An oral pharmaceutical and an oral care product

FIELD OF THE INVENTATION

[0001] The present invention relates to the field of pharmaceutical techniques, and relates to pharmaceuticals or oral care products for treating or preventing oral diseases which is prepared with a morusin compound as an active ingredient, the preparing method thereof and the use thereof in manufacturing pharmaceuticals or oral care products for treating or preventing oral diseases.

BACKGROUND OF THE INVENTION

[0002] The common human oral diseases include caries and periodontal disease. Caries is a chronic bacterial disease occurring in dental hard tissues, manifested as a color, shape, qualitative changes of dental hard tissues. Clinical symptoms of periodontal disease are gum bleeding, purulence, tooth mobility, absorption of alveolar bone and formation of periodontal pocket. Caries and periodontal disease are also one of the primary causes for the tooth loss of adults. It's considered now that the pathogeny of both caries and periodontal disease is endogenous infection diseases resulted from a case that the normal oral floras lose balance, namely the initial factor being plaque microorganism, and being resulted from specific pathogenic microorganisms. Bacteria is the necessary condition for the occurrence of caries, and *Streptococcus mutans*, *Actinomyces naeslundi, Actinomyces viscosus* and the like may break up carbohydrates to yield acids, causing teeth inorganics to demineralize and form caries cavities. *Streptococcus mutans* and *Streptococcus sanguinis* are also the pioneer bacteria in the formation of dental plaques, they form dental plaques together with *Actinomyces naeslundi, Actinomyces viscosus*, *Porphyromonas gingivalis, Actinobacillus actinomycetemcomitans* and *Fusobacterium nucleatum*. The toxins and other detrimental substances produced by the bacteria in the dental plaques may cause the inflammatory reactions of the host, lead to the increase in vascular permeability and the spread of inflammation, destroy the gum, dental bone and alveolar bone, and cause gingivitis and periodontal diseases.

[0003] Therefore, inhibiting oral pathogenic microorganisms is an important approach to prevent caries, gingivitis and periodontal diseases, but the medicaments for treating caries and periodontal disease are very limited at present. On one hand, chemical pharmaceuticals are used to eliminate or inhibit the plaque bacteria, but the long-term use of broad-spectrum antibacterial will bring drug-resistant strains and other side

effects. For example, the chemical plaque-controlling agent Chlorhexidine used both at home and abroad in recent years is a diguanido-hexane having obvious bacteriostasis, but the long-term use of gargle containing 0.12-0.20% Chlorhexidine will cause stained tooth and formation of brown tongue coat at the back of tongue, although will not form any drug-resistant strains or cause any harm to human body. On the other hand, dialectic therapeutics of Traditional Chinese Medicines are used, such as gargling Chinese medicines which are "heat-clearing" and "detoxifying" like honeysuckle, etc., as well as external-applying methods such as applying Bingpeng San (borneol and borax powder) or Asarum on the suffering part. There are many inconveniences in using these methods, and there is no conclusive evidence to prove their efficacy. However, if the gingivitis is not treated timely or properly, the inflammation symptom may spread to periodontal apex to cause the inflammation of periodontal apex tissues, and further affects the alveolar bone or the neighboring tissues. Based on the above reasons, it may be seen that it is meaningful to research and develop new medicines from natural plants for treating common oral diseases such as caries and periodontal diseases, and to develop oral pharmaceuticals or oral care products for inhibiting primary oral pathogenic microorganisms and dental plaques, gingivitis, and for countering breath odor.

[0004] Researches on natural plants inhibiting oral pathogenic microorganisms have distinct geographical characteristics. In accordance with different geographical environments and country situations all over the globe, different countries and regions found some plants of the anti-caries effects, such as *Anogeissus Wall.* and *Vernonia esculenta*, *Garcinia morella Desv.* (gamboges) of Africa and the Middle East; blood grass roots, cocoa fruit of Latin American countries; *Areca catectu L.* (betel nut) of Southeast Asia; Eucalyptus leaves of Australia. China and Japan are more concentrated on the study of Chinese herbal medicines.

