



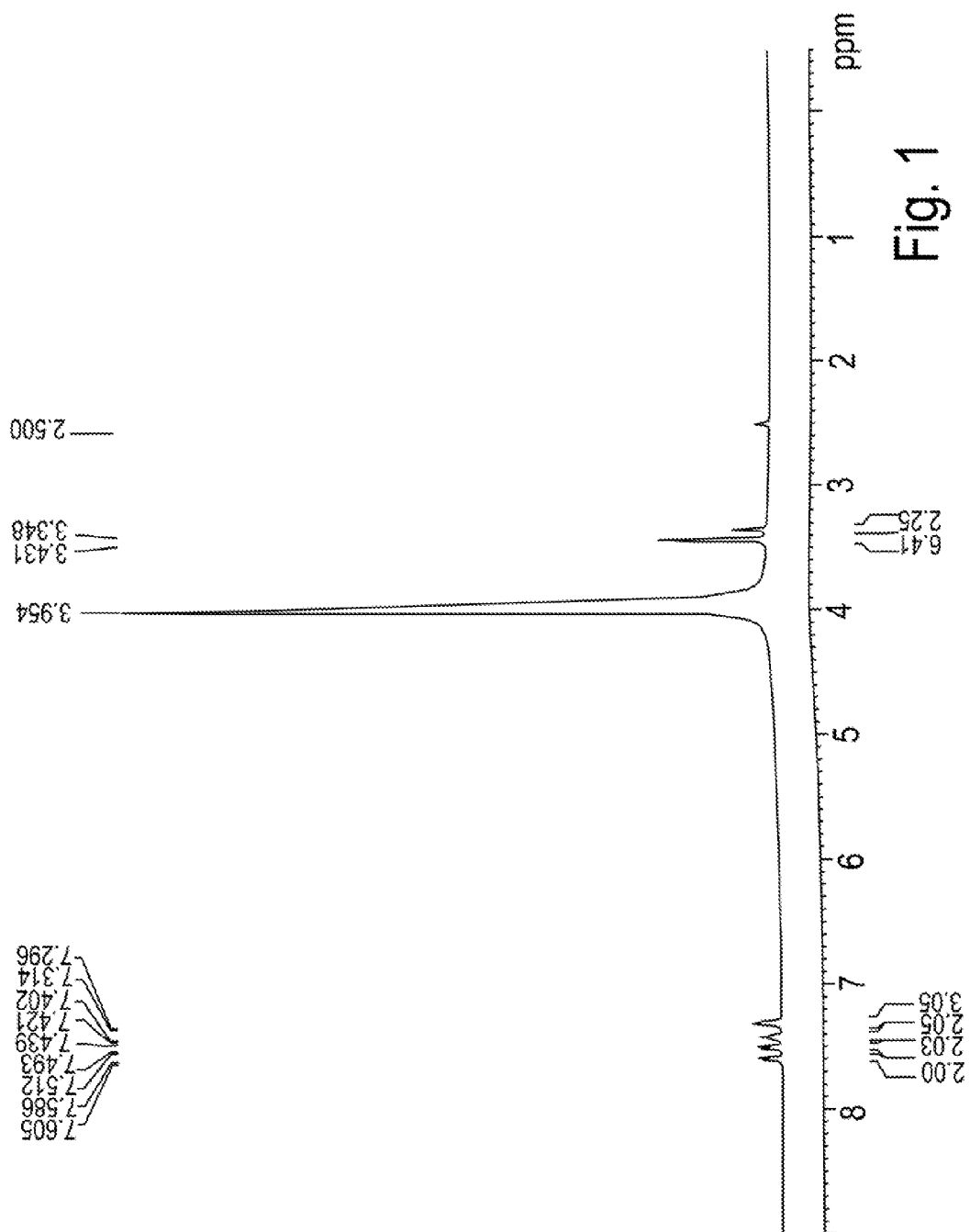
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(19) **United States**(12) **Patent Application Publication**
WANG et al.(10) **Pub. No.: US 2013/0035505 A1**(43) **Pub. Date: Feb. 7, 2013**(54) **BIPHENYL ACETATE, PREPARATION AND
USES THEREOF****Publication Classification**(76) Inventors: **Wei WANG**, Guangzhou (CN);
Wenzhan CHEN, Guangzhou (CN)(51) **Int. Cl.**
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C07C 51/41 (2006.01)(21) Appl. No.: **13/570,373**(52) **U.S. Cl.** **562/492**(22) Filed: **Aug. 9, 2012**(57) **ABSTRACT****Related U.S. Application Data**(63) Continuation of application No. 12/309,326, filed on
Jan. 12, 2009, filed as application No. PCT/CN2007/
002830 on Sep. 27, 2007.

A biphenyl acetate composition, which is a biphenyl acetic ammonia butantriol salt. The composition is prepared by reacting biphenyl acetic acid and ammonia butantriol in organic solvent, and a ratio of biphenyl acetic acid and ammonia butantriol is 1:1. The salt is capable of providing anti-inflammatory, analgesic, and antipyretic effect. The salt is unique and has stable chemical structure, can be prepared into an injection or a capsule, and has low toxicity and insignificant local and vascular irritating effect, thereby being prepared into a predetermined dosage in a controllable and precise manner.

Foreign Application Priority Data

(30) Oct. 23, 2006 (CN) 200610122917.4



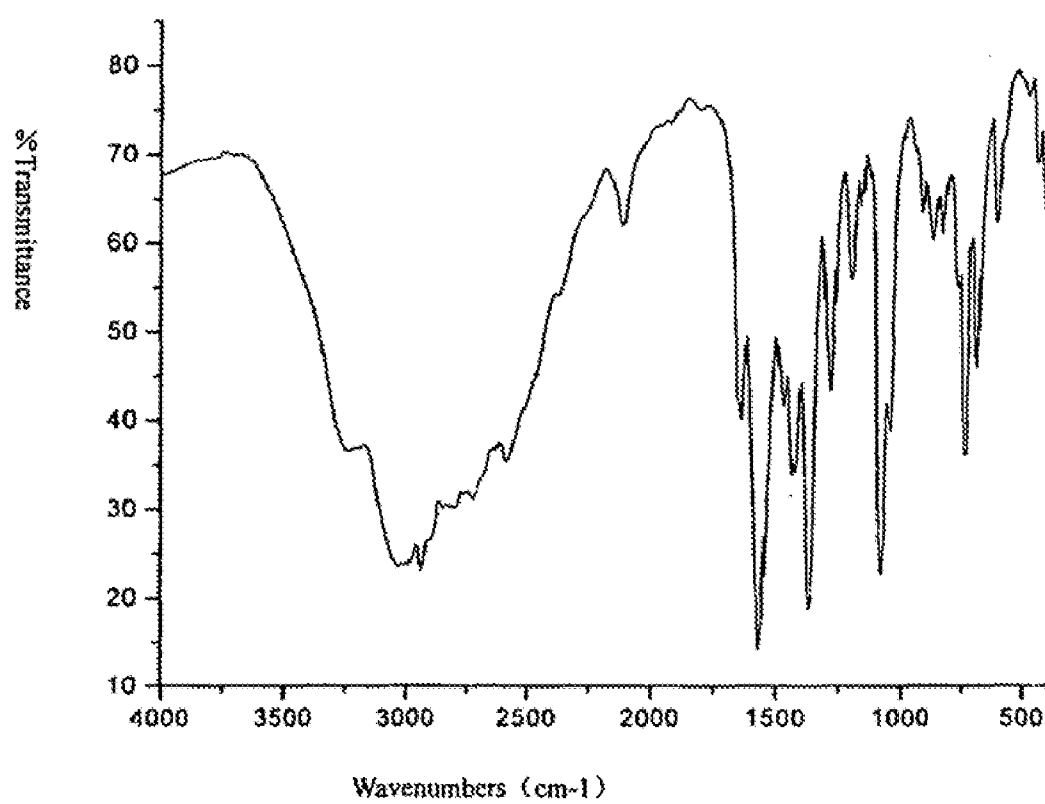


Fig 2

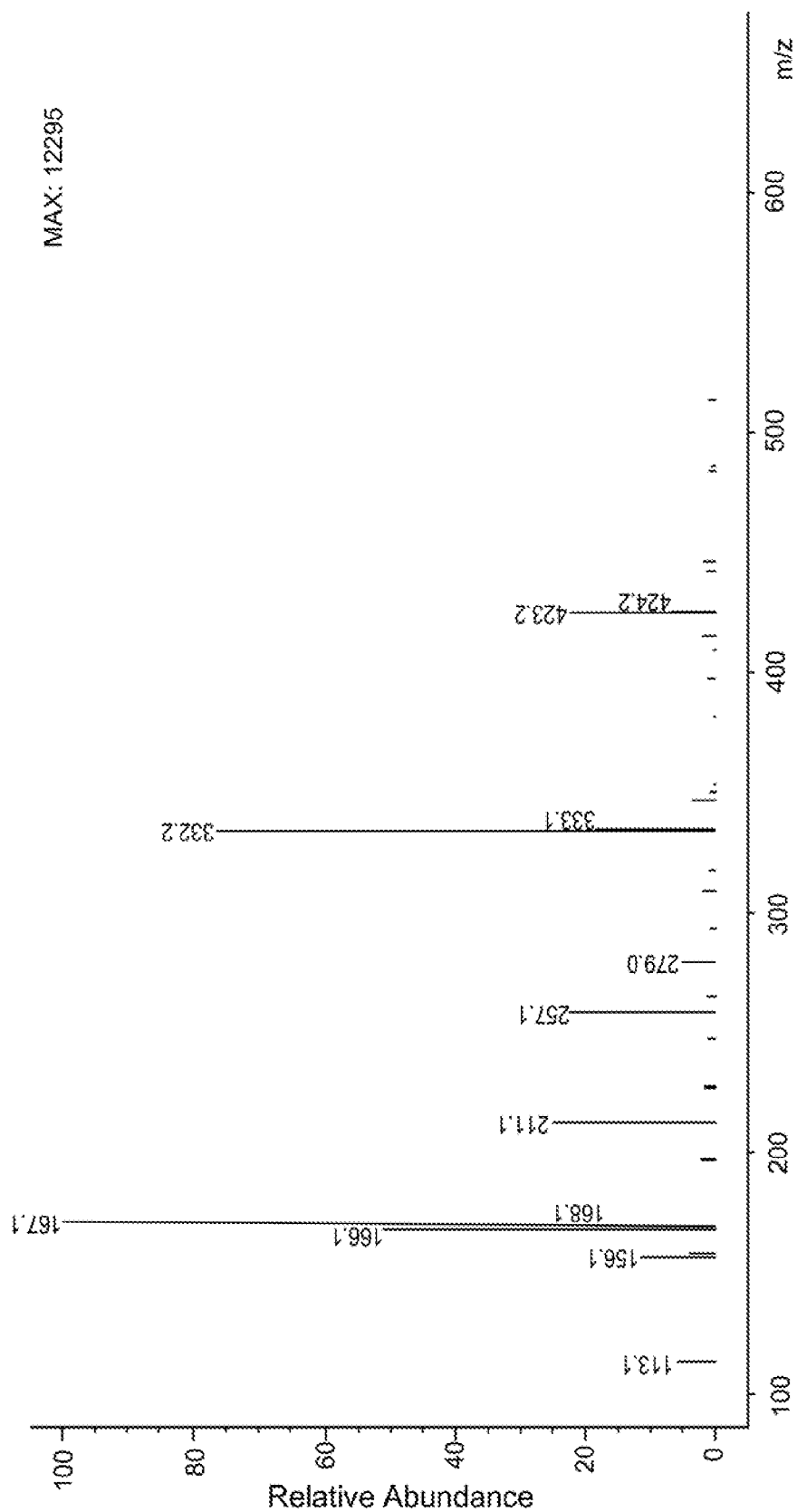


Fig 3

Solute	Solvent	The amount of biphenyl acetic ammonia butantriol salt (g)	The amount of solvent (ml)	The dissolving condition	Conclusion
The amount of biphenyl acetic ammonia butantriol salt	Methanol	0.1135	3	Completely dissolved	Dissolved
	Water	14.1	10	Completely dissolved	Slightly dissolved
	Alcohol	14.3	10	Completely dissolved	Slightly dissolved
	Acetone	8.9	150	Completely dissolved	Undissolvable or almost undissolvable
	Acetonitrile	9.1	150	Completely dissolved	Undissolvable or almost undissolvable
	Formamide	0.2137	6	Completely dissolved	Dissolved

