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Kelimycin tablet and preparation method thereof

Abstract

The invention relates to a kelimycin tablet and a preparation method thereof. The kelimycin tablet comprises kelimycin and a tablet core comprising pharmaceutically acceptable adjuvants; and the pharmaceutically acceptable adjuvants include microcrystalline cellulose, carboxymethyl starch sodium, povidone K30 and magnesium stearate. The preparation method comprises the following step of: preparing the medicated tablet core, wherein an inside and outside addition method is adopted for the carboxymethyl starch sodium in the preparation of the medicated tablet core. The kelimycin tablet disclosed by the invention has the advantages of faster disintegration and better dissolution rate, and is easy to granulate. The preparation method of the kelimycin tablet has the advantages of simple process, large production quantity and low production cost, and easily realize hygienic standard and is suitable for large-scale mechanized production.

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Claims (10)

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translated from Chinese

1. A benefit Tablets, characterized in that said Currie Tablets core comprising a pharmaceutically acceptable excipient and can benefit neomycin thereof; a pharmaceutically acceptable excipient to the microcrystalline cellulose, sodium starch glycolate, povidone and magnesium stearate K3tl.

The Currie Tablets according to claim 1, wherein the mass ratio of the microcrystalline cellulose can benefit rapamycin is 0.35~1.1: 1, preferably 0.55~1.03: 1; the the sodium carboxymethyl starch and the mass ratio of adriamycin to Currie 0.08~0.15: 1, preferably 0.11~0.135: 1; mass ratio of the povidone and can benefit K3tl rapamycin is 0.06~0.12: 1, preferably 0.075~0.1: 1; magnesium stearate and the mass ratio of adriamycin to Currie 0.01~0.022: 1, preferably 0.015~0.02: 1.

The Currie Tablets according to claim 2, characterized in that the composition of the core is as follows:

可利霉素	1 重量份
微晶纤维素	0.55 重量份
羧甲淀粉钠	0.11 重量份
聚维酮 K ₃₀	0.075 重量份
硬脂酸镁	0.015 重量份；

可利霉素	1 重量份
微晶纤维素	1.03 重量份
羧甲淀粉钠	0.135 重量份
聚维酮 K ₃₀	0.1 重量份
硬脂酸镁	0.02 重量份。

The benefit may be any of claims 1-3 **Tablets** of claims, wherein said benefit **Tablets** may further comprise a coating layer.

Description translated from Chinese

The Currie **Tablets** according to claim 4, wherein said coating layer is made of Opadry II and distilled water.

A benefit **Tablets** and preparation method of the 3 6. A method of preparing claims, characterized in that the method comprises preparing the tablet core is prepared containing, in the FIELD preparation of carboxymethyl-containing tablet core adding sodium starch inside and outside.

Tablets can benefit the production method according to claim 6, wherein the preparation containing tablet core comprises the steps of: 1) a pharmaceutically acceptable [0001] The present invention pertains to an improved pharmaceutical dosage form, specifically, to a method for preparing **Tablets** and Currie. excipient may benefit neomycin and were screened ; 2) can benefit adriamycin, microcrystalline cellulose and sodium carboxymethyl starch are mixed uniformly, followed Background by addition of aqueous solution of the povidone K3tl soft material, granulated with 18 mesh sieve, the resultant wet granules were dried; 3) sulfate in the 18-mesh sieve, added after the sodium carboxymethyl starch and magnesium stearate are mixed, tableting to prepare **tablets** containing the cores.

[0002] Currie adriamycin (Kelimycin), also known as Bitespiramycin (Bitespiramycin), biotechnology neomycin (Shengjimycin) by the present applicant in cooperation with the China Institute of Medicinal Biotechnology, as described in the paper "Preparation of a new drug, 18-membered lactone ring structure, under was cloned and identified as a producing bacterium, the orientation Acylspiramycins 4 "-OH, 4 " 4 " position of isovaleryl spiramycin novel antibiotic as a main component was added isovaleryl position side chain formation.

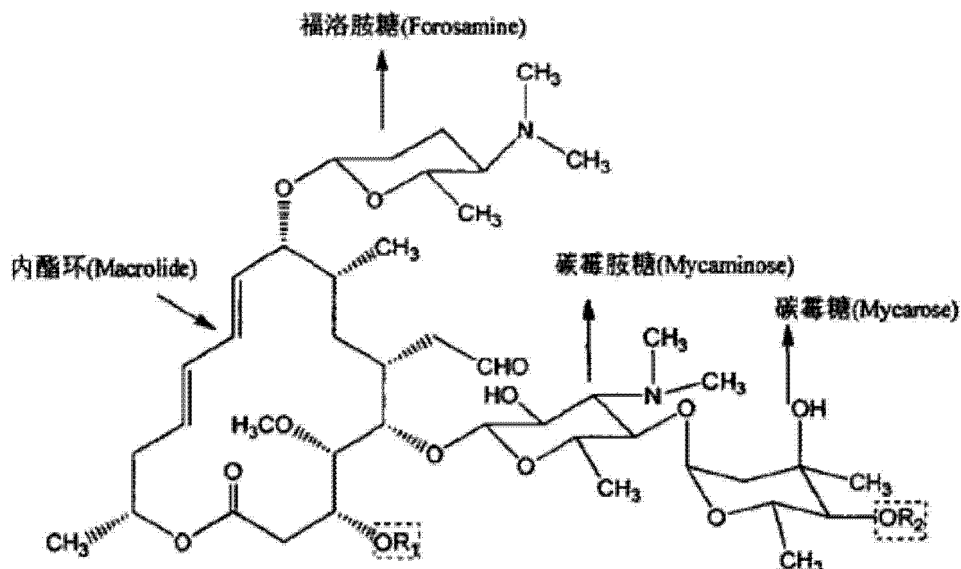
9. A process according to any one of claims 6-8, wherein said preparation further comprises a further coating the resulting tablet cores prepared containing film-coated [0003] AD**Tablets** benefit by a variety of spiramycin derivatives, the main active ingredient isovaleryl spiramycin (I + II + III) total content of not less than 65%, 4 "

