

DESCRIPTION

TITLE OF INVENTION: PESTICIDE TECHNICAL MATERIAL OR PARENT DRUG AND PREPARATION METHOD THEREFOR AND USE THEREOF

TECHNICAL FIELD

[0001] The present application belongs to the technical field of agriculture, and specifically relates to a pesticide technical material or parent drug and preparation method therefor and use thereof.

BACKGROUND

[0002] 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines (where n represents the number of L-lysyl and its value may be any integer from 0 to 4) exhibit excellent bactericidal activity against Gram-positive bacteria, Gram-negative bacteria, mycobacteria, saccharomycetes, and filamentous fungi, making it a promising agricultural antibiotic.

[0003] Currently, only one technical material or parent drug product of 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines has been registered in China, with a relatively low active ingredient content of 12% and poor product quality.

[0004] CN113896753A discloses a method for efficiently separating zhongshengmycin from fermentation broth. This method combines ceramic membrane filtration and cation resin exchange adsorption methods to obtain a technical material containing 25% to 65% of 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines. The color and purity of the technical material are significantly improved compared to commercial products with an active ingredient content of 12% to 24%. However, the applicant found in experiments that the active ingredients of the technical material obtained in CN113896753A degrade rapidly and its antibacterial activity declines significantly during storage. In order to better meet practical production needs, it is imperative to develop a technical material or parent drug of 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines with stable

active ingredient content and antibacterial effect.

SUMMARY

[0005] In order to solve the above technical problems, one aspect of the present application provides a pesticide technical material or parent drug containing at least two 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosaamines;

[0006] based on the total mass of the technical material or parent drug, the total content of the 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosaamines is 70% or more;

[0007] where n represents the number of L-lysyl, and the value of n is any integer from 0 to 4.

[0008] Optionally, based on the total mass of the technical material or parent drug, the total content of the 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosaamines is 70% to 94%.

[0009] Optionally, based on the total mass of the technical material or parent drug, the total content of the 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosaamines is 70% to 90%.

[0010] Optionally, the pesticide technical material or parent drug includes at least three 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosaamines.

[0011] Optionally, the pesticide technical material or parent drug includes at least four 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosaamines.

[0012] Optionally, the pesticide technical material or parent drug includes at least five 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosaamines

[0013] Another aspect of the present application provides a method for preparing the foregoing pesticide technical material or parent drug, including a fermentation step and a purification step.

[0014] Another aspect of the present application provides application of the foregoing pesticide technical material or parent drug or the pesticide technical material or parent drug obtained by the foregoing method in the preparation of bactericides

[0015] The present application achieves the following positive and progressive

effects:

[0016] According to the pesticide technical material or parent drug provided in the present application, based on the total mass of the technical material or parent drug, controlling the total content of the 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines at 70% or more ensures better effects than technical materials or parent drugs with lower active ingredient content in terms of stable active ingredient content and antibacterial effect, and is more conducive to extending the shelf life of the technical material or parent drug. Furthermore, controlling the total content of the 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines within the range of 70% to 94% can better ensure weak hygroscopicity of the technical material or parent drug, greatly reduce the degradation of active ingredients, maintain the antibacterial activity, and achieve excellent overall performance in processing performance, storage convenience, and storage stability.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] FIG. 1 shows a liquid chromatogram of a pesticide technical material or parent drug prepared in Example 2, where bold peaks in the data table correspond to 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines, and the value of n is 0, 1, 2, 3, or 4 in ascending order of retention time;

[0018] FIG. 2 shows a liquid chromatogram of a pesticide technical material or parent drug prepared in Example 3, where bold peaks in the data table correspond to 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines, and the value of n is 0, 1, 2, 3, or 4 in ascending order of retention time;

[0019] FIG. 3 shows a liquid chromatogram of a pesticide technical material or parent drug prepared in Example 5, where bold peaks in the data table correspond to 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines, and the value of n is 0, 1, 2, 3, or 4 in ascending order of retention time;

[0020] FIG. 4 shows a liquid chromatogram of a pesticide technical material or parent drug prepared in Example 6, where bold peaks in the data table correspond to 1-N glycosidic

streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines, and the value of n is 0, 1, 2, 3, or 4 in ascending order of retention time;

[0021] FIG. 5 shows hygroscopicity of samples from Example 2, Example 3, Example 5, and Example 6; and

[0022] FIG. 6 shows antibacterial effects of samples from Example 2, Example 3, Example 5, and Example 6, where FIG. 6A shows antibacterial effects of samples not placed under 60°C/25% relative humidity (RH) conditions, while FIG. 6B shows antibacterial effects of samples placed under 60°C/25% RH conditions.