Table 1: the solubility testing

FIG. 4

Group	The number of animals (amount)	Dosage (mg/kg)				
				1 hour	2 hours	3 hours
The blank control group	12	-	19.15±2.97	20.18±2.97	20.24±3.16	20.43±2.85
Low dose group	12	4	19.38±2.96	25.16±5.67	23.00±2.79	22.25±3.16
Medium dose group	12	12	20.24±2.56	33.50±5.54**	32.12±2.95**	30.75±3.15**
High dose group	12	36	19.76±3.74	39.83±4.15***	34.65±3.84***	33.58±2.15** *
Lysine Acetylsalicylate	12	240	19.15±3.46	31.08±4.26**	30.35±3.29**	28.16±2.97**

* P<0.05, ** P<0.01

Table 2: analgesia affection of mice heating plate method

FIG. 5

Group		Dosage (mg/kg)	The number of animals (amount)	Degree of expansion (mg)
Model group		--	10	17.1±3.8
Biphenyl acetic ammonia butantriol salt injection	No. 1	3	10	13.9±2.6*
	No. 2	6	10	13.5±2.9*
	No. 3	12	10	13.0±2.7*
	No. 4	24	10	12.7±2.9*
	No. 5	18	10	10.9±2.5**
Flurbiprofen Axetil injection	No. 1	3	10	14.2±2.7*
	No. 2	6	10	13.2±3.6**
	No. 3	12	10	11.7±3.6**
	No. 4	24	10	11.4±4.7**
	No. 5	48	10	10.9±3.3**

Compare with model group: * $p < 0.05$, ** $p < 0.01$

Table 3: the affection of expansion

FIG. 6

Group	Dosage Dose (mg/kg)	The number of animals (amount)	The number of twist (times)	Inhibitory rate (%)	ED50 and 95% degree of confidence
Model group	—	10	19.9±5.9	—	—
Biphenyl acetic ammonia butantriol salt injection	No.1 3	10	13.2±5.5*	33.7	7.9 mg/kg (4.7-13.5)
	No.2 6	10	11.5±5.4**	42.2	
	No.3 12	10	7.1±3.4**	64.3	
	No.4 24	10	6.8±3.0**	65.8	
	No.5 48	10	5.1±3.0**	74.4	
Flurbiprofen Axetil injection	No.1 3	10	12.7±4.8**	36.2	6.3 mg/kg (4.3-9.3)
	No.2 6	10	9.6±3.0**	51.8	
	No.3 12	10	7.4±3.7**	62.8	
	No.4 24	10	6.5±2.6**	66.8	
	No.5 48	10	4.4±3.2**	77.9	

Compare with model group: * p<0.05, ** p<0.01

Table 4: the affection of expansion

FIG. 7

Allergic reaction						
0	Normal	7	Hyperphea	14	Step unstable	
1	Mania	8	Micturate	15	Jumping	
2	Piloerection	9	Defecation	16	Polypona	
3	Shivering	10	Lacrimation	17	Spasm	
4	Itching mouse	11	Dyspnea	18	Spin	
5	Sneezing	12	Voar	19	Respiration cheyne	
6	Coughing	13	Peliosis	20	Death	

Table 5: allergic reaction symptom

FIG. 8

Reaction symptom	Evaluation standard
0	Allergic reaction negative (-)
1-4	Allergic reaction weak positive (+)
5-10	Allergic reaction positive (++)
11-19	Allergic reaction strong positive (+++)
20	Allergic reaction extremely strong positive (++++)

Table 6: allergenicity evaluation standard of cavia porcellus

FIG. 9

Group	Animals' number	Gender	Weight (g)			D17 weight change (g)
			D1	D5	D17	
Negative control group	1	♀	332	342	395	63
	3	♀	355	360	422	67
	6	♀	323	337	344	21
	7	♂	345	366	428	83
	8	♂	301	310	363	62
	12	♂	348	344	412	64
	Average value		334	343	394	60
	SD		20	20	34	21
Positive control group	2	♀	347	348	405	58
	10	♀	315	319	355	40
	12	♀	334	283	340	6
	1	♂	320	328	367	47
	2	♂	310	334	380	70
	9	♂	360	372	418	58
	Average value		331	331	378	47
	SD		20	30	30	22
Given medicine group (7.5mg/kg·bw)	5	♀	330	333	352	22
	7	♀	335	349	406	71
	8	♀	337	327	376	39
	6	♂	318	358	380	62
	10	♂	351	367	427	76
	11	♂	329	330	366	37
	Average value		333	344	385	51
	SD		11	16	27	22
Given medicine group (22.5mg/kg·bw)	4	♀	338	347	356	18
	9	♀	331	307	318	-13
	11	♀	333	328	448	115
	3	♂	332	324	283	-49
	4	♂	351	338	375	15
	5	♂	315	294	312	56
	Average value		323	349	24	
	SD		12	20	59	57

Table 7: the active allergic testing

FIG. 10

Group	Animals' number	Reaction symptom	Reaction's degree or times	Allergic reaction incidence rate (%)
Negative control group	1	-	-	0
	3	-	-	
	6	-	-	
	7	-	-	
	8	-	-	
	12	-	-	
Positive control group	2	Died	+++++	100
	10	Died	+++++	
	12	Died	+++++	
	1	Died	+++++	
	2	Died	+++++	
	9	Died	+++++	
Reagent group (7.5mg/kg·bw)	5	-	-	0
	7	-	-	
	8	-	-	
	6	-	-	
	10	-	-	
	11	-	-	
Reagent Group (22.5 mg/kg·bw)	4	-	-	0
	9	-	-	
	11	-	-	
	3	-	-	
	4	-	-	
	5	-	-	

Table 8: allergic reaction condition of active allergic testing

FIG. 11

ml	Test Tube's number						
	1	2	3	4	5	6	7
2% red blood cell's suspending liquid	2.5	2.5	2.5	2.5	2.5	2.5	2.5
0.9% NaCl injection	2.0	2.1	2.2	2.3	2.4	2.5	/
Injecting water	/	/	/	/	/	/	2.5
Solution sample	0.5	0.4	0.3	0.2	0.1	/	/

Table 9: number of 2% red blood cell's suspending liquid

FIG. 12

Tube's number		1	2	3	4	5	6	7
Test liquid (ml)								
2% red blood cell's suspending liquid		2.5	2.5	2.5	2.5	2.5	2.5	2.5
0.9% NaCl injection (ml)		2.0	2.1	2.2	2.3	2.4	2.5	0.0
Injecting water (ml)		0.0	0.0	0.0	0.0	0.0	0.0	2.5
The biphenyl acetic ammonia butantriol salt injection (high amount) (ml)		0.5	0.4	0.3	0.2	0.1	0.0	0.0
Judging conclusion	The conclusion of keeping warm at 37°C after 15 minutes	---	---	---	---	---	---	+
	The conclusion of keeping warm at 37°C after 30 minutes	---	---	---	---	---	---	+
	The conclusion of keeping warm at 37°C after 45 minutes	---	---	---	---	---	---	+
	The conclusion of keeping warm at 37°C after 1 hour	---	---	---	---	---	---	+
	The conclusion of keeping warm at 37°C after 2 hours	---	---	---	---	---	---	+
	The conclusion of keeping warm at 37°C after 3 hours	---	---	---	---	---	---	+

“+” = absolutely dissolved; “-” = insolubility

Table 10: hemolytic testing

FIG. 13

Tube's number		1	2	3	4	5	6	7
Test liquid (ml)								
2% red blood cell's suspending liquid		2.5	2.5	2.5	2.5	2.5	2.5	2.5
0.9% NaCl injection (ml)		2.0	2.1	2.2	2.3	2.4	2.5	0.0
Injecting water (ml)		0.0	0.0	0.0	0.0	0.0	0.0	2.5
The biphenyl acetic ammonia butantriol salt injection (high amount) (ml)		0.5	0.4	0.3	0.2	0.1	0.0	0.0
Judging conclusion	The conclusion of keeping warm at 37°C after 15 minutes	—	—	—	—	—	—	+
	The conclusion of keeping warm at 37°C after 30 minutes	—	—	—	—	—	—	+
	The conclusion of keeping warm at 37°C after 45 minutes	—	—	—	—	—	—	+
	The conclusion of keeping warm at 37°C after 1 hour	—	—	—	—	—	—	+
	The conclusion of keeping warm at 37°C after 2 hours	—	—	—	—	—	—	+
	The conclusion of keeping warm at 37°C after 3 hours	—	—	—	—	—	—	+

“+” = absolutely dissolved; “-” = insolubility

Table 11: hemolytic testing

FIG. 14

Rabbits No.	Left ear (reagent side)	Right ear (the control group side)
1	A sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using.	A sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using.
3	The skin color of injection area is red (0.1cm×0.5cm). A sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using.	A sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using.
4	A sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using.	The skin color of injection area is red (0.2 cm ×0.5cm). A sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using.
6	A sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using.	A sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using.

Table 12: the exciting reaction (high dosage)

FIG. 15

Rabbits No.	Left ear (reagent side)	Right ear (the control group side)
2	A sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using.	A sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using.
5	The skin color of injection area is red (0.1cm×0.2cm). A sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using.	A sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using.
7	The skin color of injection area is red (0.1 cm ×0.2cm). A sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using.	A sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using.
8	The skin color of injection area is red (0.1 cm ×0.2cm). A sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using.	A sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using.