Acylspiramycins the total content of not less than 80%, in a pharmaceutically acceptable is a pharmaceutical composition. Center 16-membered lactone ring structure, with an amine molecule Flor sugar, sugar molecule and a molecule of carbon pyrimethanif mycamillose connected to each other, the main component of isovaleryl spiramycin I, II, III and spiral mold that is different from the pixel structure mycamillose 4 " group is linked on position rather than an isovaleryl group hydroxy. AD**Tablets** can benefit the production method according to claim 9, wherein said coating comprises the steps of: a preparation of coating solution): Opadry II weighed water was added in a dosing vessel was added in, after complete addition stirring speed is reduced, so that scroll disappears, stirring was continued for 30min, to obtain a preparation of film-coated **tablets**, the **tablets** containing the 90% after a 100% of the total Acylspiramycins 80% undecylated spiramycin 5%.

temperature of 30~35 ° C spray pressure 0.02~0.04Mpa, spray flow 1~1.5ml / min coated, after constant for spray package 1.5~2h, smooth surface to the **tablets**, spiramycin in 30%, isovaleryl spiramycin I, II, III ratio of 65% of the sum of Sah, the ratio of the total Acylspiramycins Sah 80% undecylated spiramycin Sah 5%.

uniform color, in line with the standard test for qualified film coating, a coating weight gain of 5%.

[0004]



[0005] Formula (I)

[0006] Currie rapamycin macrolide antibiotics belonging to 16 yuan, having reactive carboxyl group, an alkoxy group, an epoxy group, a ketone group and an aldehyde and a pair of conjugated C = c, a molecular weight of about 884 ~982. Because of similar chemical structure, with the benefit of macrolide antibiotics neomycin having many properties: soluble in most organic solvents esters, acetone, chloroform, alcohols, slightly soluble in petroleum ether, insoluble in water ; molecular structure containing two dimethylamino and weakly alkaline, soluble in an acidic aqueous solution; having solubility decreases with increasing temperature "negative solubility" properties. Since rapamycin may benefit a main component isovaleryl spiramycin 4 " position of the carbon chain longer, poor hydrophilicity, solubility in water than the spiramycin and 4 " - acetyl small helicase. [0007] Currie rapamycin as a white amorphous powder, slightly hygroscopic, specific rotation of about -80.8 °, most UV

Absorption wavelength purple reaction 231~232nm, itself has a weak fluorescent chromophore, concentrated sulfuric acid or hydrochloric case, producing strong purple fluorescence, absorbance at the maximum at 231~232nm.

[0008] The drug is lipophilic, strong tissue penetration ability, oral absorption, long duration in vivo, after sustained antibiotic effect. The relationship between efficacy and chemical conformation, macrolide antibiotics 4 'after the acylation, lipophilicity and improved in vivo activity, and antibacterial activity in vivo clinical results have been significantly improved, and the stability of the antibiotic in vivo as of 4 " carbon chain of the enhanced growth of hydroxyester, i.e., isovaleryl spiramycin> propionyl spiramycin> Acetylspiramycin.

[0009] Preliminary in vivo pharmacodynamic test showed that the drug not only for most G + bacteria have a good activity on the part of G- bacteria also have a role, the technical parameters were significantly better than erythromycin, acetylspiramycin, medemycin, especially for Mycoplasma pneumoniae strongest antibacterial activity of erythromycin resistant bacteria, Neisseria gonorrhoeae, Haemophilus influenzae, Bacteroides fragilis, Legionella, and multi-line bacillus Clostridium perfringens also have some antibacterial activity against Staphylococcus aureus clinical resistance to erythromycin only a very small cross-resistance. Currie ADM will be mainly used for the treatment of Gram-positive bacterial infectious diseases, particularly upper respiratory tract infection, and may be used for urinary tract infections.

[0010] Clinical studies have shown, it can benefit ADM is a safe and effective oral antibiotics. However, studies performed Currie rapamycin formulation is also less, in particular, can benefit as a class of drugs neomycin, its formulation study reported less.

[0011] The present Applicant on May 25, 2011 filed an application No. 201110136228.X, entitled "L adriamycin Currie, pharmaceutical compositions, preparation method and application" patent application, wherein Example 12 L Currie discloses a neomycin tablets, prescription according to which 10,000 calculated as: L Currie ADM raw powder 1000g, low-substituted hydroxypropyl cellulose (5%) 92.5g, sodium carboxymethyl starch (3 %) 55.5g, magnesium stearate (1%) 18.5g, subtracting the total weight of other starch raw materials by weight of the total weight of 1850 g; also discloses tablets made of the sugar-coated tablets, enteric-coated tablets and a gastric method sheet. However, further studies found by the present invention, since the adhesive force can benefit rapamycin and starches having strong moisture absorption and strong adhesion, the use of the tablets formulation of soft material easily prepared sieved, granulated difficult, and the resulting slow tablet disintegration, good dissolution rate.