DETAILED DESCRIPTION

[0023] For the inventive purpose, unless otherwise specified, the terms used in the present application have the following meanings:

[0024] The term “active ingredient” refers to toxic and biocidal ingredients in pesticide products against diseases, insects, weeds, etc. In the present application, the active ingredients specifically refer to “1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines”.

[0025] The term “1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamine” refers to B to F ingredients of Zhongshengmycin, i.e., F ingredient when n=0, E ingredient when n=1, D ingredient when n=2, C ingredient when n=3, or B ingredient when n=4.

[0026] The term “technical material” refers to a product composed of active ingredients and related impurities obtained during production, added with a small quantity of additives if necessary.

[0027] The term “parent drug” refers to a product composed of active ingredients and related impurities obtained during production, including a small quantity of additives and appropriate diluents if necessary.

[0028] In the present application, in addition to 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines, the technical material or parent drug includes other substances that may be extracted from fermentation broth (such as related impurities) or other added substances (such as additives or diluents).

[0029] The term “total content” in the expression “based on the total mass of the technical material or parent drug, the total content of the 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines” refers to a percentage of the total mass of at least two 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines contained in the technical material or parent drug to the total mass of the technical material or parent drug, where the value of n is any integer from 0 to 4.

[0030] For example, if the technical material or parent drug includes a total of two 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines, the value of n is 0 or 1, the total mass of the technical material or parent drug is 100 g, and the total mass of the two 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines is 70 g, based on the total mass of the technical material or parent drug, the total content of the 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines is 70%. The technical material or parent drug including two 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines further includes, but is not limited to the following: the value of n is 0 or 2; the value of n is 0 or 3; the value of n is 0 or 4; the value of n is 1 or 2; the value of n is 1 or 3; the value of n is 2 or 3; the value of n is 2 or 4; the value of n is 3 or 4; or other combinations.

[0031] Alternatively, for example, if the technical material or parent drug includes a total of three 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines, the value of n is 0, 1, or 2, the total mass of the technical material or parent drug is 100 g, and the total mass of the three 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines is 80 g, based on the total mass of the technical material or parent drug, the total content of the 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines is 80%. The technical material or parent drug including three 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines further includes, but is not limited to the following: the value of n is 0, 1, or 3; the value of n is 0, 1, or 4; the value of n is 1, 2, or 3; the value of n is 1, 3, or 4; or other combinations.

[0032] Alternatively, for example, if the technical material or parent drug includes a

total of four 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines, the value of n is 0, 1, 2, or 3, the total mass of the technical material or parent drug is 100 g, and the total mass of the four 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines is 90 g, based on the total mass of the technical material or parent drug, the total content of the 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines is 90%. The technical material or parent drug including four 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines further includes, but is not limited to the following: the value of n is 0, 1, 2, or 4; the value of n is 0, 2, 3, or 4; the value of n is 1, 2, 3, or 4; or other combinations.

[0033] Alternatively, for example, if the technical material or parent drug includes a total of five 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines, the value of n is 0, 1, 2, 3, or 4, the total mass of the technical material or parent drug is 100 g, and the total mass of the five 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines is 90 g, based on the total mass of the technical material or parent drug, the total content of the 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines is 90%.

[0034] In a specific embodiment, in the pesticide technical material or parent drug provided in the present application, the total content of active ingredients is 70% or more. Compared to pesticide technical materials or parent drugs with lower active ingredient content, such as technical materials or parent drugs with a total active ingredient content of 60%, the technical material or parent drug provided in the present application has slower degradation of active ingredients and better maintenance of antibacterial activity during storage.

