OH)D₂
 µg() 1 -(OH)D₂ . 2 , 3 4
 8 PTH , PTH 50% 가 1 -(OH)D₂ , P
 TH PTH 3 4µg()
 , 가 PTH 1 -(OH)D₂ .
 12 , PTH 130 240pg/mL , 2 12 (가
 1 -(OH)D₂) , PTH
 D₂ 가, (1) 1 -(OH)D₂ 가 PTH , (2) 1 -(OH)

6: 2

PTH가

2 100 30 PTH (가 60
 (0.70g/cm²) .)
 2 1 500mg . 1
 PTH , 1 -(OH)D₂ 2.5µg/ 가 . PTH

가 . 가 .

1 -(OH)D₂ , , PTH

7: 2 PTH가

12 60 100 2 40 . (0.
70g/cm²)

5μg/ 1 ,24-(OH)₂D₄ (u.i.d.; 7.5μg/ 2) , : 1

(a) PTH(iPTH); (b) , ; (c) - (: 가)
가 . (a) (b)

1 ,24-(OH)₂D₄가 iPTH

, iPTH

2 3

8: 2 3 PTH가

2 PTH (: 1015 4706pg/mL) 가 14 1000 pg/mL i
-(OH)D₂ (10μg - 3 /) , 150 300pg/mL iPTH 2 3 (. 1
가 . 11 12 , 2 iPTH 1000pg/m
L , 9 iPTH 510pg/mL .

9: ARVDD 1,25(OH)₂D₃ PTH가 -

ARVDD 가 1,25(OH)₂D₃ 50 80 PTH가 -
1,25(OH)₂D₃ () PTH ()
m² (0.70g/c

2 , 30 1 1 -(OH)D₂ 20μg/ 500mg 1 가 , 30 . 1
; PTH , , ; , .
PTH 가 .

1 -(OH)D₂ PTH 가 .

10: ARVDD 1,25(OH)₂D₃ PTH가 -

ARVDD 가 1,25(OH)₂D₃ 50 80 PTH가 PTH ()
 m² 1,25(OH)₂D₃ () (0.70g/c

500mg 1,24-(OH)₂D₂ 100μg 1 가 , 30 . 12
 , 30 1 가 ;
 PTH , , ; , , PTH
 가 .

1,24-(OH)₂D₂ PTH 가

RVDD / ARVDD : (1) 1 D A , (2)
) 1,25-(OH)₂D₃ (3) 1,25-(OH)₂D₃ PTH ARVDD
 D . ,
 , 가 , 가
 , 가 가 . ,

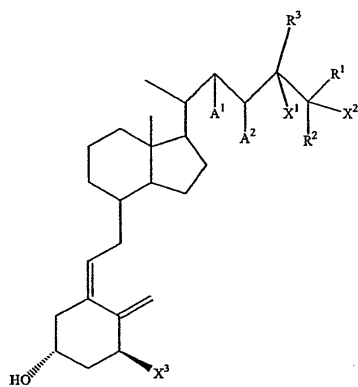
(57)

1. (PTH)
 D ,

2. D (ARVDD)

3. , ARVDD (1) 1 D , (2) 1,25- D₃ (3) 1,25
 - D₃ .

4. 2 , D가 I D .
 I



I ,

A^1 A^2 - C-22 C-23 ;

R^1 R^2 , O- , O- , O- , O- [, R^1 , R^2 , C₃-C₈ ;

R^3 , O- , O- , O- ;

X^1 ;

X^2 , R^1 R^2 ;

X^3 , X^1 , X^2 X^3 .

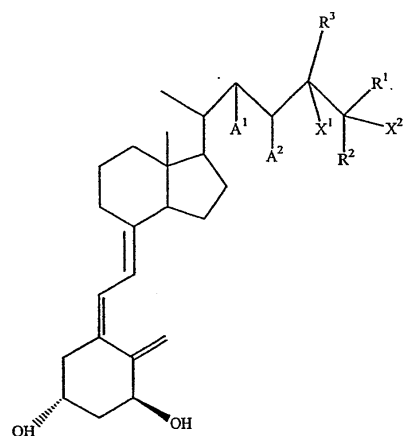
5.