[0012] In view of this, the present invention proposed Japanese.

SUMMARY

[0013] The present invention will solve the above technical problem, there is provided a granulated easy, rapid disintegration, dissolution rate can preferably benefit Tablets.

[0014] To achieve the object of the present invention, the present invention employs the following technical solutions:

[0015] A benefit Tablets, wherein said Currie Tablets comprising a core sheet by a pharmaceutically acceptable excipient and Lee neomycin thereof; the pharmaceutically acceptable excipient is a micro microcrystalline cellulose, sodium starch glycolate, povidone and magnesium stearate K3tl.

[0016] Tablets may benefit the present invention, wherein the mass ratio of the microcrystalline cellulose may be of benefit rapamycin

0.35 ~1.1: 1, preferably 0.55 ~1.03: 1;

[0017] the mass of sodium carboxymethyl starch and adriamycin can benefit ratio 0.08~0.15: 1, preferably 0.11~0.135: 1;

Mass ratio of [0018] said povidone K30 and Currie rapamycin is 0.06~0.12: 1, preferably 0.075~0.1: 1;

Magnesium stearate [0019] The mass ratio of the rapamycin to Currie 0.01~0.022: 1, preferably 0.015~0.02: 1.

[0020] CN201110136228.X Example 12 discloses a left Currie ADM tablets, prescription according to which 10,000 calculated as: L Currie ADM raw powder 1000g, low-substituted hydroxypropyl cellulose (5%) 92.5 g of, sodium carboxymethyl starch (3%) 55.5g, magnesium stearate (1%) 18.5g, subtracting the total weight of other starch raw materials by weight of the total weight of 1850 g; the invention also discloses tablets prepared into sugar-coated tablets, enteric-coated tablets and a method for gastric sheet. However, since the adhesive force can benefit rapamycin and starches having strong moisture absorption and strong adhesion, the use of the tablets formulation of soft material easily prepared sieved, granulated difficult, and the obtained slow disintegration of the tablet, poor dissolution rate.

[0021] The present inventors examined the degree of difficulty through a large number of different granulation formulation of the test, the disintegration time four Appearance sheet, sheet stiffness, sheet, tablet core finalized the present invention. By comparison, formulations of the invention compared to the prior art, the dissolution has been greatly improved.

[0022] Specifically, the present invention can benefit Tablets, wherein said tablet core consisting of the following:

[0023]

I can benefit Ga mold parts just domain

Micro cellulose product 0.55 \$: . % parts

Parts of sodium carboxymethyl starch 0J amount] ®

Povidone _ Km 0.075 parts by weight

Magnesium stearate 0.015 <f parts;

[0024] or

[0025]

可利霉素	1 重量份
微晶纤维素	0.55 重量份
羧甲淀粉钠	0.11 重量份
聚维酮 K ₃₀	0.075 重量份
硬脂酸镁	0.015 重量份;

可利霉素	1 重量份
微晶纤维素	1.03 重量份
羧甲淀粉钠	0.135 重量份
聚维酮 K ₃₀	0.1 重量份
硬脂酸镁	0.02 重量份。

[0026] In the present invention, the povidone is povidone K3tl K3tl aqueous solution, preferably 5% (w / w) aqueous solution of povidone K3tl.

[0027] More particularly, the present invention is preferred for the tablet core:

[0028] 200mg / 350mg

[0029] The tablet core:

可利霉素	200g
微晶纤维素	110g
羧甲淀粉钠	22g
聚维酮 K ₃₀ (5%)	15g
硬脂酸镁	3g
制成	1000 片

[0031] 150mg / 350mg

[0032] The tablet core:

可利霉素	150g
微晶纤维素	155g
羧甲淀粉钠	27g
聚维酮 K ₃₀ (5%)	15g
硬脂酸镁	3g
制成	1000 片

of the sheet, sheet stiffness, sheet, and ultimately determine the above-described preferred tablet core. Further, the benefit of the tablets in the present invention may further comprise a coating layer.

[0035] In the present invention, the coating layer is made of Opadry II and distilled water.

[0036] As a preferred embodiment, the coating liquid formulation of the present invention are:

欧巴代 II	21g
蒸馏水	适量
制成	10ml

[0038] Preferably the above-described tablet core and the coating solution formulation is amplified, and its dissolution test (see FIG. 8 and FIG. 9), can be seen from the figure, at the time of 30min, tablets and coated tablets cumulative dissolution percentages are close to 95%.

[0039] Further, since the content can benefit Tablets was determined by the microbiological assay, rapamycin can benefit 0.1g per titer should be 10 million units, but the actual content of the feedstock produced not fully meet this standard, We need to be adjusted prescription raw material content. The measurement results of different batches of raw content has been produced, which is the lower limit of not less than 90%, therefore, the preferred formulation will benefit adriamycin inputs adapted to

meet the requirements of the tablet content, while reducing the microcrystalline cellulose diluent the amount of pigment, in order to ensure constant tablet weight.