[0035] Further, the inventor of the present application found that the 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines are hygroscopic, especially at high content, such as when the content is more than 96%. Therefore, the present application preferably provides a technical material or parent drug with a total active ingredient content of 70% to 94%. Such a content range can ensure weak hygroscopicity of the technical material or parent drug, effectively reduce the degradation of active ingredients, and better

maintain the antibacterial activity. Further preferably, the total content of active ingredients in the technical material or parent drug is in a range of any two values consisting of 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 88.5%, 89%, 89.5%, 90%, 90.5%, 91%, 91.5%, 92%, 93%, and 94%. Further preferably, the total content of active ingredients in the technical material or parent drug is any one of 70% to 94%, 70% to 90%, 70% to 85%, 70% to 83%, 70% to 80%, and 70% to 75%.

[0036] In a specific embodiment, a preparation method for the pesticide technical material or parent drug provided in the present application includes a fermentation step and a purification step.

[0037] In a specific embodiment, strains used for fermentation are not limited, as long as they can produce the active ingredients 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosaamines. Preferably, *Streptomyces lavendulae* var. *hainanensis* strains are used.

[0038] The present application does not limit the method of purifying the pesticide technical material or parent drug from fermentation broth, as long as the total content of obtained active ingredients is within the scope of the present application. Preferably, the purification step includes: a fermentation broth cell separation step; a resin adsorption and desorption step; and/or a concentration step. The cell separation includes, but is not limited to, centrifugation, filtration, etc. The resin is preferably ion exchange resin, such as 724 weakly acidic cation exchange resin; and the desorption solution is preferably acidic, such as hydrochloric acid solution. The concentration includes, but is not limited to, nano-filtration concentration.

[0039] Specific examples:

[0040] Reagents and solvents used in the following examples can be purchased commercially or prepared by conventional methods known to those skilled in the art. All the commercially available reagents and solvents have not been further purified. Experimental methods not specified with particular conditions in the following examples shall follow conventional methods and conditions.

[0041] Samples in the examples were tested according to the following methods.

[0042] 1. Determination of active ingredient content in pesticide technical material or

parent drug

[0043] (1) Preparation of sample solution:

[0044] 0.025 g of to-be-tested sample was weighed, placed in a 50 mL volumetric flask, and diluted with water to a scale, and the diluted sample was shaken well and filtered.

[0045] (2) Test conditions:

[0046] Chromatography column: 250 mm × 4.6 mm (i.d.) stainless steel column, filled with a C18 and 5 µm packing.

[0047] Mobile phase: Gradient elution conditions are shown in Table 1.

[0048] Flow rate: 1.0 mL/min.

[0049] Column temperature: Room temperature (temperature change should not exceed 2°C).

[0050] Test wavelength: 200 nm.

[0051] Injection volume: 10 µL.

[0052] Table 1 Gradient elution conditions

Time/min	Acetonitrile (µL)	Buffer salt solution (mL)
0	85	15
2	85	15
10	78	22
20	78	22
22	85	15
30	85	15

[0053] The above operating parameters are typical and can be adjusted appropriately according to the characteristics of different instruments to obtain the best results. The retention time of active ingredients was confirmed by corresponding ingredient standards.

[0054] (3) Result calculation

[0055] The content of active ingredients was calculated through area normalization.

[0056] 2. Determination of degradation rate of active ingredients in pesticide technical material or parent drug

[0057] (1) Preparation of sample solution:

[0058] Identical to “Determination of active ingredient content in pesticide technical material or parent drug”.

[0059] (2) Test conditions:

[0060] Identical to “Determination of active ingredient content in pesticide technical material or parent drug”.

[0061] (3) Result calculation

[0062] The result was calculated according to the following equation:

[0063] $M = (A1 - A2) / A1 \times 100\%$

[0064] In the equation:

[0065] M - degradation rate of active ingredients;

[0066] A1 - Total peak area of active ingredients in the sample not placed under 60°C/25% RH conditions;

[0067] A2 - Total peak area of active ingredients in the sample placed under 60°C/25% RH conditions.

[0068] Preparation examples

[0069] Example 1 Preparation of pesticide technical material or parent drug

[0070] 1. Preparation of fermentation broth

[0071] The fermentation broth was obtained by the fermentation of *Streptomyces lavendulae* var. *hainanensis* in a medium containing glucose, corn starch, corn flour, soybean flour, inorganic salt, etc. The fermentation process was provided by Shaanxi Microbe Biotechnology Co., Ltd. (a subsidiary of the applicant Grand Industrial Holding Co., Ltd.), the applicant of CN113896753A.