Table 13: the exciting reaction (low dosage)

FIG. 16

Animal No.	Left leg quadriceps muscle (reagent side)	Right leg quadriceps muscle (control side)
1	The muscular tissue around injection area is full of flexibility and luster, no significant change	The muscular tissue around injection area is full of flexibility and luster, no significant change
3	The muscular tissue around injection area is full of flexibility and luster, no significant change	The muscular tissue around injection area is full of flexibility and luster, no significant change
4	The muscular tissue around injection area is full of flexibility and luster, no significant change	The muscular tissue around injection area is full of flexibility and luster, no significant change
6	The muscular tissue around injection area is full of flexibility and luster, no significant change	The muscular tissue around injection area is full of flexibility and luster, no significant change

Table 14: the exciting reaction (high dosage)

FIG. 17

Animal No.	Left leg quadriceps muscle (reagent side)	Right leg quadriceps muscle (control side)
2	The muscular tissue around injection area is full of flexibility and luster, no significant change	The muscular tissue around injection area is full of flexibility and luster, no significant change
5	The muscular tissue around injection area is full of flexibility and luster, no significant change	The muscular tissue around injection area is full of flexibility and luster, no significant change
7	The muscular tissue around injection area is full of flexibility and luster, no significant change	The muscular tissue around injection area is full of flexibility and luster, no significant change
8	The muscular tissue around injection area is full of flexibility and luster, no significant change	The muscular tissue around injection area is full of flexibility and luster, no significant change

Table 15: the exciting reaction (low dosage)

FIG. 18

Animal No.	Left leg quadriceps muscle (reagent side)	Right leg quadriceps muscle (control side)
1	The structure of muscle tissue is normal, and the muscle fiber is very tidily arranged	The structure of muscle tissue is normal, and the muscle fiber is very tidily arranged
3	The structure of muscle tissue is normal, and the muscle fiber is very tidily arranged	The structure of muscle tissue is normal, and the muscle fiber is very tidily arranged
4	The structure of muscle tissue is normal, and the muscle fiber is very tidily arranged	The structure of muscle tissue is normal, and the muscle fiber is very tidily arranged
6	The structure of muscle tissue is normal, and the muscle fiber is very tidily arranged	The structure of muscle tissue is normal, and the muscle fiber is very tidily arranged

Table 16: the exciting reaction (high dosage)

FIG. 19

Animal No.	Left leg quadriceps muscle (reagent side)	Right leg quadriceps muscle (control side)
2	The structure of muscle tissue is normal, and the muscle fiber is very tidily arranged	The structure of muscle tissue is normal, and the muscle fiber is very tidily arranged
5	The structure of muscle tissue is normal, and the muscle fiber is very tidily arranged	The structure of muscle tissue is normal, and the muscle fiber is very tidily arranged
7	The structure of muscle tissue is normal, and the muscle fiber is very tidily arranged	The structure of muscle tissue is normal, and the muscle fiber is very tidily arranged
8	The structure of muscle tissue is normal, and the muscle fiber is very tidily arranged	The structure of muscle tissue is normal, and the muscle fiber is very tidily arranged

Table 17: the exciting reaction (low dosage)

FIG. 20

Group	Dosage (mg/kg)	Number of ulcer animals / Sum of total animals
The biphenyl acetic ammonia butantriol salt	333	7/15
Biphenyl acetate	212	13/15

Table 18: the test of stomach channel

FIG. 21

BIPHENYL ACETATE, PREPARATION AND USES THEREOF

CROSS REFERENCE OF RELATED APPLICATION

[0001] This is a continuation application that claims the benefit of priority under 35 U.S.C. §119 to a non-provisional application, application Ser. No. 12/309,326 with a filing date of Jan. 12, 2009, which is a national phase national application of an international patent application number PCT/CN2007/002830 with a filing date of Sep. 27, 2007 based on a foreign application number 200610122917.4 with a filing date of Oct. 23, 2006 in China. The contents of these specifications, including any intervening amendments thereto, are incorporated herein by reference.

BACKGROUND OF THE PRESENT INVENTION

[0002] 1. Field of Invention

[0003] The present invention relates to preparation and use of biphenyl acetate, and more particularly to a preparation and use of biphenyl acetic ammonia butantriol salt.

[0004] 2. Description of Related Arts

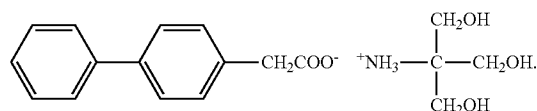
[0005] In 1993, biphenyl acetic acid is commonly used as a medicine for reducing inflammation and relieving pain in Japan and Italy. The biphenyl acetic acid is used to provide analgesia and anti-inflammatory effect related to metatarsal arthritis, omarthritis, tenosynovitis, muscle pain and cartilage tissue injury. In addition, it is also used for reducing traumatic swelling and pain. Because of its insolubility in water, biphenyl acetate can only be used for traumatic medicine. This property restricts the application of this medicine dramatically.

[0006] In Japan, biphenyl ethyl acetate has been used for injecting emulsion (insoluble in water) for reducing clinical pain of a living object. However, the manufacture of this medication has recalled this type of emulsion recently because it is discovered that the emulsion may cause a shock phenomenon to the living object. Further clinical studies found that allergy is the major cause of the shock phenomenon and the soy phosphatidol acting as the coemulsifier of the injecting emulsion acts may be one of the allergen. Therefore, the biphenyl ethyl acetate which is manufactured in an emulsion form has the drawbacks of very low stability, involving complicated preparation process and technique and being unsafe owing to the macromolecular structure of the coemulsifier. In other words, in view of the functional group of biphenyl acetic acid, there is no solution provided to make use of this functional group for preparation of injection solution or the like which is stable in structure and safe for administration as injection to a living object. It is worth mentioning that the injecting emulsion contains macromolecular protein which may not only impose toxic effect on liver but also cause allergy to the living object, therefore imposing safety issue when used in living object.

SUMMARY OF THE PRESENT INVENTION

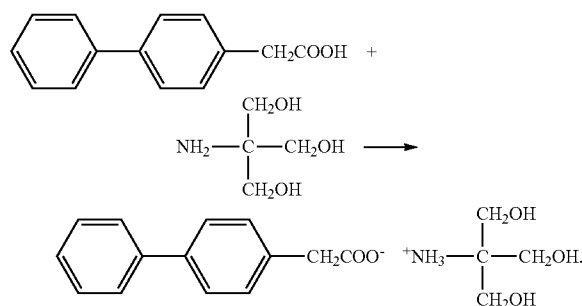
[0007] An object of the present invention is to provide a new kind of biphenyl acetate, which is biphenyl acetic ammonia butantriol salt. The biphenyl acetic ammonia butantriol salt has the following chemical structure.

(I)



[0008] Its molecular structure is $C_{18}H_{23}NO_5$, and its molecular weight is 333.14.

[0009] Another object of the present invention is to provide a manufacturing method of biphenyl acetic ammonia butantriol salt. This method is to react biphenyl phenylacetic acid with ammonia butantriol in organic solvent, and then generate biphenyl acetic ammonia butantriol salt. The reaction formula is below:



[0010] In the method above, it is available to add biphenyl phenylacetic acid with ammonia butantriol at the same time in organic solvent, or add biphenyl phenylacetic acid first. It is also available to add ammonia butantriol first in organic solvent, and then react with biphenyl phenylacetic acid to generate biphenyl acetic ammonia butantriol salt. In order to increase recovery rate, the ratio of biphenyl phenylacetic acid and ammonia butantriol should be 1:1. As for organic solvent, this organic solvent should have the ability to dissolve phenyl acetic acid, such as alcohol and benzene, and especially chose methanol, anhydrous ethanol, acetone, and n-butanol, benzyl and benzene. In the method above, there are not any special requirement for temperature and time. The normal reaction temperature is 0-80° C., but it prefers to set the temperature at 50-70° C. The reaction time is 0.5-2 hours.

[0011] The method also includes the procedure of the purification of biphenyl acetic ammonia butantriol salt. There are variety purification methods that we can use today, and here are two classic purification method: the first one is to evaporate solvent, and then generate the white powder after the reaction. Further, the procedure is to dry the white powder in vacuum, and then generate biphenyl acetic ammonia butantriol salt. The other method is to cool down the solvent below 0° C., and then generate crystallization. Consequently, we dry the crystallization in vacuum to produce biphenyl acetic ammonia butantriol salt. The second method is the best way to use, because it can get the better compound's purity and crystal analgesic.

[0012] According to the above manufacturing method, the yield of biphenyl acetic ammonia butantriol salt is 85.6-96%, and the purity is 99.2-99.8%. Further, the melting point is 162-163° C.

[0013] Another object of the present invention is to provide the pharmaceuticals application of biphenyl acetic ammonia butantriol salt. As for the research, this biphenyl acetic ammonia butantriol salt has anti-inflammatory, analgesic, and antipyretic. Accordingly, the subject matter of the present invention is the active compound of biphenyl acetic ammonia butantriol salt.

[0014] If the purpose require, we can add one or more kinds of accepting carrier in this medicine, including diluting agent, excipient, extender, adhesive, moistening agent, disintegrating agent, absorbefacient, surfactant, adsorption agent, and lubricant. This medicine also can add scenting agent, sweetening agent and so on.

[0015] This medicine can be manufactured as injection (injective liquid, injective cool powder, and injective aseptic needle), tablet, powder, pill, capsule, oral liquid, cream, and so on. These above kinds of medicines all can be manufactured in terms of the normal order in pharmaceutical field. The amount of taking this biphenyl acetic ammonia butantriol salt medicine is 0.8-3.6 mg/kg/days.

[0016] Still further objects and advantages will become apparent from a consideration of the ensuing description and drawings.

[0017] These and other objectives, features, and advantages of the present invention will become apparent from the following detailed description, the accompanying drawings, and the appended claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0018] FIG. 1 is the HNMR spectroscopy analysis of biphenyl acetic ammonia butantriol salt according to a preferred embodiment of the present invention.

[0019] FIG. 2 is the IR spectroscopy analysis of biphenyl acetic ammonia butantriol salt according to the above preferred embodiment of the present invention.

[0020] FIG. 3 is the Mass spectroscopy analysis of biphenyl acetic ammonia butantriol salt according to the above preferred embodiment of the present invention.

[0021] FIG. 4 shows Table 1 which illustrates solubility testing.

[0022] FIG. 5 shows Table 2 which illustrates the analgesia affection of mice heating plate method's for injecting the biphenyl acetic ammonia butantriol salt liquid.

[0023] FIG. 6 shows Table 3 which illustrates the affection of expansion in Kunming's mouse for biphenyl acetic ammonia butantriol salt injection in dimethyl benzene.

[0024] FIG. 7 shows Table 4 which illustrates the affection of expansion in Kunming's mouse for biphenyl acetic ammonia butantriol salt injection glacial acetic acid.

[0025] FIG. 8 shows Table 5 which illustrates allergic reaction symptom.

[0026] FIG. 9 shows Table 6 which illustrates allergenicity evaluation standard of caviaporcellus.

[0027] FIG. 10 shows Table 7 which illustrates the active allergic testing of animals' change condition in caviaporcellus for injects the biphenyl acetic ammonia butantriol salt injection.

[0028] FIG. 11 shows Table 8 which illustrates allergic reaction condition of the whole body active allergic testing in injecting the biphenyl acetic ammonia butantriol salt injection.

[0029] FIG. 12 shows Table 9 which illustrates the number of 2% red blood cell's suspending liquid.

[0030] FIG. 13 shows Table 10 which illustrates the result of hemolytic testing (application of visual) of the biphenylacetic ammonia butantriol salt injection (high amount) (ml).

[0031] FIG. 14 shows Table 11 which illustrates the result of hemolytic testing (application of visual) of the biphenylacetic ammonia butantriol salt injection (low amount) (ml).