Adjusted prescription as follows:

[0040] Adjustment of the tablet core:

可利霉素	225g
微晶纤维素	85g
羧甲淀粉钠	22g
聚维酮 K ₃₀ (5%)	15g
硬脂酸镁	3g
制成	1000 片

[0042] After the compressed core prescription, the above-described coating process after coating, dissolution test results shown in Figure 10:

[0043] As can be seen from the dissolution profile of the formulation after adjustment still satisfy dissolution requirements. Meanwhile, the object of the present invention is to provide the benefit may be rapamycin preparation, which process is simple, the production volume, low cost production, "health standards" easy to achieve, suitable for large scale mechanized production.

[0044] Tablets may be prepared benefit of the present invention include core tablets prepared containing, sodium carboxymethyl starch prepared tablet containing the core inside and outside the adder.

[0045] Specifically, the present invention is the preparation of a tablet containing a core comprising the steps of: [0046] 1) will benefit pharmaceutically acceptable excipients are sieved and neomycin;

[0047] 2) can benefit adriamycin, microcrystalline cellulose and sodium carboxymethyl starch are mixed uniformly, followed by addition of aqueous solution of the povidone K3tl soft material, granulated with 18 mesh sieve, the resultant wet granules were dried;

[0048] 3) After drying at 18 mesh sieve, was added sodium starch glycolate and magnesium stearate are uniformly mixed, tableting to prepare tablets containing the cores.

[0049] wherein, in step 1) according sieved through a 100 mesh sieve;

[0050] Step 2) is dried as in the 60 ° C under ventilation drying 2h.

[0051] The aqueous povidone K3tl preferably K3tl 5% povidone solution.

[0052] As a preferred embodiment, the core of the production method of the present invention: a main drug and each excipient than 100 mesh, the prescriptions can benefit neomycin, microcrystalline cellulose and half of the prescribed amount of carboxymethyl starch sodium mixed, followed by addition of a 5% aqueous solution of the povidone K3tl soft material, granulated with 18 mesh sieve, the wet granules at 60 ° C under ventilation drying 2h; after drying 18-mesh sieve, then add 1/2 after the

prescribed amount of prescriptions carboxymethyl starch sodium and magnesium stearate are mixed, with a diameter of dimple embossed sheet punching 11_ was prepared tablet weight 350mg, hardness of the tablet core containing 6.5kg. Which process flow diagram shown in Figure 1.

[0053] Further, the production method of the present invention further comprises further coating the resulting tablet cores prepared containing film-coated **tablets**.

[0054] In particular, said coating comprising the steps of:

[0055] a) preparation of coating solution: Opadry II weighed water was added in a dosing vessel, was added in portions, until complete addition, stirring speed is reduced, so that scroll disappears, stirring was continued for 30min, to obtain;

[0056] b) Preparation of film-coated **tablets**: the core tablet containing coating pan set, determining coating conditions were: rate of host 20~25r / min, inlet air temperature of 40~45 ° C, wind temperature 30~35 ° C, spray pressure 0.02~0.04Mpa, spray flow 1~1.5ml / min coated, after continuous constant spray package 1.5~2h, smooth surface to the **tablets**, uniform color, film-coated inspection compliance standard qualified, coat weight gain of 5%.

[0057] Compared with the prior art, can benefit **Tablets** and preparation method provided by the invention have the following advantages:

[0058] (1) **Tablets** can benefit the present invention provides a rapid disintegration, dissolution rate is better;

[0059] (2) The present invention provides a granulation **Tablets** may facilitate easy and smooth-sided sheet obtained, without anesthesia surface phenomenon;

[0060] (3) Preparation of adriamycin can benefit provided by the present invention readily granulated, simple preparation method suitable for mechanized production, yield, low cost, "health standards" can be easily reached;

[0061] (4) according to the present invention can benefit **Tablets** facilitate the clinical staff, medication of patients, there is a strong clinical utility.

BRIEF DESCRIPTION

[0062] Preparation process flow diagram of FIG. 1 of the present invention may be of benefit **Tablets**;

[0063] FIG. 2 is a dissolution profile of formulation 11;

[0064] FIG. 3 is a dissolution profile 14 a prescription;

[0065] FIG. 4 is a dissolution profile of formulation 16;

[0066] FIG. 5 is a dissolution profile 18 a prescription;

[0067] FIG. 6 is a dissolution profile of different coating weight (200mg / 350mg);

[0068] FIG. 1 is a dissolution profile of different coating weight (150mg / 350mg);

[0069] FIG. 8 is an enlarged prescription dissolution profiles (200mg / 350mg); [0070] FIG. 9 is an enlarged prescription dissolution profiles (150mg / 350mg);

[0071] FIG. 10 is a dissolution profile of the formulation of raw materials to adjust the content of the coated **tablets**;

Dissolution profile [0072] FIG. 11 of the present invention may benefit ADM prior art **tablets** and **tablets** of rapamycin may benefit.

Detailed ways

[0073] DETAILED DESCRIPTION The following present invention, according to further embodiments of the present invention is described, and not to limit the present invention.