[0072] 2. Purification

[0073] According to steps 1) to 4) of Example 3 in CN113896753A, the fermentation broth was filtered with a ceramic membrane to collect high-titer supernatant liquid and low-titer supernatant liquid separately, the low-titer supernatant liquid was adsorbed and desorbed through LX-731-X1 modified resin, the high-titer supernatant liquid was mixed with an eluent, and the mixture was concentrated and dried to obtain a pesticide technical material or parent drug. After determination, the obtained pesticide technical material or parent drug contained 1-N glycosidic

streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines, where the value of n was 0, 1, 2, 3, or 4, and based on the total mass of the technical material or parent drug, the total content of active ingredients was 48.8%.

[0074] Example 2 Preparation of pesticide technical material or parent drug

[0075] 1. Preparation of fermentation broth

[0076] Identical to Example 1.

[0077] 2. Purification

[0078] According to steps 1) to 4) of Example 1 in CN113896753A, the fermentation broth was filtered with a ceramic membrane to collect high-titer supernatant liquid and low-titer supernatant liquid separately, the low-titer supernatant liquid was adsorbed and desorbed through LX-731-X1 modified resin, and the desorbed solution was concentrated and dried to obtain a pesticide technical material or parent drug. After determination, the obtained pesticide technical material or parent drug contained 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines, where the value of n was 0, 1, 2, 3, or 4, and based on the total mass of the technical material or parent drug, the total content of active ingredients was 60.0%. A liquid chromatogram is shown in FIG. 1.

[0079] Example 3 Preparation of pesticide technical material or parent drug

[0080] 1. Preparation of fermentation broth

[0081] Identical to Example 1.

[0082] 2. Purification

[0083] (1) Acidification of fermentation broth: The fermentation broth was acidified to a pH value of 3.5;

[0084] (2) Cell separation: The acidified material was centrifuged to obtain supernatant liquid, which was then filtered with an ultra-filtration membrane twice;

[0085] (3) Resin adsorption and desorption: The filtrate was adsorbed with 724 weakly acidic cation exchange resin, unadsorbed impurities were rinsed with water until effluent was colorless, and then the effluent was desorbed with 5% hydrochloric acid. After the effluent from the 0.5 bed volume (BV) of the desorption solution was discarded, a sample was collected until 5 BV;

[0086] (4) Nano-filtration concentration: The desorption solution was subjected to

nano-filtration concentration;

[0087] (5) Drying: The concentrated solution was spray-dried to obtain a pesticide technical material or parent drug. After determination, the obtained pesticide technical material or parent drug contained 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines, where the value of n was 0, 1, 2, 3, or 4, and based on the total mass of the technical material or parent drug, the total content of active ingredients was 72.9%. A liquid chromatogram is shown in FIG. 2.

[0088] Example 4 Preparation of pesticide technical material or parent drug

[0089] 1. Preparation of fermentation broth

[0090] Identical to Example 1.

[0091] 2. Purification

[0092] (1) Acidification of fermentation broth: The fermentation broth was acidified to a pH value of 3.5;

[0093] (2) Cell separation: The acidified material was centrifuged to obtain supernatant liquid, which was then filtered with an ultra-filtration membrane twice;

[0094] (3) Resin adsorption and desorption: The filtrate was adsorbed with 724 weakly acidic cation exchange resin, unadsorbed impurities were rinsed with water until effluent was colorless, and then the effluent was desorbed with 5% hydrochloric acid. After the effluent from the 0.5 BV of the desorption solution was discarded, a sample was collected until 5 BV. The above resin adsorption process was repeated once more for the collected desorption solution;

[0095] (4) Nano-filtration concentration: The desorption solution was subjected to nano-filtration concentration;

[0096] (5) Drying: The concentrated solution was spray-dried to obtain a pesticide technical material or parent drug. After determination, the obtained pesticide technical material or parent drug contained 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines, where the value of n was 0, 1, 2, 3, or 4, and based on the total mass of the technical material or parent drug, the total content of active ingredients was 82.3%.

[0097] Example 5 Preparation of pesticide technical material or parent drug

[0098] 1. Preparation of fermentation broth

[0099] Identical to Example 1.