[0005] There has been no report in the prior art on oral pharmaceuticals or oral care products prepared with a compound morusin as an active ingredient by now.

DESCRIPTION OF INVENTION

[0006] The object of the present invention is to provide a pharmaceutical or oral care product for treating or preventing oral diseases which is prepared with a morusin compound as an effective ingredient, the preparing method thereof and the use thereof in manufacturing medicaments or oral care products for treating or preventing oral diseases.

[0007] In order to achieve the above object, the present invention provides the following technical solution:

[0008] An oral product, containing a morusin compound and a medical adjuvant or a caring adjuvant.

[0009] The oral product includes, but not limited to oral pharmaceuticals, oral care products.

[0010] The adjuvant includes, but not limited to pharmaceutically applicable carriers and/or excipients, common adjuvants of oral care products.

[0011] The present invention provides a method for preparing the above oral product at the same time, i.e., taking Cortex Mori, extracting the Cortex Mori with 90% ethanol for 3 times under reflux, 3h each time, and recovering to dryness to obtain an extractum; dissolving and suspending the resultant extractum, extracting 3 times with ethyl acetate, recovering to dryness to obtain an ethyl acetate extractum; dissolving the resultant extractum with acetone and adsorbing on silica gel, evaporating to dryness at room temperature, and subjected to a silica gel column chromatography, eluting with petroleum ether: acetone in 8:2(v/v); take every 50 liters as a fraction, obtaining 27 fractions (Fr.1~Fr.27) in all; subjecting the fraction Fr.4 to a silica gel column chromatography, and eluting with petroleum ether:acetone in 8:2, then subjecting to a polyamide column chromatography again with 60:40 ethanol:water, and a silica gel column chromatography with 95:5 chloroform:acetone, obtaining a morusin compound; then common adjuvants of oral pharmaceuticals or common adjuvants of oral care products are added to make the oral product.

[0012] The morusin compound of the present invention may be used in manufacturing pharmaceuticals for treating or preventing diseases, or may be used to prepare oral care products.

[0013] The inventor of the present invention finds for the first time that morusin compound has certain inhibiting effect on oral pathogenic microorganisms, and may be applied in anti-caries and breath odor-inhibiting oral pharmaceuticals or oral care products as an effective ingredient, and may also be used in oral pharmaceuticals or oral care products for countering gingivitis and dental plaques, removing oral sensitivity, countering tartar and whitening tooth.

[0014] The invention will be illustrated in combination with examples in the following.

EXAMPLE 1 Preparation of morusin compound and structure identification of the compound

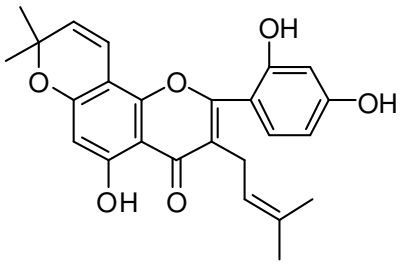
[0015] 50kg Cortex Mori (White Mulberry Root-bark) is extracted with 500kg 90% ethanol under reflux for 3 times, 3h each time, and the extract is recovered to dryness to obtain 10.5kg extractum. The extractum is dissolved and suspended with 8kg hot water and 4kg 90% ethanol, and extracted with 50kg ethyl acetate for three times, recovered to dryness, obtaining 4kg ethyl acetate extractum. The resultant extractum is dissolved with acetone and adsorbed on 6kg silica gel, evaporated to dryness at room temperature, and subjected to a silica gel column chromatography (30 meshes, 30kg), eluted with petroleum ether: acetone (v/v, 8:2); Every 50 liters is taken as a fraction, obtaining 27 fractions (Fr.1~Fr.27) in all. The fraction Fr.4 is subjected to a silica gel column chromatography, and eluted with petroleum ether: acetone (v/v, 8:2), giving 10g fraction which mainly contains compound 1 (morusin). The fraction is subjected to a polyamide column chromatography (60:40 ethanol: water) and a silica gel column chromatography (95:5 chloroform: acetone), obtaining the compound morusin (5g).