[0074] [Example 1]

[0075] Specifications: 200mg / 350mg

[0076] The tablet core:

[0077]

可利霉素

200g

微晶纤维素

110g

羧甲淀粉钠

22g

聚维酮 K₃₀ (5%)

15g

硬脂酸镁

3g

制成	1000 片
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[0078] The coating solution formulation:

[0079]

欧巴代 II	21g
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蒸馏水	适量
-----	----

制成	105ml
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[0080] Preparation process:

[0081] Preparation of tablet core: a main drug and each excipient than 100 mesh, the prescriptions can benefit amphotericin, sodium carboxymethyl starch, microcrystalline cellulose and 1/2 mixed uniformly prescribed amount, followed by addition of 5% PVP aqueous solution of the ketone K3tl soft material, granulated with 18 mesh sieve, the wet granules are dried for 2h at 60 ° C under ventilation; after drying 18-mesh sieve, then add 1/2 prescriptions prescribed amount of sodium starch glycolate and after magnesium stearate was mixed, washed with a dimple diameter 11mm stampers prepared tablet weight 350mg, hardness of the tablet core containing 6.5kg.

[0082] The formulation of coating solution: weighed desired Opadry II (white) was added to the vessel with the desired amount of water, was added in portions, until complete addition, stirring speed is reduced, so that scroll disappear and continue stirring 30min, that is.

Preparation [0083] The film-coated tablets: The tablet core coating pan set, determining coating conditions, speed of the host is 20r / min, inlet air temperature 40 ° C, outlet temperature 30 ° C, spray pressure 0.02Mpa, spraying flow rate of 1ml / min coated for constant spray package after 1.5h, smooth surface to the tablets, uniform color, film coating meet inspection standards qualified. Coating weight of about 5%.

[0084] [Example 2]

[0085] Specifications: 150mg / 350mg

[0086] tablet core: [0087]

可利霉素	150g
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微晶纤维素	155g
-------	------

羧甲淀粉钠	27g
-------	-----

聚维酮 K ₃₀ (5%)	15g
--------------------------	-----

硬脂酸镁	3g
------	----

制成	1000 片
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[0088]

[0089] The coating solution formulation: the same as in Example 1.

[0090] Preparation process:

Preparation of formulations [0091] The core and the coating solution same as in Example 1.

Preparation [0092] The film-coated tablets: The tablet core coating pan set, determining coating conditions, speed of the host is 25r / min, inlet air temperature 45 ° C, outlet temperature 35 ° C, spray pressure 0.04Mpa, spraying flow rate of 1.5ml / min coated for constant spray package after 2h, smooth surface to the tablets, uniform color, film coating meet inspection standards qualified. Coating weight of about 5%.

[0093] [Example 3]
[0094] Specifications: 225mg / 350mg
[0095] The tablet core:
[0096]

可利霉素	225g
微晶纤维素	85g
羧甲淀粉钠	22g
聚维酮 K ₃₀ (5%)	15g
硬脂酸镁	3g
制成	1000 片

[0097] The coating solution formulation: the same as in Example 1.
[0098] Preparation process:
[0099] formulated core and a coating liquid prepared in Example 1.

Preparation [0100] The film-coated tablet: the tablet core coating pan set, determining coating conditions, speed of the host is 22r / min, inlet air temperature 43 ° C, outlet temperature 32 ° C, spray pressure 0.03Mpa, spraying flow rate of 1.2ml / min coated, after continuous constant spray package 1.8H, smooth surface to the tablets, uniform color, film coating meet inspection standards qualified. Coating weight of about 5%.

[0101] Examples 4-10 The following is a tablet core formulation I shown in the following table, the coating liquid formulation and preparation process as in Example 1.
[0102] Table 1, Examples 4-10
[0103]

实施例编号 片芯处方	4	5	6	7	8	9	10
可利霉素	150g	200g	225g	200g	225g	150g	150g
微晶纤维素	165g	112g	78.75g	112g	83.25g	164g	157g
羧甲淀粉钠	21g	24 g	24.75g	24g	18g	20.75g	22.5g
聚维酮 K ₃₀ (5%)	12g	12g	18.5g	11.9g	20.375g	11.95g	18g
硬脂酸镁	2g	2g	3g	2.1g	3.375g	3.3g	2.5g

[0104] Test Example I
[0105] Prescription screening test
[0106] a, 200mg / 350mg prescription screening
[0107] (I) Screening diluent
[0108] starch, microcrystalline cellulose, lactose, respectively Currie adriamycin, low substituted hydroxypropylcellulose, sodium carboxymethyl starch, and magnesium stearate as shown in Table 2 formulation design

structure as shown in Table 2 formulation design.

[0109] Table 2, diluent screening

[0110]

	处方 1	处方 2	处方 3
可利霉素	10g	10g	10g
淀粉	6g	0.8g	0.8g
乳糖	——	——	5.2g
微晶纤维素	——	5.2g	——
低取代羟丙甲纤维素	0.8g	0.8g	0.8g
羧甲淀粉钠	0.6g	0.6g	0.6g
硬脂酸镁	0.1g	0.1g	0.1g
制粒难易	制得的软材不易过筛，制粒较难	制得的软材较易过筛，制粒较容易	制粒较容易
片的形态	制得的片表面光洁	制得的片表面光洁	制得的片略显粗糙
片的硬度（kg）	7.9	6.5	6.0
崩解时间（min）	18.15	18	18

[0111] Note: The above formulation is made in the amount of 50

[0112] By comparing the appearance inspection system ease of formulation of a soft material and the granulation process combined sheet, microcrystalline cellulose as a diluent find the best; but these were slowly disintegrating formulation problems, it screening of disintegrant based on the formulation 2. [0113] (2) Screening disintegrant

[0114] ① adjustment ratio and low substituted hydroxypropylcellulose, sodium carboxymethyl starch, respectively, shown in Table 3 and the formulation may be designed to benefit adriamycin, microcrystalline cellulose and magnesium stearate.