[00100] 2. Purification

[00101] (1) Acidification of fermentation broth: The fermentation broth was acidified to a pH value of 3.5;

[00102] (2) Cell separation: The acidified material was centrifuged to obtain supernatant liquid, which was then filtered with an ultra-filtration membrane 3 times;

[00103] (3) Resin adsorption and desorption: The filtrate was adsorbed with 724 weakly acidic cation exchange resin, unadsorbed impurities were rinsed with water until effluent was colorless, and then the effluent was desorbed with 5% hydrochloric acid. After the effluent from the 1 BV of the desorption solution was discarded, a sample was collected until 4 BV. The above resin adsorption process was repeated once more for the collected desorption solution;

[00104] (4) Nano-filtration concentration: The desorption solution was subjected to nano-filtration concentration;

[00105] (5) Drying: The concentrated solution was spray-dried to obtain a pesticide technical material or parent drug. After determination, the obtained pesticide technical material or parent drug contained 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines, where the value of n was 0, 1, 2, 3, or 4, and based on the total mass of the technical material or parent drug, the total content of active ingredients was 89.2%. A liquid chromatogram is shown in FIG. 3.

[00106] Example 6 Preparation of pesticide technical material or parent drug

[00107] 1. Preparation of fermentation broth

[00108] Identical to Example 1.

[00109] 2. Purification

[00110] (1) Acidification of fermentation broth: The fermentation broth was acidified to a pH value of 3.5;

[00111] (2) Cell separation: The acidified material was centrifuged to obtain supernatant liquid, which was then filtered with an ultra-filtration membrane 3 times;

[00112] (3) Resin adsorption and desorption: The filtrate was adsorbed with 724

weakly acidic cation exchange resin, unadsorbed impurities were rinsed with water until effluent was colorless, and then the effluent was desorbed with 5% hydrochloric acid. After the effluent from the 1 BV of the desorption solution was discarded, a sample was collected until 4 BV. The above resin adsorption process was repeated twice more for the collected desorption solution;

[00113] (4) Nano-filtration concentration: The desorption solution was subjected to nano-filtration concentration;

[00114] (5) Drying: The concentrated solution was spray-dried to obtain a pesticide technical material or parent drug. After determination, the obtained pesticide technical material or parent drug contained 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines, where the value of n was 0, 1, 2, 3, or 4, and based on the total mass of the technical material or parent drug, the total content of active ingredients was 96.2%. A liquid chromatogram is shown in FIG. 4.

[00115] Effect examples

[00116] The technical materials or parent drugs of Example 2 (active ingredient content 60.0%), Example 3 (active ingredient content 72.9%), Example 5 (active ingredient content 89.2%), and Example 6 (active ingredient content 96.2%) were placed under 60°C/25% RH conditions for 30 days to observe their hygroscopicity, test their degradation rates of active ingredients, and evaluate the changes in their antibacterial effect.

[00117] 1. Hygroscopicity

[00118] After the technical materials or parent drugs were placed under 60°C/25% RH conditions for 30 days, their hygroscopicity in Example 2, Example 3, Example 5, and Example 6 was shown in FIG. 5. As shown in FIG. 5, the samples from Example 2, Example 3, and Example 5 exhibited low hygroscopicity. In Example 2 and Example 3, only a very small amount of sample on the periphery of the sample pile became slightly moist, while in Example 5, a small amount of sample on the periphery and surface of the sample pile became moist. Nevertheless, the majority of the samples in the three examples remained in a powdered state. After the moist portions were removed with a glass rod, the remaining powdered samples still maintained excellent fluffiness and could be normally used for subsequent formulation processing. The sample from Example 6 had mostly transformed into

paste and readily adhered to the glass rod. Such highly hygroscopic technical material or parent drug tended to adhere to machinery or conveying devices during processing, resulting in operational inconvenience and manufacturing difficulties and posing a huge challenge to storage conditions. Evidently, due to the excessively high active ingredient content, the sample from Example 6 exhibited significantly increased hygroscopicity, poor processing properties, and more stringent storage requirements. The hygroscopicity of the 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines may be due to excessive hydroxyl groups in its molecular structure.

[00119] 2. Degradation rates of active ingredients

[00120] To-be-tested samples:

[00121] Samples from Example 2, Example 3, Example 5, and Example 6 not placed under 60°C/25% RH conditions;

[00122] Samples from Example 2, Example 3, Example 5, and Example 6 placed under 60°C/25% RH conditions for 30 days (dried).

[00123] The degradation rates of active ingredients in the samples were shown in Table 2.