[0032] FIG. 15 shows Table 12 which illustrates the exciting reaction of rabbits' ear for the biphenyl acetic ammonia butantriol salt injection (Application of visual after 48 hours regent time).

[0033] FIG. 16 shows Table 13 which illustrates the exciting reaction of rabbits' ear for the biphenylacetic ammonia butantriol salt injection (Application of visual after 48 hours' last regent time).

[0034] FIG. 17 shows Table 14 which illustrates the exciting reaction of rabbits' muscle (Application of visual) for the biphenyl acetic ammonia butantriol salt injection (high amount).

[0035] FIG. 18 shows Table 15 which illustrates the exciting reaction of rabbits' muscle (Application of visual) for the biphenyl acetic ammonia butantriol salt injection (low amount).

[0036] FIG. 19 shows Table 16 which illustrates the exciting reaction of rabbits' muscle (sickness investigation) for the biphenyl acetic ammonia butantriol salt injection (high amount).

[0037] FIG. 20 shows Table 17 which illustrates the exciting reaction of rabbits' muscle (sickness investigation) for the biphenyl acetic ammonia butantriol salt injection (low amount).

[0038] FIG. 21 shows Table 18 which illustrates the test of stomach channel.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

[0039] The embodiment of the present invention as shown and described below is exemplary only and not intended to be limiting. Therefore, this invention includes all modifications or any combination encompassed within the spirit and scope of the followings.

[0040] The following description illustrates a preparation of biphenyl acetic ammonia butantriol salt according to a first preferred embodiment of the present invention.

[0041] 21.2 g (0.1 ml) of Biphenyl acetate and 210 ml of methanol are added into a dry and clean 250 ml three opening round bottom crucible bottle. Stir and heat the mixture to 60° C. until the mixture is totally dissolved. Add ammonia butantriol into the mixture solution until the solution is in a clarified transparent manner. Stir the solution for one hour and make TLC fully reacting with the solution. (eluent: DMF—acetic ester 2:1). Set the end point when the raw material biphenyl acetate is totally reacted with another reactants. Cool down to -5° C. for 5 hours and get huge amount of white crystal. Remove chloride and put the solution into vacuum dry machine at 80° C. Finally, we can get the biphenyl acetic ammonia butantriol salt in a white crystal manner. The melting point thereof is between 162 and 163° C. The yield is 91.6%. The theoretical value of element analysis is C, 64.9%, H, 6.9%, N, 4.2%, O, 24%. The actual value of element analysis is C, 64.1%, H, 7.3%, N, 3.6%, O, 25%).

[0042] FIG. 1 shows the ¹HNMR spectroscopy analysis of biphenyl acetic ammonia butantriol salt.

[0043] There are eight hydrogen peaks signal in the ^1H NMR spectroscopy of the biphenyl acetate in the solvent of DMSO- d_6 . According to the chemical shift in ^1H NMR spectroscopy, all peaks' chemical shift (δ) below 4 ppm are H signal of saturated carbon, and the total sum of peaks are 14. Therefore, if δ value is smaller than 6 ppm, there are all H signal of aromatic ring, and the total number of these peaks is 9. At $\delta=3.35$ ppm, the 2H single hydrogen peak can be determined as an isolated CH_2 group. In the structure of biphenyl acetate, the carbon No. 13 which connects with benzene and COO — in CH_2 does not accept the coupling of other hydrogen's core. At $\delta=3.43$ ppm, the 3H single peak can be determined as three equal value isolated CH_2 group. In the structure of biphenyl acetate, carbon NOs. 18, 19, 20 all connect with the carbon No. 17 of the CH_2 , and these three CH_2 are equal values. Because of these three CH_2 does not accept the coupling and have the equal value, it reveals single peak signal. The wide peak at $\delta=3.43$ ppm can be determined as three OH group and a protonation's NH_3^+ , because these active H probably combine with the water which is in the solvent, it reveals a wider peak. The integral value cannot explain the real number of these active H, because there is water in this solvent. There are four splitting signal groups in the low magnetic field, and according to these peaks' area it only can be known that there are 3, 2, 2, 2, H from high to low magnetic field. Further, there are only three left groups which can be clarify their peak shape, so they can be clarified as two duplicate and one triple peaks. In addition, it can be explained that there are H on the benzene due to their chemical shift, so two duplicate peaks near 8.0 Hz which named as peak No. 7 and No. 8 can indicate as two positions. One position is on a side of benzene which has H, and the other is a side of benzene which does not have H but have other substituted group. The two duplicate peaks can be explained as four H in the structure of biphenyl acetate which are H2/H6, H3/H5, and H8/H12. Furthermore, the triple peaks near by 7.6 Hz can be explained as positions that those benzenes have H on their both side, and there are H9, H10, and H11 in this molecular structure.

[0044] IR spectroscopy analysis of biphenyl acetic ammonia butantriol salt is shown in FIG. 2.

[0045] (1) It can be determined the structure of this molecule has amine salts of carboxylic acids, if there is a wide and strong COO — stretching vibration peak at 1560.13 cm^{-1} , and wide, strong, and scattered NH_3^+ characteristic peak at the region of $2927.41\text{--}2113.60\text{ cm}^{-1}$. The COO — and NH_3^+ form a COO — NH_3^+ free monomer molecular structure, and COO — and NH_3^+ also easily form hydrogen bonds between dimmer to polymer. In addition, the stretching vibration frequency region of NH_3^+ and OH of $\text{CH}_2\text{—OH}$ reveal at $2927.41\text{--}2113.60\text{ cm}^{-1}$, and then form multiple, overlapping, scattered, and strong peaks.

[0046] (2) The stretching vibration wide strong peak of OH is at 3214.94 cm^{-1} . The other deformed vibrations about OH group (60H) are at 1423.21 cm^{-1} and 1278.57 cm^{-1} , and further a flat shaking vibration is at about 690.39 cm^{-1} (rOH). It can be explained that the wide, strong, and stretching vibration peak at 1083.80 cm^{-1} is C—O ($\nu\text{C—O}$), so it also can declare that OH directly connect with CH_2 .

[0047] (3) The series spectrum peaks at $2987\text{--}2896\text{ cm}^{-1}$, which are determined there are saturated carbon hydrogen group in this molecular structure, are both the asymmetric and symmetric stretching vibration group, such as CH_3 and CH_2 . At the same time, the deformed absorbing vibration of CH_3

and CH_2 reveal at the region of $1467\text{--}1367\text{ cm}^{-1}$. Even though, it can be reasoned from NMR spectrum that this compound does not contain methyl, there are some disrupted peaks near by $2965\pm\text{cm}^{-1}$ and $1375\pm\text{cm}^{-1}$ from IR, so it cannot be clarify that this compound does not include methyl.

[0048] (4) At $3100\text{--}2980\text{ cm}^{-1}$, there are a series of peaks that can be declared this molecular structure has unsaturated hydrocarbon group, such as aromatic ring, benzene ring, and alkene structure. At $1650\text{--}1423\text{ cm}^{-1}$, there are many unsaturated group that can be determined as C=C and C=N . At $1201\text{--}977\text{ cm}^{-1}$, it can be determined that has an internal bending vibration (β) of $=\text{CH}$ group in benzene. At 738.6 and 690.39 cm^{-1} , it can be determined that has two outer bending strong vibration peaks of monosubstituted benzene ring (γ). At the region of $2000\text{--}1666\text{ cm}^{-1}$, a series' peaks in this region are the same as the overlapping and combined of a monosubstituted benzene ring and a p-disubstituted benzene ring.

[0049] (5) There is stretching vibration of amine salt's C—N bond which reveals at 1045.2 cm^{-1} , and further, there is an outer bending vibration (γ) of NH_3^+ reveals at 605.5 cm^{-1} .

[0050] Mass spectroscopy analysis of biphenyl acetic ammonia butantriol salt is shown in FIG. 3.

[0051] The positive molecular ion ($\text{C}_{18}\text{H}_{23}\text{NO}_5^+$) of the biphenyl acetate molecule are examined that its charge-mass ratio (m/z) is 332.2 and relative abundance is 20. Therefore, the ratio value is 333.16 for calculating with accurate mass theory, because the low measuring accuracy of low resolution mass spectrometer generates mass relative error which is 5×10^{-4} . In the theory, the calculating value of $\text{C}_{18}\text{H}_{22}\text{NO}_5^+$ ion mass fragment is 332.15 m/z , so it only has 0.6×10^{-4} relative error.

[0052] The structure of the biphenyl acetic ammonia butantriol salt is I, and the purification is 99.5%.

[0053] The solution test of biphenyl acetic ammonia butantriol salt:

[0054] According to Chinese medicine book in 2005 edition, the preparation of biphenyl acetic ammonia butantriol salt is made by different solvent. In other words, they use acetone, formylamine, ethane nitrile, methanol, alcohol as the solvent to test their solubility. At first, mill the biphenyl acetic ammonia butantriol salt into flour and weight it, and add solvent into the biphenyl acetic ammonia butantriol salt. Second, at $25\pm 2^\circ\text{C}$., wave the mixer solution every 5 minutes for 30 seconds, and inspect the dissolve situation. Repeat three times and the result is illustrated in Table 1. Referring to Table 1, the biphenyl acetic ammonia butantriol salt is soluble in formamide and methanol, slightly soluble in water and alcohol, and is insoluble in acetone and acetonitrile.

Preferred Embodiment 2

[0055] 21.2 g (0.1 ml) of Biphenylacetate, 12.1 g (0.1 mole) of ammonia butantriol, and 150 ml of absolute alcohol are added into a dry and clean 250 ml three opening round bottom crucible bottle. Stir the solution mixture at 50°C . 30 minutes for totally dissolving until the solution is in a clarified transparent manner. Evaporate the mixture solution and get white powder. Put the solution into vacuum dry machine at 80°C . Finally, we can get 32 grams of biphenyl acetic ammonia butantriol salt. The melting point thereof is between 163 and 164°C . The yield is 96.0%. The theoretical value of element analysis is C, 64.9%, H, 6.9%, N, 4.2%, O, 24%. The actual

value of element analysis is C, 64.1%, H, 7.3%, N, 3.6%, O, 25%) The product is biphenyl acetic ammonia butantriol salt, and the purity is 99.2%.

Preferred Embodiment 3

[0056] 21.2 g (0.1 ml) of Biphenyl acetate and 210 ml of benzene are added into a dry and clean 250 ml three opening round bottom crucible bottle. Stir and heat the mixture until the solution is perfect dissolved. Add ammonia butantriol into the mixture solution until the solution is in a clarified transparent manner. Stir the solution for two hours and make TLC fully reacting with the solution. Set the end point when the raw material biphenyl acetate is totally reacted with other reactants judge by TLC. Cool down to get huge amount of white crystal. Remove chloride and use absolute ether washing the white crystal and then put it into vacuum dry machine at 80° C. Finally, we can get the biphenyl acetic ammonia butantriol salt 28.5 grams. The melting point is between 163 and 164° C. The yield is 85.6%. The theoretical value of element analysis is C, 64.9%, H, 6.9%, N, 4.2%, O, 24%. The actual value of element analysis is C, 64.1%, H, 7.3%, N, 3.6%, O, 25%) The product is biphenyl acetic ammonia butantriol salt, and the purity is 99.8%.