[0115] Table 3, disintegrating agents screening

[0116]

	处方 4	处方 5
可利霉素	10g	10g
淀粉	0.8g	0.8g
微晶纤维素	5.2g	5.2g
低取代羟丙甲纤维素	0.7g	0.9g
羧甲淀粉钠	0.7g	0.5g
硬脂酸镁	0.1g	0.1g
片的硬度(kg)	6.0	6.2
崩解时间(min)	15.17	35.87

[0117] Note: The above formulation is made in the amount of 50

[0118] The disintegrating formulation did not meet two requirements, compared to formulation 4 5 disintegrating formulation has greatly improved.

[0119] ② alternatively with sodium starch glycolate low-substituted hydroxypropyl methyl cellulose as disintegrant

[0120] sodium carboxymethyl starch were designed with a prescription benefit adriamycin, microcrystalline cellulose and magnesium stearate, respectively, the amount of disintegrant is 8%, 7%, 6%, 5%, 4%.

[0121] Table 4, the amount of sodium carboxymethyl starch Screening

[0122]

	处方 6	处方 7	处方 8	处方 9	处方 10
可利霉素	10g	10g	10g	10g	10g
微晶纤维素	5.2g	5.4g	5.6g	5.8g	6.0g
羧甲淀粉钠	0.7g+0.7g	0.6g+0.6g	0.5g+0.5g	0.4g+0.4g	0.3g+0.3g
淀粉	0.8g	0.8g	0.8g	0.8g	0.8g
硬脂酸镁	0.1g	0.1g	0.1g	0.1g	0.1g
片的硬度(kg)	5.6	5.9	7.5	7.5	6.0
崩解时间(min)	8.83	9.92	6.74	10.17	12.48

[0123] Note: The above formulation was made in the amount of 50 [0124] disintegration time and hardness of comprehensive study by prescription to prescription 6 about 10 was found to 6% of sodium starch glycolate disintegrant than the prescription 8 it is good. Screening adhesive 9 on the basis of the prescription

sheet 10 was found to 0% of sodium starch glycolate disintegrant than the prescription 6 it is good. Screening adhesive 6 on the basis of the prescription.

[0125] Filter (3) binder

[0126] Table 5 filter, the binder

[0127]

	处方 11	处方 12	处方 13
可利霉素	10g	10g	10g
微晶纤维素	5.6g	5.6g	5.6g
羧甲淀粉钠	0.5g+0.5g	0.5g+0.5g	0.5g+0.5g
聚维酮 K ₃₀ (水)	0.8g	——	——
聚维酮 K ₃₀ (醇)	——	0.8g	——
蒸馏水	——	——	0.8g
硬脂酸镁	0.1g	0.1g	0.1
制粒难易	制软材比淀粉浆容易	制软材过程中形成黄色团块，无法制粒	制软材容易，容易过筛制粒
片的形态	制得的片表面光洁	——	制得的片表面光洁
片的硬度 (kg)	6.5	——	6.1
崩解时间 (min)	2.25	——	5.92

[0128] Note: The above formulation is made in the amount of 50

[0129] Integrated disintegration time and ease of comparison granulated sheet 11 is preferably found prescription; formulation 11 but less than 85% found Percent Dissolved (see FIG. 2) at the time when the percentage dissolving inspect 15min, was not dissolution time to pharmacopoeia requirements.

[0130] (4) Comparative Example 11 each prescription materials to fine-tune

[0131] Prescription 14: 10g

可利霉素	10g
微晶纤维素	5.5g
羧甲淀粉钠	0.55g+0.55g
聚维酮 K ₃₀ （水）	0.75g
硬脂酸镁	0.15g

制成 50 片

[0133] (see FIG. 3) was found by examining the optimal dissolution formulation 14, when the water temperature at 37 ° C, the dissolution time meet the requirements, and the smooth-sided, non-pitted surface phenomenon.

[0134] two, 150mg / 350mg prescription screening

[0135] Table 6,150mg / 350mg prescription screening

[0136]

	处方 15	处方 16	处方 17
可利霉素	7. 5g	7. 5g	7. 5g
微晶纤维素	8. 1g	7. 9g	7. 7g
羧甲淀粉钠	0. 5g+0. 5g	0. 6g+0. 6g	0. 7g+0. 7g
聚维酮 K ₃₀ （水）	0. 8g	0. 8g	0. 8g
硬脂酸镁	0. 1g	0. 1g	0. 1g
制粒难易	制软材容易，易过筛制粒	制软材容易，易过筛制粒	制软材容易，易过筛制粒
片的形态	制得的片表面光洁	制得的片表面光洁	制得的片表面光洁
片的硬度（kg）	6. 4	6. 5	6. 5

崩解时间 (min)	6.10	2.28	3.35
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[0137] Note: The above formulation is made in the amount of 50

[0138] Investigation disintegrating tablet formulation by 15 to 17 times better find 16 a prescription, but the dissolution percentage of less than 85% (see FIG. 4) at the time of 15min, and narrowly pharmacopoeia standards.