[0016] The morusin prepared by this method may have a very high concentration. In certain examples, the concentration of the morusin prepared by this method is higher than 98%. In certain other examples, the concentration of the morusin prepared by this method is 50%-99.9%. In some other examples, the concentration of the morusin prepared by this method is 75%-99.9%.

[0017] In the examples above, Cortex Mori (White Mulberry Root-bark) is used to extract the morusin compound. It may be understood by those of ordinary skills in the art that other plants may also be applicable, such as those of the same genus or the same family with Cortex Mori (White Mulberry Root-bark).

[0018] Auto SPEC type 3000 mass spectrometer is used for mass spectrometry (MS) analysis. Bruker DRX-500 superconductive NMR spectrometer is used to determine the nuclear magnetic resonance spectrometry (^{1}H NMR and ^{13}C NMR), with TMS as an internal standard. The silica gel for column chromatography and thin layer column chromatography is product of Qingdao Meigao Group Co. Ltd.

[0019] Structure formula of morusin:



Properties: light-yellow powder
mp.168-169°C
Molecular formula: $C_{25}H_{24}O_6$
Molecular weight: 420
^{1}H-NMR (MeOD, 400 MHz) δ: 7.20(1H, s, H-6'),7.09(1H, s, H-3'), 6.96(1H, d, J = 8.0 Hz, H-5'), 6.73(1H, d, J = 9.6 Hz, H-14), 6.49(1H, s, H-6), 5.56(1H, t, J = 6.4 Hz, H-10), 5.50(1H, d, J = 10.0 Hz, H-15), 3.56(2H, dd, J = 6.8, 1.0 Hz, H-9), 1.64(3H, s, H-12),1.62(3H, s, H-13), 1.40(6H, s, H-17, 18).
^{13}C-NMR (MeOD, 100MHz) δ:162.3(s, C-2), 121.2(s, C-3), 182.7(s, C-4), 105.3(s, C-4a), 162.3(s, C-5), 99.4(d, C-6), 158.2(s, C-7), 100.9(s, C-8), 152.6(s, C-8a), 24.6(t, C-9), 122.4(d, C-10), 132.0(s, C-11), 25.6(q, C-12), 17.6(q, C-13), 115.1(d, C-14), 126.8(d, C-15), 77.9(s, C-16), 27.8(s, C-17), 27.8(s, C-18), 112.4(s, C-1'), 158.2(s, C-2'), 104.1(d, C-3'), 159.1(s, C-4'), 107.8(d, C-5'), 131.7(s, C-6').

[0020] In accordance with the compound structure formula disclosed in the present invention, those skilled in the art may synthesize said compound easily by chemical methods without creative work, to substitute the extract or purified substance used in the present invention. Therefore, those skilled in the art should understand that, in addition to extraction or purification from Cortex Mori (White Mulberry Root-bark) as listed in the examples of the present invention, the present invention may also be achieved through chemical synthesis methods. Other obvious modifications of the compound disclosed in the present invention will also be included within the protection scope of the present invention.