[0057] Preferred embodiment 4: Preparation of the injection liquid: biphenyl acetic ammonia butantriol salt.

[0058] Recipe: 94 grams of biphenyl acetic ammonia butantriol salt and 1 to 2 grams of sodium carbonate to form 1000 syringes.

[0059] Use the method of preferred embodiment 1 to adjust the biphenyl acetic ammonia butantriol salt into a container, add a predetermined amount of water. Stir the mixture and meanwhile add 0.1% (0.1 g/100 ml) sodium carbonate until the biphenyl acetic ammonia butantriol salt is perfect dissolved. Control the pH value between 8.5 and 8.8. Add water up to 4000 ml. Add 2 gram of active carbon. Heat the solution for 15 minutes. Remove chloride and carbon from the solution. The liquid is filtered by 0.22 um micro filter, and is contained and sealed it to different syringe tubes. (Each tube includes 94 grams of biphenyl acetic ammonia butantriol salt). Finally, the solution is treated under a predetermined pressure and germ-free at 115° C. to form the final product.

[0060] Preferred embodiment 5: Preparation of the dry powder of biphenyl acetic ammonia butantriol salt to form 1000 dropper bottles.

[0061] Recipe: 94 grams of biphenyl acetic ammonia butantriol salt and 20 grams of mannite.

[0062] Use the method of preferred embodiment 1 to adjust 94 grams of biphenyl acetic ammonia butantriol salt into a container, add 20 grams of mannite and a predetermined amount of water for solvent. Add water up to 3000 ml. Add 2 gram of active carbon. Heat the solution for 15 minutes. Remove chloride and carbon. The solution is filtered by 0.22 um micro filters, and is contained and sealed it to different dropper bottles. (each bottle includes 94 grams of biphenyl acetic ammonia butantriol salt).

[0063] Preferred embodiment 6: Preparation of the capsule of biphenyl acetic ammonia butantriol salt.

[0064] Recipe: 188 grams of biphenyl acetic ammonia butantriol salt and 20 grams of lactose to form 1000 capsules.

[0065] Use the method of preferred embodiment 2 to adjust 94 grams of biphenyl acetic ammonia butantriol salt and go through 100 sieves. Add prescription lactose at 80° C. and go through 80 sieves, mixed, and test its component. Finally, fill it into the No. 1 capsule.

[0066] Preferred embodiment 7: The test of medicine effects of biphenyl acetic ammonia butantriol salt.

[0067] 1. Pain Effects in a Mouse Injection Biphenyl Acetic Ammonia Butantriol Salt

[0068] Pick the female Kunming mouse, each having the weight between 20 to 22 grams. At first, test their sensitive towards pain. Put the mouse on the hot plate with the temperature of 55±0.5° C., and calculate how much pain does the mouse has by determining how many times they lick their back leg. Eliminate the mice seem to like to jump and the mice has no respond for 30 seconds. Pick a total of 60 mice having sensitive to pain and divide them into 5 groups randomly. Use the method of preferred embodiment 4 to adjust the biphenyl acetic ammonia butantriol salt. The dosage of biphenyl acetic ammonia butantriol salt is divided into low, medium, and high dosage, correspondingly to 4, 12, 36 mg/kg, and normal dosage 1/3, 1, 3 respectively. And there is a positive contrast group. The mixture solution is injected into the vein of each of the mice according to its weight ratio 0.1 ml liquid/10 gram weight. On the other hand, the saline is injected into the vein in the contrast group. Use epilation to remove the hair of the back leg of the mouse. Record the painful of every mouse before giving drug, and record the painful after giving drug 1 hour. After the mouse licks its foot, remove the hot plate immediately. Do the same record again at the second and third hour after giving drug. Do the t inspect, and judge its effects on easing pain.

[0069] As shown in Table 2, it shows that the pain results are very similar on different mouse before giving drugs. After giving drugs, the biphenyl acetic ammonia butantriol salt is significantly extends the time which mouse is standing on the hot plate at first, second, and the third hour compared to the contrast group. In other words, it increases the ability of those mice to fight with pain.

[0070] 2. The Pain Effects in a Kunming Mouse Injection Biphenyl Acetic Ammonia Butantriol Salt Towards their Swelling Ears.

[0071] (1) Material and Recipe:

[0072] (1.1) Test Animals:

[0073] Kunming mouse: SPF LEVEL, male, 15-17 grams, a total numbers of 110 mice are used.

[0074] Certification number: SCXK 2003-0002, 2005A012

[0075] (1.2) Drugs: Use the Method of Preferred Embodiment 4 to Adjust the Biphenyl Acetic Ammonia Butantriol Salt

[0076] 2. Methods and Results

[0077] Total numbers of 110 Kunming mice are used, male, 15-17 g, medical inspection for 3 days.

[0078] After testing, the mice are divided into eleven groups randomly and each group contains 10 mice. The numbers and dosage of the biphenyl acetic ammonia butantriol salt are 1, 2, 3, 4, 5 and 3, 6, 12, 24, 48, respectively. The numbers and dosage of flurbiprofenaxetil are 1, 2, 3, 4, 5, and 3, 6, 12, 24, 48 respectively. Use the dimethybenzene to make the mouse ear swelling, and use the mouse left ear as the contrast group. After 30 minutes, the mixing liquid is injected into the vein according to its weight ratio 0.1 ml liquid/10 gram weight. Use a punch, having the diameter of 8 mm, to punch the same hole in two different ears. Weight it by very high quality scale. Finally, the swelling ratio is: the weight of right ear plus the weight of left ear.

[0079] Referring to Table 3, it shows the swelling ratio of the biphenyl acetic ammonia butantriol salt NO. 1, NO. 2, NO. 3, NO. 4, and NO. 5 and its swelling ratio caused by dimethybenzene respectively. (p lower than 0.05 and p higher than 0.01) On the same manner, the flurbiprofenaxetil NO. 2, NO. 3, NO. 4, and NO. 5 is significantly reduces the swelling ratio towards Kunming mouse caused by dimethybenzene.

[0080] There is no significantly difference between biphenyl acetic ammonia butantriol and flurbiprofenaxetil. To sum up, the effect of the biphenyl acetic ammonia butantriol towards the swelling ear caused by dimethybenzene is almost the same as the flurbiprofenaxetil towards the swelling ear caused by dimethybenzene.

[0081] 3. The Injection of Biphenyl Acetic Ammonia Butantriol Towards the NIH Mice Twisted Caused by the Acetic Acid.

[0082] 1. Methods and Results

[0083] (1.1) Test Animals

[0084] NIH mice, SPF level, half of the mice are male and half of the mice are female, 15-17 g, a total numbers of 110 mice are used.

[0085] Certification number: SCXK 2003-0002, 2006A017

[0086] (1.2) Medicine

[0087] Use the method of preferred embodiment 4 to adjust the biphenyl acetic ammonia butantriol salt.

[0088] Flurbiprofenaxetil Injection Liquid

[0089] The experiment method and result

[0090] After testing, the 110 NIH mice are divided into eleven groups randomly, which means each group has 10 mice, and each of the mice has a weight between 15 and 17 grams. The numbers and dosage of the biphenyl acetic ammonia butantriol salt are 1, 2, 3, 4, 5 and 3, 6, 12, 24, 48 mg/kg respectively. The numbers and dosage of flurbiprofenaxetil are 1, 2, 3, 4, 5, and 3, 6, 12, 24, 48 respectively also. The medicine and weight ratio is 0.1 ml medicine/10 g weight. Meanwhile, we give the same quantity of saline solution to the contrast group. After 30 minutes, the mixture solution is injected into the vein according to its weight ratio 0.1 ml liquid/10 gram weight for HAc painful. Record the twist reaction every 15 minutes, count the twist reaction, and calculate the inhibition rate.

[0091] Table 4 shows the biphenyl acetic ammonia butantriol salt solution NOs. 1, 2, 3, 4, 5 and its control group can dramatically control the twist caused by the injection glacial acetic acid. ($P < 0.05$ or $P > 0.01$) ED 50 and 95% degree of confidence is 7.9 (4.7-13.5) mg/kg. Meanwhile, the flurbiprofenaxetil solution NOs. 1, 2, 3, 4, 5 and its control group can dramatically control the twist caused by the injection glacial acetic acid. ($P < 0.01$) ED 50 and 95% degree of confidence is 6.3 (4.9-6.3) mg/kg.

[0092] There is no significantly difference between biphenyl acetic ammonia butantriol and flurbiprofenaxetil injection. To sum up, the effect of the biphenyl acetic ammonia butantriol towards the mouse twisted caused by glacial acetic acid is almost the same as the flurbiprofenaxetil towards the mouse caused by glacial acetic acid.

[0093] Preferred embodiment 8: the safety test of injection of biphenyl acetic ammonia butantriol salt.

[0094] The safety test is published by Chinese drug inspection department issued on August 2003. (GLP)

[0095] The Drug

[0096] (1) Use the Method of Preferred Embodiment 4 to Adjust the Biphenyl Acetic Ammonia Butantriol Salt

[0097] The initial dosage to the animal: vein injection, 94 mg/injection, use 0.9% NACL solution dilates to 100-200 ml, once or twice injection per day.

[0098] (2) The Positive Contrast Group: White Egg, No: 050114

[0099] (3) The Positive Contrast Group: 0.9% (0.9 g/100 ml) NACL Solution

[0100] 2. Test Animal and Feed Condition:

[0101] Guinea Pig

[0102] a. level, race: the common level guinea pig.

[0103] b. Age: 10 to 12 weeks old.

[0104] c. First weight when purchasing/sex: 280-330 g, half of guinea pigs are male and half of guinea pigs are female.

[0105] d. original from, and evidence of certification: certification number: SCXK 2006-0015, 2006B-007.

[0106] e. animal pick explanation: guinea pig is one of the priority experiments for allergy test, it is recommended by the drug research guide.

[0107] f. Inspection procedure: do the investigation to the test animal before inspection. Review the appearance and behavior of the animal including defecation, food intake, and so on, and eliminate viral animal. The entire animal doing the investigation are required to have the permit from the investigation person.

[0108] g. Standard method: use the drying method, and use saturated sorrow and bitter solution to mark spot on different parts of animal for different number. Each group has 3 guinea pigs, and mark them respectively.

[0109] 2. Rabbit

[0110] a. level, race: the common level rabbit.

[0111] b. Age: 3 months old.

[0112] c. First weight when purchasing, sex: 2.0-2.2 kg, half of the rabbits are male and half of the rabbits are female.

[0113] d. original from, and evidence of certification: certification number: 2006A001

[0114] e. animal pick explanation: rabbit is one of the priority experiments of allergy test, it is recommended by the drug research guide.

[0115] f. Inspection procedure: the procedure is the same as guinea pig does.

[0116] g. Standard method: the method is the same as rabbit does. Feed the rabbits separately, and mark them.

[0117] (3) Feed Condition:

[0118] a. Feed management: the animal is feeding by people who own the certificate of feeding animal.

[0119] b. Feed condition, level, and certification: guinea pig and the rabbit are living in common guinea pig room and rabbit room respectively, all the utility meets the requirement of safety animal living, and good air ventilation and light, temperature is between 16-26°C., humidity is 40 to 70%, The animal safety certification number is: 2005C133. The test animal approval number is: SYXK-2003-0003 (ISSUED BY 2005).