[0139] Improvement: ratio of each of materials 16 to fine tune the recipe.

可利霉素	7.5g
微晶纤维素	7.75g
羧甲淀粉钠	0.675g+0.675g
聚维酮 K ₃₀ (水)	0.75g
硬脂酸镁	0.15g

制成 50 片

[0142] (see FIG. 5) found by examining the optimal prescription dissolution 18, when the water temperature 37 ° C, elution time compliance and smooth-sided, non-pitted surface phenomenon.

[0143] Third, the screening of coating solution

[0144] Prescription 14:

可利霉素	100g
微晶纤维素	55g
羧甲淀粉钠	5.5g+5.5g
聚维酮 K ₃₀ (水)	7.5g
硬脂酸镁	1.5g

制成 50 片

[0146] Preparation process:

[0147] the main drug and excipients are over 100 mesh sieve, the amount of prescription can benefit neomycin, microcrystalline cellulose and sodium carboxymethyl starch are mixed uniformly, followed by addition of 5% povidone solution K3tl softwood to 18 mesh Sieve tablets, the wet granulation at 60 ° C under ventilation drying 2h. After drying in a 18-mesh sieve, then add prescriptions carboxymethyl starch sodium mixed with magnesium stearate, with a diameter of dimple embossed sheet punching 11_ was prepared tablet weight 350mg, hardness of the tablet core containing 6.5kg .

[0148] The coating material selection:

[0149] Since rapamycin may benefit bitter, so the need for film-coated tablet cores, choice white color coating agent. Traditional coating solution often dissolved in organic solvents (e.g., acetone, methylene chloride), giving a coating step brings unsafe factors, such as organic solvents toxic, pollute the environment, a large amount of residual organic solvent and the like, and complicated operation, Thus in recent years, more and more aqueous polymer dispersion coating people of all ages. A dispersion medium which is aqueous, aqueous polymer dispersion coating system consisting of water at <spherical particles in the form of solid or semi-solid I μ m, also called latex or pseudo-latex. In addition to avoiding the use of an aqueous dispersion of an organic solvent, but also has a high solids content and low viscosity, ease of preparation, and the coating operation is conducive to shortening the coating time, it is important to industry. This was chosen Opadry II (white) of coating material, self-inspection can facilitate dissolution of rapamycin film-coated tablets.

[0150] Preparation of coating solution:

[0151] weighed desired Opadry II (white) was added to the vessel with the desired amount of water, was added in portions, until complete addition, stirring speed is reduced, so that the vortex disappeared, stirring was continued for 30min, i.e. too.

[0152] Preparation of film-coated tablets:

[0153] The tablet core coating pan set, determining coating conditions, speed of the host 20~25r / min, inlet air temperature 40~450C, air temperature 30~35 ° C, spray pressure 0.02~0.04Mpa, spray slurry flow 1~1.5ml / min coated, after continuous constant spray package 1.5~2h, smooth surface to the tablets, uniform color, film coating meet inspection standards qualified. Coat weight gain of 3%, 5%, 7%. Dissolution of the results shown in Figure 6:

[0154] Ibid measurable amount of ADM Currie different coating weight of the dissolution profile 150mg / 350mg, the results shown in Figure 7:

[0155] Results: The dissolution test, three kinds of coating weight average dissolution meet the quality requirements. 3% of the coating just completely surround the core, in order to produce easy to control the coating weight set at 5%.

[0156] By examining the different prescription ease of granulation, disintegration time four Appearance sheet, sheet stiffness, sheet, and ultimately determine the optimal formulation process is as follows:

[0157] 200mg / 350mg

[0158] tablet core:

可利霉素 200g

微晶纤维素 110g

羧甲淀粉钠 22g

聚维酮 K₃₀ (5%) 15g

硬脂酸镁 3g

制成 1000 片

[0161] 150mg / 350mg

[0162] tablet core:

可利霉素	150g
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微晶纤维素	155g
-------	------

羧甲淀粉钠	27g
-------	-----

聚维酮 K ₃₀ (5%)	15g
--------------------------	-----

硬脂酸镁	3g
------	----

制成	1000 片
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[0164] Coating liquid formulation:

欧巴代 II	21g
--------	-----

蒸馏水	适量
-----	----

制成	105ml
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[0166] Preparation process:

[0167] Preparation of tablet core: a main drug and each excipient than 100 mesh, the prescriptions can benefit neomycin, microcrystalline cellulose and sodium carboxymethyl starch are mixed uniformly, followed by addition of a 5% aqueous solution of the povidone K3tl softwood , granulated with 18 mesh sieve, the wet granules at 60 ° C under ventilation drying 2h. After drying in a 18-mesh sieve, and then added an amount of the formulation of the core tablet containing sodium carboxymethyl starch and magnesium stearate are mixed, washed with a dimple diameter 11mm stampers prepared tablet weight 350mg, hardness of 6.5kg.

[0168] The coating solution prepared: Opadry weighed required II (white) was added to the vessel with the desired amount of water, was added in portions, until complete addition, stirring speed is reduced, so that scroll disappear and continue stirring 30min, that is.