EXAMPLE 2 The inhibition experiment of morusin on primary oral pathogenic microorganisms

A. The Cultivation of the bacteria species:

Table 1: Related Oral Pathogenic microorganisms

Strains	**ATCC number**	**Gram properties**	**Culture medium**
***Actinomyces naeslundii* (A. n)**	12104	G(+)	TSB
***Actinobacillus actinomycetemcomitans* (A. a)**	43717	G(-)	TSB / RCM (3:1)
***Streptococcus mutans* (S. m)**	25175	G(+)	TSB
***Porphyromonas gingivalis* (P. g)**	33277	G(-)	FTM / RCM (3:1)
***Fusobacterium nucleatum subsp. Polymorphum* (F.n)**	10953	G(-)	BHI
***Actinomyces viscosus* (A.v)**	27044	G(+)	TSB
***Streptococcus sanguis* (S.sa)**	10556	G(+)	TSB

[0021] A single colony is picked from the Trypticase Digested Soybean peptone agar blood plate (TSA5B) of ordinarily stored bacteria species to corresponding broth culture medium, cultivated in microaerobic environment (P.g and F.n. need anaerobic cultivation) with 95% air, 5% CO_2 at 37.0 ˚C ± 1.0 ˚C, wherein S.m and S.sa. are cultivated for 18-24 h, and the remaining three are cultivated for 40-48 h. Then corresponding broth cultivate medium is used to adjust the turbidity of the bacteria suspension to 0.5#McFarland standard, equivalent to 1.0×10^8 CFU/mL.

B. Experiment method: Broth dilution method

[0022] After they are performed a series of 2-fold dilutions, the anti-bacteria pharmaceuticals are quantitatively inoculated with tested bacteria, and are observed after incubated at 37 ˚C for 18-24 h, wherein the lowest pharmaceutical concentration that inhibits the growth visible to the naked eye of the tested bacteria is the minimum inhibitive concentration (MIC) of the tested pharmaceuticals to the tested bacteria. The operating steps are:

a. Preparation of the stock solution of antibacterial pharmaceutical: Preparing 1%

stock solution of various antibacterial pharmaceuticals with 100% pure ethanol as solvent. The prepared stock solution is filtered to eliminate bacteria, and is distributed into small portions to be used.
b. Range of measured concentration: the present experiment chooses 250 ppm as the ceiling measured concentration of the anti-bacteria pharmaceutical.
c. Measuring method: micro-dilution method.

[0023] Firstly, 100 μL broth medium is added to each hole of the 96-well plate, and 100 μL sterile anti-bacteria pharmaceutical solution which is diluted 10-folds (1000mg/l) is added to each hole of the first column, then each hole of the first column is blowed repeatedly for 7-8 times using multi-channel micropipet, and 100μL sample is transferred to the second column after sufficiently mixing the pharmaceutical with TSB. After similarly being blowed for 7-8 times, 100μL sample is transferred to the third column, and analogously to the last column. Thus the concentration of the pharmaceutical is 2-fold gradiently diluted, from 500 mg/L of the first column to 0.24 mg/L of the last column (the 12th column).

[0024] The bacteria to be tested and standard bacteria are prepared as above. The bacteria solution is diluted with broth medium to a bacteria content of about 10^6 CFU/mL. Then 100μL for each hole is inoculated. Thus the final diluted concentration of the anti-bacteria pharmaceutical in each line are 250, 125, 62.5…0.12 mg/L, and the final inoculation quantity is about 5×10^7 CFU/mL or 5×10^6 bacteria each hole. The 96-well plate is placed on a microshaker and is shaken for 1min to mix the solution in each hole. The microwell plate is covered and is sealed with adhesive paper to reduce the evaporation during the incubation process and is placed in a humid box, cultivated in microaerobic environment with 95% air, 5% CO_2 (or in anaerobic environment with 90% N_2, 5% H_2, 5% CO_2) at 37.0 ˚C ± 1.0 ˚C for 18-24h . The 96-well plate is placed under an enzyme-labeling instrument, and by comparing the growing characteristics of the tested bacteria with the standard bacteria, the lowest anti-bacteria pharmaceutical concentration contained in the hole without bacteria is taken as MIC.