3 , I D .

6.

2 , D가 II 1 - D .

II



II ,

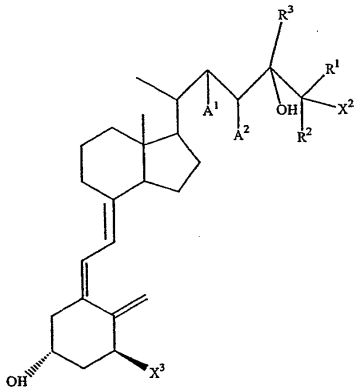
A^1 A^2 - C-22 C-23 ;

R^1 R^2 , O- , O- , O- , O- [, R^1 , R^2 ,

R^3 , O-, , , , , O-, O-, O-
 X^1 ;
 X^2 , R^1 R^2 .

7.

2 , D IV 24- D .
 IV



IV ,

A^1 A^2 - C-22 C-23 ;
 R^1 R^2 , O-, , O-, , O-, , O- [, R^1 , R^2 ,
 R^3 , O-, , , , O-, O-, O-
 X^3 ;
 X^2 , R^1 R^2 .

8.

2 , D 1 - $\text{D}_{4;1}$,25- $\text{D}_{2;1}$ -
 $\text{D}_{2;1}$,24- $\text{D}_{2;1}$,24,25- $\text{D}_{2;1}$,25-
 $\text{D}_{3;1}$ - $\text{D}_{3;1}$,25- $\text{D}_{4;1}$,24,25-
 $\text{D}_{4;1}$,24- $\text{D}_{2;1}$,24- $\text{D}_{4;1}$.

9.

3 , ARVDD 가 1 D .

10.

3 , ARVDD 가 1,25- D_3 .

11.

3 , ARVDD 가 1,25- D_3 .

- 2 12. , D .
- 12 13. , 가 D , , , , .
- 12 14. , D , .
- 2 15. , D가 (episodic) .
- 15 16. , D 10 μ g 300 μ g .
- 16 17. , D 1 ,25- D₃ 1 - D₃ .
- 15 18. , 1 12 1 .
- 2 19. , D .
- 19 20. , D .
- 20 21. , D .
- 19 22. , D .
- 20 23. , D 1 μ g 300 μ g .
- 23 24. , D 20 μ g 100 μ g .
- 19 25. , D .
- 20 26. , D , , .
27. D (ARVDD) D

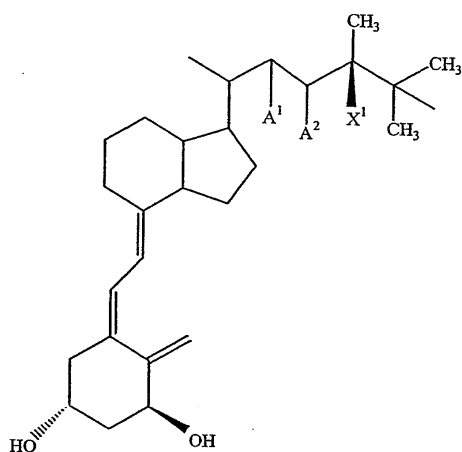
28.

27 , D ,

29.

, 1 μ g 300 μ g III

III



III ,

A¹ A² C-22 C-23 - ,X¹ .

30.

29 , , 가 가 .

31.

30 , 가 , , , , , .

32.

29 가 .

33.

32 , 가 .

34.

, D D (ARVDD) .

35.

(i) D (ii) , 가 , , , .

36.

35 , D ,
.

37.
1,25-(OH)₂D₃ , 1,25-(OH)₂D₃ . D

38.
D / D (ARVDD) , D
.

39.
(i) D 가 D / 가 D (ARVDD) (ii)
.