[0120] c. Feed and drinking water: drinking water is the stuffs of feed.

[0121] Use the method of preferred embodiment 4 to adjust the biphenyl acetic ammonia butantriol salt and to do the safety experiment.

[0122] No. 1 the biphenyl acetic ammonia butantriol salt injection towards the guinea pig for the whole body allergy experiment

[0123] 1. Method:

[0124] Take 24 experimental guinea pig, evenly divide into 4 groups by sex and weight randomly, each group has six male guinea pig and six female guinea pig. It divided into the positive contrast group, the negative contrast group, the low and high dosage group from the method of preferred embodiment 4 to adjust the biphenyl acetic ammonia butantriol salt, and it is 7.5 and 22.5 mg/kg bw equaling to one times and three times of the clinical usage respectively.

[0125] Injection through abdominal cavity, and the dosage per animal is 0.5 ml, for every other day for three sequence injections. Sensitizer dosage: the positive contrast group: NaCl solution is given (0.9 g/ml); the positive contrast group: 2% (2 g/100 ml) white egg is given; the low dosage group: 7.5 mg the biphenyl acetic ammonia butantriol salt/kg bw. The high dosage group: 22.5 mg the biphenyl acetic ammonia butantriol salt/kg bw.

[0126] The concentration of medicine: the low dosage group: 5.0 mg biphenyl acetic ammonia butantriol salt/ml; the high dosage group: 15.0 mg biphenyl acetic ammonia butantriol salt/ml, wherein the method of making the high dosage solution is that use 1 bottle of biphenyl acetic ammonia butantriol salt solution (4 ml: 94 mg/bottle) from the method of preferred embodiment 4. Take 4 ml the biphenyl acetic ammonia butantriol salt solution and dilute it with 0.9% NaCl solution to 6.3 ml. The concentration of the biphenyl acetic ammonia butantriol salt solution is: 15.0 mg the biphenyl acetic ammonia butantriol salt solution/ml solution). The method of making the low dosage solution is that use 1 bottle of biphenyl acetic ammonia butantriol salt solution (2 ml: 15 mg/bottle) from the method of preferred embodiment 4. Take 2 ml the biphenyl acetic ammonia butantriol salt solution and dilute it with 0.9% NaCl (0.9 g/100 ml) solution to 6.0 ml. The concentration of the biphenyl acetic ammonia butantriol salt solution is: 5.0 mg the biphenyl acetic ammonia butantriol salt solution/ml solution).

[0127] After 12 days of the cavity injection, the medicine is given by vein injection. medicine volume: 1.0 ml/per animal. Dosage: two times of allergy dosage. Inspection the animal responds.

[0128] 2. Target of Investigation:

[0129] 2.1 Allergy Period: Weigh the Animal Before Allergy, and Record the Animal Responds in Detail.

[0130] 2.2 Allergic Reaction: Weight the Animal Before Exciting. Inspect the Animal Responds for 30 Minutes and Record in Table 5 in Detail.

[0131] 3. Result:

[0132] We can judge the level of allergy and the reaction rate of allergy. If there is any animal having allergy after rejection, we can take two healthy guinea pigs to do the vein injection for medicine 2 ml. Do the Inspection of that are there any allergy situation caused by the feeding material.

[0133] 4. Result:

[0134] 4.1 Investigation in Normal Condition

[0135] In the period of investigation, the activity, the breath, and the stool examination of the guinea pigs have not showed significantly unusual. The weight change is shown in Table 7.

[0136] 4.2 Active Allergic Reactions:

[0137] The allergic action and the active allergic towards the guinea pigs are shown in Table 8. There is no allergy symptom occurred in the negative control group. There is allergy symptom occurred in the positive control. The symptoms for six guinea pigs are hyperpnea, polypnea, step unstable, jumping, and death. There is no allergic symptom in low dosage reagent group and the high dosage reagent group.

[0138] The results show that there is no allergy symptom in the negative control group, but the entire guinea pigs of the positive control group went death. There is no allergic symptom in low dosage reagent group and the high dosage reagent group.

[0139] The results show that we use the method of preferred embodiment 4 to adjust the biphenyl acetic ammonia butantriol salt and do the whole body allergy test towards the guinea pig is negative effect.

[0140] 2. The Blood Absorbing Test Towards the Biphenyl Acetic Ammonia Butantriol Salt

[0141] The blood absorbing test outside the body: put the biphenyl acetic ammonia butantriol salt making from the method of preferred embodiment 4 solution 0.63 mg/ml, 1.88 mg/ml into 2% red blood cell's suspending liquid, respectively. There is no blood absorbing reaction within 3 hours in each tube. The results show that we use the method of preferred embodiment 4 to adjust the biphenyl acetic ammonia butantriol salt and do the absorbing test outside the body towards the guinea pig is negative effect. The detail experimental methods and results are shown in the following:

[0142] The method of making the medicine:

[0143] (1) high dosage group: the high dosage group: use 1 bottle of biphenyl acetic ammonia butantriol salt solution (4 ml: 94 mg/bottle) from the method of preferred embodiment 4. Take 0.5 ml the biphenyl acetic ammonia butantriol salt solution and dilute it with 0.9% NaCl solution (0.9 g/100 ml) to 6.25 ml. The concentration of the biphenyl acetic ammonia butantriol salt solution is: 1.88 mg/the biphenyl acetic ammonia butantriol salt solution/ml solution).

[0144] (2) low dosage group: use 1 bottle of biphenyl acetic ammonia butantriol salt solution (4 ml: 94 mg/bottle) from the method of preferred embodiment 4. Take 2 ml the biphenyl acetic ammonia butantriol salt solution and dilute it with 0.9% NaCl (0.9 g/100 ml) solution to 6.0 ml. The concentration of the biphenyl acetic ammonia butantriol salt solution is: 0.63 mg the biphenyl acetic ammonia butantriol salt solution/ml solution).

[0145] 2. The Injection Method:

[0146] (1) The Preparation of 2% Red Blood Cell's Suspending Liquid

[0147] Take few milliliters of rabbit blood into a triangular flask and shake it for 10 minutes. Remove the fiber egg white, and get non-fiber blood. Separate the blood solution into few centrifuge tubes. Add ten times of 0.9% NaCl solution, well mixing, and centrifuge (1500 turns/minutes, 15 minutes) to remove the supernatant. Use 0.9% NaCl solution to wash the precipitation red blood two or three times until the supernatant is not red anymore. Use the red blood to mix the 0.9% NaCl solution to make 2% suspending liquid for test use.

[0148] Take the same size of opening of 7 clean test tubes and number them. Add the 0.9% NaCl solution, the injection water, medicine, and the 2% suspending liquid followed by Table 9. After well mixing, put them in the temperature chamber at 37° C. Inspect them every 15 minutes. After 1 hour, inspect them every one hour for 3 hours.

[0149] (2) Result Observation

[0150] If testing solution presents clearly red, no cellular residual under the tube, and few cellular residual, it can determine that haemolysis happens. If red cells all sink, and supernatant fluid presents no color, it can present that haemolysis doesn't happen. If there are red brown precipitates in the solution, and non-dispersed after shaking, it represents that the red cellular condensed matter happens. If red cellular coagulation happens, and further, it must be decided that it is true or faked coagulation. If condensed matters are uniform distribution after shaking the tube, it can be decided as faked coagulation. Or putting aggregate on this wave plate and put 2 drops 0.9% NaCl injection on the fringe of cap wave plate, and then observe in the scope, if red cellular condensed matter can be flushed scattering, it is faked coagulation. If condensed matter cannot be flushed scattering, it is true coagulation.

[0151] 3. Result Decision

[0152] While negative control tube has no haemolysis and coagulation, positive control tube has haemolysis, and the subject tube does not have haemolysis and coagulation in three hours, this sample (tested animal) can be used for injecting. If the subject tube has haemolysis and coagulation in three hours, this sample cannot be used for injecting.

[0153] 4. The Results

[0154] After adding low concentration 0.63 mg/ml and high concentration 1.88 mg/ml the biphenyl acetic ammonia butantriol salt into different tubes, there is no blood absorbing reaction within 3 hours. In other words, the outside body blood test is negative effect as shown in Table 10 and Table 11.

[0155] The blood test of the biphenyl acetic ammonia butantriol salt injection solution

[0156] The test of the blood of rabbit's ear

[0157] Pick 8 healthy rabbits; use the contrast method towards each right and left ear. Vein injection to the rabbit's left ear. The concentration of the medicine is 5 ml/kg weight. Use the method of preferred embodiment 4 to adjust the biphenyl acetic ammonia butantriol salt solution. The low dosage and high dosage of the biphenyl acetic ammonia butantriol salt solution is 3.15 mg/kg bw, and 9.4 mg/kg bw, respectively. Meanwhile the concentration of them is 0.63 mg/ml, and 1.88 mg/ml respectively which is 0.7-1.4 and 2-4 times of clinical vein injection. Vein injection to the rabbit's right ear for 0.9 g/100 ml NaCl is formed as the control group. Once a day, and repeats it for consecutive three days. After injection high and low dosage of solution, each rabbits is given 0.9% NaCl liquid. Pick each two given high dosage and low dosage rabbits, and dissect it after 48 hours. Giving another two given high dosage and low dosage rabbits for two weeks recovery period, and then dissect it too. Finally, a sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using. There is no any poison on the animal's blood according to pathology. The method of preferred embodiment 4 to adjust the biphenyl acetic ammonia butantriol salt solution is conforming to the regulation standard.

[0158] The method of the experiment and the result is showing on the following:

[0159] 1. The Preparation of Test:

[0160] (1) High dosage group: use 2 bottles of biphenyl acetic ammonia butantriol salt solution (4 ml: 94 mg/bottle) from the method of preferred embodiment 4. Take 8 ml the biphenyl acetic ammonia butantriol salt solution and dilute it with 0.9% NaCl solution (0.9 g/100 ml) to 100 ml. The

concentration of the biphenyl acetic ammonia butantriol salt solution is: 1.88 mg/the biphenyl acetic ammonia butantriol salt solution/ml solution).

[0161] (2) Low dosage group: take 30 ml of the above solution having concentration of 1.88 mg/ml. Take 30 ml of the biphenyl acetic ammonia butantriol salt solution and dilute it with 0.9% NaCl (0.9 g/100 ml) solution to 90 ml. The concentration of the biphenyl acetic ammonia butantriol salt solution is: 0.63 mg the biphenyl acetic ammonia butantriol salt solution/ml solution).

[0162] 2. Weight the Animal: Weight the Animal Before Injection, and after Injection for 48 Hours and 14 Days.

[0163] 3. Regular Inspection and Animal Pick

[0164] Observe and record the response of the animal every day before injection every day. After the final injection for 48 hours, the high concentration and the low concentration rabbits are being killed by bleeding. Record the blood reaction. Cut the left ear first, and then cut the right ear from the boundary part of the ear, and then mark it. Cut a portion of the ears sample into 10% methylene liquid. The sample is 8 cm in length, and 1 cm in width, wherein a first cut is formed at 0.5 cm from the first needle point, a second cut is formed at 2 cm from the third needle point, and the thread side is the second cut. On the other hand, after 14 days of giving medicine, the high and low dosage animals do the following inspection. Use the first needle point as the boundary, cut one section from the first cut. And use the third needle point as boundary, cut two sections from the second cut. Use paraffin to form the sampling slice. The thickness of sampling slice is between 4 and 5 μ m. The sampling slice is treated by H-E dying for inspection.