C. Experiment results (see Table 2)

Table 2: the effect of compound morusin on oral pathogenic microorganisms

	A. v ATCC 27044	**S. m ATCC 25175**	**A. a ATCC 43717**	**A. n ATCC 12104**	**P. g ATCC 33277**	**F. n ATCC 10953**	**S. sa ATCC 10556**
Negative control (DMSO)	-	-	-	-	-	-	-
Positive control (Triclosan)	3.9	3.9	1.95	3.9	7.8	7.8	7.8
Morusin	2.4	3.9	2.4	1.9	1.9	15.6	3.9

EXAMPLE 3: Anti-inflammatory experiment of morusin

[0025] A. The experiment uses KB cell (the epidermic cancer cell in human oral cavity):

During the experiment, the KB cell inoculated in the cultivating plate is treated with or without (control) compound morusin. After the treatment, the supernatant of the cultivating liquid is collected and stored in -80C refrigerator. The PGE_2 in the supernatant is detected by Enzyme-linked immunsorbent assay, and Luminex multifunctional liquid-phase chip analysis system is used for the detection of GM-CSF, TNF-α, IL-1β and IL-6 (the results are shown in Table 3).

[0026] B. Detection of PGE_2 by Enzyme-linked immunsorbent assay:

The assay is performed as standard Enzyme-linked immunsorbent assay.

Result (the smaller the value, the better the anti-inflammatory activity): The 50% inhibitory concentration of morusin to the growth of oral KB cell is 0.02 ppm, equivalent to the positive control Triclosan. The result shows that morusin has significant anti-inflammatory activity.

[0027] C. Luminex multifunctional liquid-phase chip analysis of GM-CSF, TNF-α, IL-1 and IL-6:

The 96-well plate is enclosed with disclosing liquid for 30min. The fluorescent microspheres are added into the 96-well plate after dilution. The standard sample and

the sample to be measured are added, and are stayed overnight at 4°C. In the next day, the supernatant is discarded and 50 μl GM-CSF, TNF-α, IL-1β and IL-6 antibodies are added to each hole. After being rinsed for 4 times, the 96-well plate is placed in a shaking table under ambient temperature to shade from light for 1h; rinsed 4 times, and added PE labeled with streptavidin and shaded from light for 15 min at room temperature, and then rinsed 4 times. The microspheres are suspended in the rinsing buffer, and the 96-well plate is added immediately on Luminex (Luminex Corporation, Austin, Tx.) to analyze.

[0028] D. Result: The compound Morusin has a very strong anti-inflammatory ability. The specified results are shown in Table 3.

Table 3: the anti-inflammatory effect of morusin (the larger the value, the stronger the anti-inflammatory ability)

Extract/compound	GM-CSF	IL-1β (interleukin)	IL-6 (interleukin)	TNF-α(Tumor Necrosis Factor)
Compound morusin	9%	20%	49%	91%
Triclosan (Positive control)	5%	7%	31%	81%

[0029] It may be verified by the above experiment results that: compound morusin according to the present invention has excellent inhibitory effect on oral pathogenic microorganisms (*Actinomyces viscosus, Actinobacillus actinomycetemcomitans, Streptococcus mutans*, *Porphyromonas gingivalis*), has significant anti-inflammatory activity to oral KB cells, and also has significant inhibitory effect on inflammatory factors.

EXAMPLE 4: Use of morusin

[0030] When used as pharmaceuticals, compound morusin of the present invention may be used directly, or may be employed in oral pharmaceuticals or oral care products such as toothpaste, mouthwash, paste, instant tablet or thin film, chewing gum and the like as the effective ingredient. It may be used in effective amount together with other ingredients such as humectant, abrasive, surfactant, pharmaceutically acceptable carrier and/or additive to prepare oral pharmaceuticals or oral hygiene products. The resultant oral medicaments or oral hygiene products include but not limited to toothpaste, mouthwash, chewing gum and oral pastes, etc.