[00124] Table 2 Degradation rates of samples

Technical material/parent drug sample	Degradation rate%
Example 2	7.69%
Example 3	4.03%
Example 5	3.27%
Example 6	6.88%

[00125] According to the above results, after the samples from Example 2 and Example 6 were placed under 60°C/25% RH conditions for 30 days, their degradation rates of active ingredients were more than 5%, making them difficult to meet production requirements. The sample from Example 2 exhibited the highest degradation rate due to its lower active ingredient content and higher impurity content, compromising the stability of active ingredients. The sample from Example 6 exhibited the next highest degradation rate. As indicated by the earlier hygroscopicity results, the excessively high active ingredient

content in Example 6 led to strong hygroscopicity, and the sample had mostly transformed into paste after being placed under 60°C/25% RH conditions for 30 days, so the high-moisture environment was likely a major contributing factor to the degradation of active ingredients. In contrast, Example 3 and Example 5 exhibited lower degradation rates of active ingredients (less than 5%), indicating greater stability of active ingredients and better suitability for practical production needs.

[00126] 3. Determination of antibacterial effect

[00127] (1) To-be-tested samples

[00128] The samples from Example 2, Example 3, Example 5, and Example 6 not placed under 60°C/25% RH conditions were prepared into the following solutions for later use:

[00129] 0.1 g of the sample from Example 2 was dissolved in 1.2 L of sterile water to obtain a solution with an active ingredient concentration of 50 µg/mL, designated as solution 1 (pre);

[00130] 0.1 g of the sample from Example 3 was dissolved in 1.458 L of sterile water to obtain a solution with an active ingredient concentration of 50 µg/mL, designated as solution 2 (pre);

[00131] 0.1 g of the sample from Example 5 was dissolved in 1.784 L of sterile water to obtain a solution with an active ingredient concentration of 50 µg/mL, designated as solution 3 (pre);

[00132] 0.1 g of the sample from Example 6 was dissolved in 1.924 L of sterile water to obtain a solution with an active ingredient concentration of 50 µg/mL, designated as solution 4 (pre);

[00133] The samples from Example 2, Example 3, Example 5, and Example 6 placed under 60°C/25% RH conditions for 30 days (dried) were diluted by the same factors as the corresponding samples not placed under 60°C/25% RH conditions to prepare the following solutions for later use:

[00134] 0.1 g of the sample from Example 2 was dissolved in 1.2 L of sterile water to obtain a solution, designated as solution 1 (post);

[00135] 0.1 g of the sample from Example 3 was dissolved in 1.458 L of sterile

water to obtain a solution, designated as solution 2 (post);

[00136] 0.1 g of the sample from Example 5 was dissolved in 1.784 L of sterile water to obtain a solution, designated as solution 3 (post);

[00137] 0.1 g of the sample from Example 6 was dissolved in 1.924 L of sterile water to obtain a solution, designated as solution 4 (post).

[00138] (2) Preparation of an bacterial layer

[00139] 200 mL of a medium, after being melted and cooled to 48°C to 50°C, was mixed with 1 mL of 1×10^{-8} CFU/mL xanthomonas citri suspension, and the mixture was shaken well, poured into a culture dish, and allowed to stand until solidified, to obtain a bacterial layer.

[00140] (3) Addition of the solutions

[00141] 4 pieces of sterile filter paper were placed on one culture medium containing the bacterial layer, and 10 μ L of solution 1 (pre), solution 2 (pre), solution 3 (pre), and solution 4 (pre) were added dropwise to the filter paper, respectively. This operation was repeated 3 times.

[00142] 4 pieces of sterile filter paper were placed on another culture medium containing the bacterial layer, and 10 μ L of solution 1 (post), solution 2 (post), solution 3 (post), and solution 4 (post) were added dropwise to the filter paper, respectively. This operation was repeated 3 times.

[00143] The culture dishes were placed in a 28°C incubator for culture 48 hours.

[00144] (4) Investigation on antibacterial effect

[00145] After the culture was completed, the diameters of inhibition zones were measured using a cross method and an average value was calculated. Results are shown in Table 3 and FIG. 6, where FIG. 6A shows an inhibition zone image of the sample not placed under 60°C/25% RH conditions, and FIG. 6B shows an inhibition zone image of the sample placed under 60°C/25% RH conditions for 30 days.