Preparation [0169] The film-coated tablet: the tablet core coating pan set, determining coating conditions, speed of the host 20~25r / min, inlet air temperature of 40~45 ° C, air outlet temperature of 30~35 ° C spray pressure 0.02~0.04Mpa, spray flow I~

1.5ml / min coated, after continuous constant spray package 1.5~2h, smooth surface to the tablets, uniform color, film coating meet inspection standards qualified. Coating weight of about 5%.

[0170] amplified on the dissolution of the prescription (see FIG. 8 and FIG. 9), can be seen from the figure, at the time of 30min, tablets and coated tablets cumulative dissolution percentages were approximately 95%.

[0171] Further, since the content can benefit Tablets was determined by the microbiological assay, rapamycin can benefit 0.1g per titer should be 10 million units, but the actual content of the feedstock produced not fully meet this standard, We need to be adjusted prescription raw material content. The measurement results of different batches of raw content has been produced, which is the lower limit of not less than 90%, therefore, the optimal formulation according to Currie adriamycin inputs adapted to meet the requirements of the tablet content, while reducing diluent microcrystalline amount of cellulose, in order to ensure constant tablet weight. Adjusted prescription as follows:

[0172] Adjustment of the tablet core:

-

可利霉素	225g
微晶纤维素	85g
羧甲淀粉钠	22g
聚维酮 K ₃₀ (5%)	15g
硬脂酸镁	3g
制成	1000 片

[0174] After the compressed core prescription, the above-described coating process after coating, dissolution test results shown in Figure 10: can be seen from the dissolution profile of the formulation after adjustment still satisfy dissolution requirements.

[0175] Comparative Example I

[0176] The Comparative Examples may benefit ADM tablets of the present invention and the prior art can benefit ADM dissolution tablets were investigated.

[0177] Test drugs: doxorubicin Currie plain tablet core formulation and manufacturing process of the tablet core obtained in Example 1 of the embodiment of the present invention;

[0178] Control Drugs: CN102247396A according to Example 12 can be obtained in Lee L ADM tablets.

[0179] The dissolution test drugs and the control drug were examined. The results shown in Figure 11.

[0180] As can be seen from FIG. 11, can facilitate dissolution of the ADM tablets according to the present invention is significantly better than CN102247396A Example 12 L-prepared tablets can benefit ADM.

[0181] Tablets may be prepared ADM benefit to other embodiments of the present invention are also subjected to the above tests, the results of which obtained similar.

Patent Citations (2)

Publication number	Priority date	Publication date	Assignee	Title
CN1554355A *	2003-12-23	2004-12-15	沈阳同联集团有限公司	Bite spiramycin and its use in anti inflammatory disease
CN101810628A *	2010-04-13	2010-08-25	北京四环科宝制药有限公司	Melbine glipizide tablet and preparation method thereof
Family To Family Citations				

* Cited by examiner, † Cited by third party

Cited By (2)

Publication number	Priority date	Publication date	Assignee	Title
CN105497053A *	2015-12-31	2016-04-20	沈阳同联集团有限公司	Application of kelimycin in mycobacterium tuberculosis infection resistance
WO2018184587A1 *	2017-04-06	2018-10-11	沈阳福洋医药科技有限公司	Use of carrimycin and pharmaceutically acceptable salt thereof for manufacture of medicament for treatment and/or prevention of tumors
Family To Family Citations				

* Cited by examiner, † Cited by third party, ‡ Family to family citation

Similar Documents

Publication	Publication Date	Title
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Wilson et al.	2005	Exploiting gastrointestinal bacteria to target drugs to the colon: An in vitro study using amylose coated tablets
JP2008528494A	2008-07-31	Pharmaceutical formulations and methods of use
WO2015028473A1	2015-03-05	Pharmaceutical composition containing dimethyl fumarate for administration at a low daily dose
HU0301177A2	2003-10-28	independent of ionic strength, sustained-release pharmaceutical compositions for
CN103655539B	2019-09-13	A kind of oral solid formulation of canagliflozin and preparation method thereof
KR20130028901A	2013-03-20	Rifaximin powder, process for preparing the same and controlled release compositions containing said rifaximin useful for obtaining a long-lasting effect
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CN101691429B	2011-12-07	Premixed film coating materials and preparation method
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CN102391389B	2013-06-12	Colloidal bismuth pectin compound and medicinal composition thereof, and preparation methods and application thereof
CN104940158B	2018-05-15	A kind of pharmaceutical composition containing CEFUROXIME AXETIL

Priority And Related Applications

Priority Applications (1)

Application	Priority date	Filing date	Title
CN 201310082805	2013-03-15	2013-03-15	Kelimycin tablet and preparation method thereof

Applications Claiming Priority (1)

Application	Filing date	Title
CN 201310082805	2013-03-15	Kelimycin tablet and preparation method thereof

Legal Events

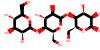
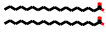
Date	Code	Title	Description
2013-06-12	C06	Publication	
2013-07-17	C10	Entry into substantive examination	
2015-04-01	C14	Grant of patent or utility model	
2015-10-14	PLDC	Enforcement, change and cancellation of contracts on pledge of patent right or utility model	

Concepts

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Starch		abstract	2	0
adjuvant		abstract	2	0
adjuvant		abstract	2	0
carboxymethyl group		abstract	2	0
sodium	Na	abstract	2	0
sodium		abstract	2	0
sodium		abstract	2	0
starch		abstract	2	0

■ Dextrin	abstract	1	0
			
■ Magnesium stearate	abstract	1	0
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