[0031] The term “effective amount” indicated herein refers to an amount sufficient to produce a positive effect. Such an effective amount will vary in particular embodiments. In addition, there may be multiple effective dosages or effective dosage range. In some examples, morusin may be mixed with other ingredients in an added amount of 0.0005-20% (mass percentage). In some other embodiments, the content of morusin is 0.001-10% (mass percentage). In some preferred examples, the content of morusin is 0.025-5% (mass percentage). In some other examples, the content of morusin is 0.05-0.5% (mass percentage).

[0032] Preferably, in tablets, the content of morusin is 4% (mass percentage); in nasal sprays, the content of morusin is 4% (mass percentage); in dropping pills, the content of morusin is 10% (mass percentage); in toothpastes, the content of morusin is 0.5% (mass percentage); in mouthwash, the content of morusin is 0.5% (mass percentage); and in oral pastes, the content of morusin is 0.01% (mass percentage).

[0033] Other effective amount may also be applicable in the present invention.

[0034] The composition of formulation according to the present invention may also contain cationic surfactants and/or non-ionic surfactants. Cationic surfactants include, but not limited to, cetyltrimethylammonium chloride, di(isobutyl-phenoxy-ethoxy-ethyl)-di(xylene-benzyl) ammonium bromide. Non-ionic surfactants include Poloxamer, polyethoxy ether, and ethoxy fatty acid and the like. Poloxamer is a block copolymer of polyoxyethylene and polyoxypropylene, having industrial applications, such as that produced by BASF under the trade name “Pluronic”. Polyethoxy ether includes polyoxyethylene sorbitol fatty acid ester (a typical monoester of polyethoxy alcohol), which is produced by ICL company with the trade name Tween. Other non-ionic surfactants include polyoxyethylene alkylphenol, polyoxyethylene alcohols, fatty acids, polyoxyethylene esters, polyoxyethylene alkyl amine glyceride, polyglyceride, tetritol ester, pentitol ester, hexitol ester, dehydrated tritol ester and polyoxyalkylamine polyalkyl ester. Typically, the mass content of surfactant in the formulation is 0.001%-3.0%. Divalent metal ions, such as zinc, copper, selenium, calcium or magnesium, may be included in the formulation. They will be in the form of soluble inorganic salts such as zinc chloride or the form of organic/inorganic compounds. The amount of divalent metal ions added into the mixture will be 0.001% - 3.0%. The formulation may contain oligosaccharides, which will be in the water-soluble state, and may convert into soluble salt, if added, in an amount of at least 0.01%.

[0035] The present invention may include various commonly used oral pharmaceuticals or oral hygiene products, such as mouthwash, oral spray, toothpaste, gels, oral mucosa plasters, oral pellicle, instant tablet and film, chewing gum and the like products for mammals, especially human and animals, to inhibit plaque and prevent dental caries and periodontal diseases.

[0036] Other additives may be used due to different approaches: mouthwash may contain acidic substances; mouthwash may also contain desensitizing substance such as potassium nitrate; toothpaste may contain abrasive such as sodium carbonate, calcium phosphate, alumina and silica; solubilizer such as PEG, glycerol, ethanol; other taste masking agent such as xylitol; thickener such as carrageenan, and surfactant such as SLS, etc. may all be used.

[0037] Waxes such as beeswax may be used in toothpaste or oral mucosa plaster; thickener and pellicle-forming agents such as carrageenan, CMC, HPMC, xanthan gum and the like may also be added.

[0038] For essences, it may use essences such as mint, spearmint, eucalyptus leaf oil, menthol, carvone, wintergreen, cloves, cinnamon, lemon, grapefruit, orange and some essences decomposed and digested from yeast and protein.

[0039] In tablets and pellicles, inert excipients may be used for the formation of the products. Adjuvants such as colorant, taste masking agent and the like are mainly included to improve the taste and appearance.