[0165] 4. Judge the Results

[0166] Do the comprehensive judge by visual examination and inspection.

[0167] 5. The Results**[0168]** 5.1 Visual Examination:

[0169] Observe and record the response of the animals every day before injection. Between the drugs given periods, we can see the skin of the rabbit's ear for the high concentration and low concentration is red. The size is between 0.1×0.2 and 0.2×1.0 cm. After 48 hours of final injection, the investigation of four rabbits of high concentration and low concentration: a sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using as shown in Table 12 and Table 13. After 14 days of final injection, the investigation of four rabbits of high concentration and low concentration: a sharp outline of a blood vessel, the thickness of rabbit's ear is even. There is no significant difference after using.

[0170] 5.2 The Investigation:

[0171] After 48 hours of giving high and low dosages of the biphenyl acetic ammonia butantriol salt solution, we dissect the rabbits. On the same method, after two weeks of giving high and low dosages of the biphenyl acetic ammonia butantriol salt solution, we dissect the rabbits. There is no degenerate and necrosis on the structure of the blood.

[0172] The muscle test of the biphenyl acetic ammonia butantriol salt solution

[0173] Pick 8 healthy rabbits; use the contrast method towards rabbit's muscle. Vein injection to the rabbit's left muscle once a day for 3 days. The concentration of the medicine is 1 ml/kg weight. Use the method of preferred embodiment 4 to adjust the biphenyl acetic ammonia butantriol salt solution. The concentration of low dosage and high dosage of

the biphenyl acetic ammonia butantriol salt solution is 0.63 mg/ml, and 1.88 mg/ml respectively which is 0.7-1.4 and 2-4 times of clinical vein injection. Vein injection to the rabbit's right muscle for 0.9 g/100 ml NaCl is set as the control group. After injection of high and low dosages of solution, each rabbits is given 0.9% NaCl liquid. Pick each two given high dosage and low dosage rabbits, and dissect it after 48 hours. Giving another two given high dosage and low dosage rabbits two weeks recovery period, and then dissect them too. Do the visual inspection of eight rabbits: the muscular tissue around injection is full of flexibility and luster, no significant change. There is no degenerate and necrosis on the structure of the deep muscle of the rabbit according to pathology. The method of preferred embodiment 4 to adjust the biphenyl acetic ammonia butantriol salt solution is conforming to the regulation standard.

[0174] The method of the experiment and the result is showing on the following:

[0175] 1. The Preparation of Test:

[0176] (1) High dosage group: use 1 bottle of biphenyl acetic ammonia butantriol salt solution (4 ml: 94 mg/bottle) from the method of preferred embodiment 4. Take 1 ml the biphenyl acetic ammonia butantriol salt solution and dilute it with 0.9% NaCl solution (0.9 g/100 ml) to 12.5 ml. The concentration of the biphenyl acetic ammonia butantriol salt solution is: 1.88 mg/the biphenyl acetic ammonia butantriol salt solution/ml solution).

[0177] (2) Low dosage group: take 2 ml of the above solution having concentration 1.88 mg/ml. Take 2 ml the biphenyl acetic ammonia butantriol salt solution and dilute it with 0.9% NaCl (0.9 g/100 ml) solution to 6 ml. The concentration of the biphenyl acetic ammonia butantriol salt solution is: 0.63 mg the biphenyl acetic ammonia butantriol salt solution/ml solution).

[0178] 2. Weight the Animal: Weight the Animal Before Injection, and after Injection for 48 Hours and 14 Days.

[0179] 3. The Injection Method

[0180] Pick 8 healthy white rabbits. Inject high dosage and low dosage biphenyl acetic ammonia butantriol salt solutions into left muscle using aseptic method. On the contrary, inject the same volume 0.9% NaCl into the right muscle as the contrast group.

[0181] 4. Regular Inspection

[0182] Observe and record the injection portions around the muscle portions of the animals every day before injection. After the final injection for 48 hours, the high concentration and the low concentration rabbits are being killed by blood-letting, and expose the muscle. Cut it through longitudinal direction. Record the injection portion by visual examination. On the other hand, after 14 days of giving medicine, two rabbits were given by the high and low dosage medicine animal do the inspection around the injection portion.

[0183] 5. Judge the Results

[0184] Do the comprehensive judge by visual examination and inspection.

[0185] 6. The Results

[0186] The result is shown in the Table 14, Table 15, Table 16, Table 17, and the diagnosis report.

[0187] After 48 hours and 14 days of giving high and low dosage of the biphenyl acetic ammonia butantriol salt solution, we do the visual examination and read the report: After using the biphenyl acetic ammonia butantriol salt solution on the rabbit's muscle portion, there is no degenerate and necrosis on the structure of the muscle portion.

[0188] The results show that we use the method of preferred embodiment 4 to adjust the biphenyl acetic ammonia butantriol salt (7.5/22.5 mg/kg bw) and do the whole body allergy test towards the guinea pig is negative effect. The results show that we use the method of preferred embodiment 4 to adjust the biphenyl acetic ammonia butantriol salt 0.63/1.88 mg/ml) and do the inspection towards the rabbit's ear boundary is negative effect. The results show that we use the method of preferred embodiment 4 to adjust the biphenyl acetic ammonia butantriol salt 0.63/1.88 mg/ml) and do the inspection towards the rabbit for outside body blood absorption is negative effect.

[0189] Preferred embodiment 9: The poison test towards the mouse for the biphenyl acetic ammonia butantriol salt

[0190] We cannot judge the effects of the biphenyl acetic ammonia butantriol salt injection towards the NIH mice (half mouse are died) Therefore, we use the maximum dosage of the biphenyl acetic ammonia butantriol salt injection towards the NIH mice to do the research about the poison of the biphenyl acetic ammonia butantriol salt towards the NIH mice.

[0191] A total amount of 40 NIH mice, 19-21 gram, (half of the mice are male and half of the mice are female), it is divided into two groups: medicine group and the contrast group. The medicine is given by the maximum dosage of the biphenyl acetic ammonia butantriol salt (94 mg/4 ml) medicine volume: 0.2 ml/once/10 g weight), twice a day, two injections are six hours difference, i.e. the total dosage for one day is 940 mg/kg. The contrast is given by the 0.1% NaCl liquid. Investigation and record the poison effect on the mice and the amount of mice death. The result is that the entire mice in the medicine group are barely to move. Some mice are very hard to breath. After injection for 2 to 4 hours, the condition of the entire mice is getting better. The entire condition of the mice in the contrast group is normal. After injection for 14 days, no mouse went death in both group, and they look good for gaining weight. And dissect all of them; there is no significantly change by visual examination. The research show that the maximum enduring quantity of the NIH mice towards the biphenyl acetic ammonia butantriol salt is over 940 mg/kg. (calculated for the enduring quantity for biphenyl acetic ammonia is 598 mg/ml) Meanwhile biphenyl acetic acid ester for vein injection LD50 is 337 mg/ml for male, and 433 mg/ml for female. The position of the biphenyl acetic ammonia butantriol is significantly decreased, and its poison is also lower than other anti-inflammatory agent.

[0192] Preferred embodiment 10: the stable test of the biphenyl acetic ammonia butantriol salt injection

[0193] According to the Chinese pharmacopia appendix XI X C, second edition, 2005 (the rule of medicine stability testing direction), Committing the implement sample 4 of the stability investigation item for biphenyl acetic ammonia butantriol salt injection includes the influence factors testing (includes high temperature, high humidity, and highlights), accelerating testing, long term testing and so on. The purpose is to investigate the regular change of this product which has the influence of temperature, humidity, and light intensity, and offer producing, packaging, and transporting condition for this medicine. At the same time, the effective date is established by passing this testing.

[0194] According to the Chinese pharmacopia appendix XI X C, second edition, 2005 (the rule of medicine stability testing direction) and "The important stability item-list of bulk drug and pharmaceutical preparation" which is in "The

researching directive rule of chemical medicine and therapeutic biological products” determines the important item-list, which includes gender character, PH value, relative materials, asepsis, thermal source, assay, and so on. The testing result is below:

[0195] 1. Influence Test:

[0196] After putting the biphenyl acetic ammonia butantriol salt at high temperature 60° C., high humidity (relative humidity 92.5±5%), and light intensity (4500±5001×) for 10 days, there is no significantly change for the product in different standard evolution. In other words, the quality of the product is very stable.

[0197] 2. Acceleration Test

[0198] After putting the biphenyl acetic ammonia butantriol salt at high temperature 40±2° C., high humidity (relative humidity 75±5%), and for 3 months, there is no significantly change for the product in every month examination. In other words, the quality of the product is very stable.

[0199] 3. Long Term Test

[0200] After putting the biphenyl acetic ammonia butantriol salt at high temperature 25° C., high humidity (relative humidity 25%) for 3 months, there is no significantly change for the product in every month examination. In other words, the quality of the product is very stable.

[0201] Preferred embodiment 11: the test of stomach channel towards the biphenyl acetic ammonia butantriol salt oral administration

[0202] NIH mice are divided into two groups randomly. After fasting for 24 hours, the NIH mice are fed by 333 mg/kg of the biphenyl acetic ammonia butantriol salt, and 212 mg/kg of the biphenyl acetic. Dissect stomach after 48 hours. Use 10% methylene oxide. Cut the stomach along the curve of stomach, and calculate the percentage of an ulcer canker. The result is shown in Table 18.

[0203] Industry Application

[0204] The biphenyl acetic ammonia butantriol salt of the present invention can dissolve in water, so this benefit can solve the problem of incapable of dissolving the biphenyl phenylacetic acid in water. At the same time of solving the solubility problem, the present invention proves the analgesic and anti-inflammatory equivalence of biphenyl acetic ammonia butantriol salt and biphenyl phenylacetic ester. In addition, we can know the result is that biphenyl acetic ammonia butantriol salt has the lower acute toxicity than biphenyl phenylacetic ester (see Example 9), and lower oral irritation (see Example 11). On this basis, we go a step further to do the allergic reactive experiment which follows the GLP testing rule, and finally, we don't find the allergic reaction and shocking phenomena which cause from allergy. At the same time, according to a normal injection requirement, we did the haemolysis and irritating testing of biphenyl acetic ammonia butantriol salt, and then we found that there is no irritation of haemolysis, muscle, and blood vessel, so it can use for injection.

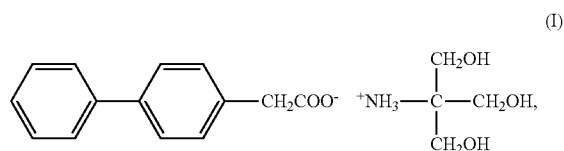
[0205] All of the above experiment proceeds in the national new medicine safety evaluation pharmacy research important laboratory, so the data have the high reliability. This medicine can be used for injection, and avoid to use big molecular coemulsifier of producing emulsion. If we want to use biphenyl phenylacetic ester for emulsion, stability is the big problem for pharmaceuticals workers, such as acidification. The present invention does a three months stability testing of biphenyl acetic ammonia butantriol salt injection, and we find that biphenyl acetic ammonia butantriol salt injection has

high stability. The procedure of producing emulsion is restraining, but the procedure of producing biphenyl acetic ammonia butantriol salt and coemulsifier is easy to proceed.