[00146] Table 3 Antibacterial effect of samples

Sample	Average diameter of antibacterial zones (mm)	Sample	Average diameter of antibacterial zones (mm)
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solution 1 (pre)	27.3	solution 1 (post)	21.2
solution 2 (pre)	27.9	solution 2 (post)	24.1
solution 3 (pre)	28.2	solution 3 (post)	24.8
solution 4 (pre)	28.7	solution 4 (post)	23.3

[00147] According to the above results, the samples from Example 2, Example 3, Example 5, and Example 6 not treated under 60°C/25% RH conditions exhibited comparable antibacterial activity, while the samples from Example 2 and Example 6 treated under 60°C/25% RH conditions exhibited a decrease in the average diameter of inhibition zones by more than 5 mm, indicating poor stability in antibacterial activity. Among them, Example 2 exhibited the most obvious decline in antibacterial activity, with the average diameter of inhibition zones decreasing from 27.3 mm to 21.2 mm (a reduction of 6.1 mm), followed by the sample from Example 6, with the average diameter of inhibition zones decreasing from 28.7 mm to 23.3 mm (a reduction of 5.4 mm). In contrast, the samples from Example 3 and Example 5 exhibited better retention of antibacterial activity, with the average diameter of inhibition zones decreasing from 27.9 mm to 24.1 mm (a reduction of 3.8 mm) and from 28.2 mm to 24.8 mm (a reduction of 3.4 mm), respectively.

[00148] Based on the above experimental results, the technical material or parent drug of Example 2 (with an active ingredient content of 60.0%) exhibited low hygroscopicity for easy processing and storage subsequently, but exhibited poorest performance in terms of retaining active ingredients and maintaining the antibacterial effect, where the poorest performance was likely attributed to high impurity content and excessively low content of the active ingredients 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines, and the stability of the active ingredients was significantly compromised by the impurities, making it prone to degradation. Therefore, only by increasing the content of 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines to 70% or more, can the stability of active ingredients and the antibacterial activity be better maintained, to meet practical production needs.

[00149] Furthermore, although the technical material or parent drug of Example 6

(with an active ingredient content as high as 96.2%) was less affected by other impurities, its high active ingredient content and strong hygroscopicity not only affect subsequent formulation processing and create storage challenges, but also promote the degradation of active ingredients. Consequently, the technical material or parent drug of Example 6 also exhibited poor performance in retaining active ingredients and maintaining the antibacterial activity. Therefore, controlling the content of 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines within the range of 70% to 94% not only ensures low hygroscopicity, but also significantly reduces the degradation of active ingredients and maintains the antibacterial activity, thereby further enhancing the overall performance of the technical material or parent drug.

[00150] The foregoing embodiments are preferred implementations of the present application, but the implementations of the present applications are not limited by the foregoing embodiments. Any other changes, modifications, substitutions, combinations, or simplifications made without departing from the spirit essence and principle of the present application shall be equivalent replacements, and shall fall within the scope of protection of the present application.

WHAT IS CLAIMED IS:

1. A pesticide technical material or parent drug, containing at least two 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines, wherein

based on the total mass of the technical material or parent drug, the total content of the 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines is 70% or more;

wherein n represents the number of L-lysyl, and the value of n is any integer from 0 to 4.

2. The pesticide technical material or parent drug according to claim 1, wherein based on the total mass of the technical material or parent drug, the total content of the 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines is 70% to 94%.

3. The pesticide technical material or parent drug according to claim 1, wherein based on the total mass of the technical material or parent drug, the total content of the 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines is 70% to 90%.

4. The pesticide technical material or parent drug according to any one of claims 1 to 3, wherein the technical material or parent drug comprises at least three 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines.

5. The pesticide technical material or parent drug according to any one of claims 1 to 3, wherein the technical material or parent drug comprises at least four 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines.

6. The pesticide technical material or parent drug according to any one of claims 1 to 3, wherein the technical material or parent drug comprises at least five 1-N glycosidic streptolidine-2-amino-(L-lysyl)_n-L-lysine-2-deoxygulosamines.

7. A method for preparing the pesticide technical material or parent drug according to

any one of claims 1 to 6, comprising a fermentation step and a purification step.

8. Application of the pesticide technical material or parent drug according to any one of claims 1 to 6 or the pesticide technical material or parent drug obtained by the method according to claim 7 in the preparation of bactericides.