[0040] The composition of the formulation related with the use of the present invention in tablets may contain filler, adhesive, lubricant, disintegrant. Fillers include, but not limited to, starch, lactose, microcrystalline cellulose and the like. Adhesives include, but not limited to, starch slurry, cellulose derivatives, polyvidone, gelatin and the like. Lubricants include, but not limited to, magnesium stearate, micropowder silica gel, talcum powder, polyethylene glycols and the like. Disintegrants include, but not limited to, sodium carboxymethyl starch, low substituted hydroxylpropyl cellulose, cross-linked polyvidone, cross-linked sodium carboxymethyl cellulose and the like. All these ingredients are pharmaceutically acceptable adjuvants recorded in the Chinese Pharmacopoeia and the Pharmacopoeia of many countries such as United Kingdom and United States.

[0041] Matrix such as polyethylene glycol and the like may be used in the pastes of the present invention. Polyethylene glycol in solid may be combined with its liquid forms to adjust the consistency. Ingredients such as magnesium stearate may also be added to adjust the consistency.

EXAMPLE 5: Specific Uses

[0042] Following experiments and examples will make those skilled in the art understand the present invention more comprehensive, but they will not limit the present invention in any way.

Morusin toothpaste formulation 1：

Components	**Content (mass percentage, %)**
Morusin	0.0005 – 20
Abrasive	10-30
Humectant	50-69
Water, Flavor, Flavoring	proper amount

Morusin toothpaste formulation 2：

Components	**Content (mass percentage, %)**
Morusin	5
Silica	30
Glycerol	5
Sorbitol	50
Water, Flavor, Flavoring	proper amount

Morusin toothpaste formulation 3：

Components	**Content (mass percentage, %)**
Morusin	0.001
Silica	10
Sorbitol	69
Water, Flavor, Flavoring	proper amount

Morusin toothpaste formulation 4：

Components	**Content (mass percentage, %)**
Morusin	10
Abrasive	25
Humectant	65

Morusin toothpaste formulation 5：

Components	Content (mass percentage, %)
Morusin	0.0005
Silica	10
Sorbitol	70
Water, Flavor, Flavoring	proper amount

Morusin toothpaste formulation 6：

Components	Content (mass percentage, %)
Morusin	20
Abrasive	25
Humectant	55

Morusin toothpaste formulation 7：

Components	Content (mass percentage, %)
Morusin	0.025
Silica	20
Glycerol	5
Sorbitol	60
Sodium fluoride	0.221
Sodium saccharin	0.3
Water	7.954
Polyethylene glycol	3
Sodium dodecyl sulfate	2
Essence	1.5

Morusin toothpaste formulation 8：

Components	Content (mass percentage, %)
Morusin	0.3
Silica	20
Glycerol	5
Sorbitol	60
Sodium fluoride	0.221
Sodium saccharin	0.3
Water	7.679
Polyethylene glycol	3

Sodium dodecyl sulfate	2
Essence	1.5

Morusin toothpaste formulation 9：

Components	**Content (mass percentage, %)**
Morusin	0.5
Silica	20
Glycerol	5
Sorbitol	60
Sodium fluoride	0.221
Sodium saccharin	0.3
Water	7.479
Polyethylene glycol	3
Sodium dodecyl sulfate	2
Essence	1.5

Morusin mouthwash formulation 1:

Components	**Content (mass percentage, %)**
Morusin	0.0005 – 20
Water	70-94
other additives	proper amount

Morusin mouthwash formulation 2:

Components	**Content (mass percentage, %)**
Morusin	5
Water	80
Pluronics	3.00
other additives	proper amount

Morusin mouthwash formulation 3:

Components	**Content (mass percentage, %)**
Morusin	0.001
Water	94
Alcohol	5.00
other additives	proper amount

Morusin mouthwash formulation 4:

Components	**Content (mass percentage, %)**
Morusin	0.5
Water	90
Pluronics	3.00
Alcohol	3.00
other additive	proper amount

Morusin mouthwash formulation 5:

Components	**Content (mass percentage, %)**
Morusin	0.025
Water	85
Pluronics	5.00
Alcohol	3.00
other additives	proper amount