[0206] The manufacturing technique of biphenyl acetic ammonia butantriol salt is very easy to proceed. The raw material is very easy to find, and the reaction is stability, high yield, and the product purity is high. So, we can directly to get the medical biphenyl acetic ammonia butantriol salt. In addition, there is no serious environmental pollutant in this producing procedure. According to the pharmaceutical testing, it can be proved that biphenyl acetic ammonia butantriol salt injection has the influence to ease analgesic, anti-inflammatory, and no allergy for mice.

[0207] For the external testing, there is no red blood cell haemolysis influence on Japan big ears' rabbit. Because of no obviously irritant influence on giving many times and one time of medicine to rabbits' vein vessel and muscle, it explain that biphenyl acetic ammonia butantriol salt can apply to muscle and vein injection. After giving one time medicine to rabbits' vein, the result of acute toxicity testing reveals that the tolerance value of NIH mice in injecting biphenyl acetic ammonia butantriol salt is 940 mg/kg. This result reveals the LD50 value of biphenyl acetic ammonia butantriol salt is higher than 940 mg/kg (biphenyl phenylacetic acid is 589 mg/kg), but the LD50 value of biphenyl phenylacetic ester is 337 mg/kg for male and 433 mg/kg for female. The acute toxicity of biphenyl acetic ammonia butantriol salt dramatically decreases, and its acute toxicity is lower than the same kinds of anti-inflammatory and analgesics medicines. Biphenyl acetic ammonia butantriol salt has the lower irritant of stomach, intestine, mouth, and abdomen than biphenyl phenylacetic acid, and further easy to take this medicine.

[0208] Accordingly, the present invention provides A composition for providing anti-inflammatory, analgesic, and antipyretic effect, wherein the composition is a biphenyl acetic ammonia butantriol salt having a chemical structure of:



[0209] wherein the biphenyl acetic ammonia butantriol salt has a molecular mass of 333.14. The biphenyl acetic ammonia butantriol salt is soluble in methanol and methanamide, slightly soluble in water and ethanol, and insoluble in propanol and acetonitrile. It is worth mentioning that the biphenyl acetic ammonia butantriol salt has low toxicity to and low stimulative effect on a living object. In addition, the biphenyl acetic ammonia butantriol salt is stable in structure and is non-allergic to the living object, thereby the biphenyl acetic ammonia butantriol salt is capable of being prepared into an injection form for administration by injection without causing allergy to the living object.

[0210] The biphenyl acetic ammonia butantriol salt is prepared by a method of preparation comprising the steps of: mixing biphenyl phenylacetic acid and ammonia butantriol in organic solvent to produce biphenyl acetic ammonia butantriol salt, wherein a ratio of the biphenyl phenylacetic acid and the ammonia butantriol is 1:1. It is worth mentioning

that the biphenyl acetic ammonia butantriol salt produced by the method of preparation has a purity of more than 99.5% by weight.

[0211] The reaction temperature is set at 0-80° C., and is preferably at 50-70° C. The reaction time is set as 0.5-2 hours.

[0212] Preferably, the biphenyl phenylacetic acid is firstly dissolved in the organic solvent, and then the ammonia butantriol is added into the organic solvent for chemical reaction to generate the biphenyl acetic ammonia butantriol salt. The ratio of the biphenyl phenylacetic acid and the ammonia butantriol is 1:1.

[0213] Preferably, the organic solvent is selected from the group consisting of alcohol group and benzene group. Preferably, the alcohol group is selected from the followings: methanol, anhydrous ethanol, acetone, and n-butanol. Preferably, the benzene group is selected from the group consisting of benzyl and benzene.

[0214] Preferably, the method of preparation further comprises the step of purifying the biphenyl acetic ammonia butantriol salt such that a purity of the biphenyl acetic ammonia butantriol salt is greater than 99.5%.

[0215] In particular, the method further comprises the steps of: evaporating a mixture of the biphenyl phenylacetic acid and the ammonia butantriol to obtain white powder after purification, and drying the white powder in a vacuum condition to obtain the biphenyl acetic ammonia butantriol salt. Alternately, the method further comprises the steps of: crystallizing a mixture of the biphenyl phenylacetic acid and the ammonia butantriol at a temperature below 0° C. to form a crystal of the mixture, and drying the crystal in a vacuum condition to obtain the biphenyl acetic ammonia butantriol salt.

[0216] It is worth mentioning that the method may further include the steps of: preparing the biphenyl acetic ammonia butantriol salt into an injection form adapted for injection to a living object, wherein the biphenyl acetic ammonia butantriol salt in the injection form is stable in structure and has insignificant local and vascular irritating effect such that the injection form is capable of providing anti-inflammatory, analgesic, and antipyretic effect by injecting into a living object, thereby the biphenyl acetic ammonia butantriol salt having a unique and stable chemical structure is capable of being prepared into a predetermined dosage in a controllable and precise manner. The injection form includes injection liquid, injection cool powder and injection aseptic needle.

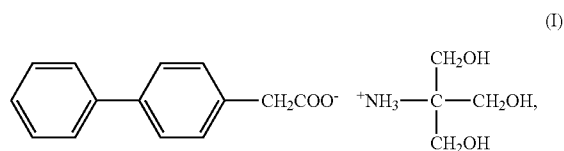
[0217] On the other hand, the method may further include the steps of: preparing the biphenyl acetic ammonia butantriol salt into a capsule form adapted for oral administration, wherein the biphenyl acetic ammonia butantriol salt in the capsule form is stable in structure and has insignificant local and vascular irritating effect such that the biphenyl acetic ammonia butantriol salt is capable of providing anti-inflammatory, analgesic, and antipyretic effect to a living object, thereby the biphenyl acetic ammonia butantriol salt having a unique and stable chemical structure is capable of being prepared into a predetermined dosage in a controllable and precise manner.

[0218] It will thus be seen that the objects of the present invention have been fully and effectively accomplished. Its embodiments have been shown and described for the purposes of illustrating the functional and structural principles of the present invention and is subject to change without depart-

ture from such principles. Therefore, this invention includes all modifications encompassed within the spirit and scope of the following claims.

What is claimed is:

1. A composition for providing anti-inflammatory, analgesic, and antipyretic effect, wherein the composition is a biphenyl acetic ammonia butantriol salt having a chemical structure of:



wherein said biphenyl acetic ammonia butantriol salt has a molecular mass of 333.14.

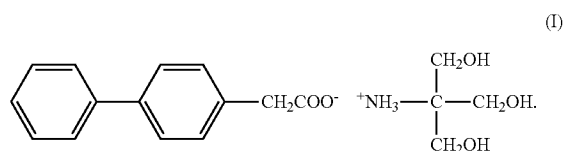
2. The composition according to claim 1, wherein said biphenyl acetic ammonia butantriol salt is soluble in methanol and methanamide, slightly soluble in water and ethanol, and insoluble in propanol and acetonitrile, wherein said biphenyl acetic ammonia butantriol salt has low toxicity to and low stimulative effect on a living object.

3. The composition according to claim 2, wherein said biphenyl acetic ammonia butantriol salt is stable in structure and is non-allergic to the living object, thereby said biphenyl acetic ammonia butantriol salt is capable of being prepared into an injection form for administration by injection without causing allergy to the living object.

4. The composition according to claim 3, is prepared by a method of preparation comprising the steps of: mixing biphenyl phenylacetic acid and ammonia butantriol in organic solvent to produce biphenyl acetic ammonia butantriol salt, wherein a ratio of the biphenyl phenylacetic acid and the ammonia butantriol is 1:1.

5. The composition according to claim 4, wherein said biphenyl acetic ammonia butantriol salt produced by said method of preparation has a purity of more than 99.5% by weight.

6. A method of preparation of biphenyl acetic ammonia butantriol salt, comprising the steps of: mixing biphenyl phenylacetic acid with ammonia butantriol in organic solvent to generate biphenyl acetic ammonia butantriol salt, wherein biphenyl acetic ammonia butantriol salt having a chemical structure of:



7. The method according to claim 6, wherein said biphenyl phenylacetic acid is firstly dissolved in said organic solvent, and then said ammonia butantriol is added into said organic solvent for chemical reaction to generate said biphenyl acetic ammonia butantriol salt.

8. The method according to claim 6, wherein a ratio of said biphenyl phenylacetic acid and said ammonia butantriol is 1:1.

9. The method according to claim 7, wherein a ratio of said biphenyl phenylacetic acid and said ammonia butantriol is 1:1.

10. The method according to claim 8, wherein said organic solvent is selected from the group consisting of alcohol group and benzene group.

11. The method according to claim 10, wherein said alcohol group of said organic solvent is selected from the group consisting of methanol, anhydrous ethanol, acetone, and n-butanol, wherein said benzene group of said organic solvent is selected from the group consisting of benzyl and benzene.

12. The method according to claim 10, wherein a reaction temperature is set at 0-80° C. and a reaction time is set as 0.5-2 hours.

13. The method according to claim 12, wherein a reaction temperature is set at 50-70° C.

14. The method according to claim 8, further comprising a step of purifying said biphenyl acetic ammonia butantriol salt such that a purity of said biphenyl acetic ammonia butantriol salt is greater than 99.5%.

15. The method according to claim 12, further comprising a step of purifying said biphenyl acetic ammonia butantriol salt such that a purity of said biphenyl acetic ammonia butantriol salt is greater than 99.5%.

16. The method according to claim 13, further comprising the steps of evaporating a mixture of said biphenyl phenylacetic acid and said ammonia butantriol to obtain white powder after purification, and drying said white powder in a vacuum condition to obtain said biphenyl acetic ammonia butantriol salt.

17. The method according to claim 13, further comprising the steps of crystallizing a mixture of said biphenyl phenylacetic acid and said ammonia butantriol at a temperature below 0° C. to form a crystal of said mixture, and drying said crystal in a vacuum condition to obtain said biphenyl acetic ammonia butantriol salt.

18. The method according to claim 15, further comprising the steps of: preparing said biphenyl acetic ammonia butantriol salt into an injection form adapted for injection to a living object, wherein said biphenyl acetic ammonia butantriol salt in said injection form is stable in structure and has insignificant local and vascular irritating effect such that said injection form is capable of providing anti-inflammatory, analgesic, and antipyretic effect by injecting into a living object, thereby said biphenyl acetic ammonia butantriol salt having a unique and stable chemical structure is capable of being prepared into a predetermined dosage in a controllable and precise manner.

19. The method according to claim 18, wherein said injection form is selected from the group consisting of injection liquid, injection cool powder and injection aseptic needle.

20. The method according to claim 15, further comprising the steps of: preparing said biphenyl acetic ammonia butantriol salt into a capsule form adapted for oral administration, wherein said biphenyl acetic ammonia butantriol salt in said capsule form is stable in structure and has insignificant local and vascular irritating effect such that said biphenyl acetic ammonia butantriol salt is capable of providing anti-inflammatory, analgesic, and antipyretic effect to a living object, thereby said biphenyl acetic ammonia butantriol salt having a unique and stable chemical structure is capable of being prepared into a predetermined dosage in a controllable and precise manner.

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