Morusin mouthwash formulation 6:

Components	**Content (mass percentage, %)**
Morusin	0.05
Water	91.7
Pluronics	3.00
Alcohol	5.00
Essence	0.25

Morusin mouthwash formulation 7:

Components	**Content (mass percentage, %)**
Morusin	0.0005
Water	94
Alcohol	5.00
other additives	proper amount

Morusin mouthwash formulation 8:

Components	**Content (mass percentage, %)**
Morusin	20
Water	70
Pluronics	3.00
Alcohol	3.00
other additives	proper amount

Morusin paste formulation 1:

Components	**Content (mass percentage, %)**
Morusin	10
Polyethylene glycol	90

Morusin paste formulation 2:

Components	**Content (mass percentage, %)**
Morusin	0.001
Polyethylene glycol	80
other additives	proper amount

Morusin paste formulation 3:

Components	**Content (mass percentage, %)**
Morusin	0.01
Polyethylene glycol	90
other additives	proper amount

Morusin paste formulation 4:

Components	**Content (mass percentage, %)**
Morusin	5
Polyethylene glycol	95

Morusin paste formulation 5:

Components	**Content (mass percentage, %)**
Morusin	0.025
Polyethylene glycol	99.975

Morusin paste formulation 6:

Components	**Content (mass percentage, %)**
Morusin	20
Polyethylene glycol	80

Morusin paste formulation 7:

Components	**Content (mass percentage, %)**
Morusin	0.0005
Polyethylene glycol	99

other additives	proper amount

[0043] Morusin tablet:

[0044] Tablet: active ingredient morusin 10mg, lactose 180mg, starch 55mg, magnesium stearate 5mg.

[0045] Preparing method： Active ingredient, lactose and starch are mixedand wetted uniformly with water. The wetted mixture is subjected to sieve and dry, subjected to sieve again, added in magnesium stearate. The mixture is then compressed into tablets weighing 250 mg each with a content of the active ingredient content of 10 mg.

[0046]Morusin nasal spray：

Morusin	80 mg
sodium chloride	8 mg
EDTA	1 mg
Sodium phosphate buffer(pH6.5)	10 mg
Polyethoxy ether	10 mg
redistilled water	to 2ml

[0047] Preparing method: One ingredient at a time is added into proper volume of redistilled water under stirring until completely dissolved, then another ingredient is added. After being added water to 2ml，the solution is filtered on a sterile filter, filled into bottles and separated according to suitable dosage.

[0048]Morusin dropping pills：

Morusin	1g
polyethylene glycol 6000	9g

[0049] Preparing method: preparation of molten liquid of morusin and polyethylene glycol 6000: Morusin is weighed according to the prescribed amount above, to which a proper amount of dehydrated ethanolis added.; After being dissolved by tepefaction, the resultant substances are added into prescribed amount of polyethylene glycol molten liquid (incubated in 60˚C water bath). The mixture is stirred to mix uniformly until ethanol is completely evaporated. The resultant is allowed to stay in 60˚C water bath to incubate for 30 min. After bubbles being are completely removed, the uniformly mixed molten liquid above in which bubbles are completely removed is

transferred into a storing tank. Under a condition that the temperature is maintained at 80-85˚C, the molten liquid is dropped dropwise into a condensing liquid under the controlling of the dropping speed. After the condensation being completed, the condensing liquid is decanted and the dropping pills are collected. Condensing liquid on the pills is trickled and removed with filter paper. Then, the pills are placed in a silica gel desiccator or dried naturally.

[0050] The above detailed description of the present invention sets forth a lot of specified details, the object thereof is to give clear and integrated explanation of the invention to facilitate the public to read and understand. However, what will be clear to one skilled in the art is that in some cases, the present invention may also be practiced without these specified details, or by making some non-essential modification or substitution to these specified details. These variations should be all considered to fall into the sprite and scope of the present invention. The scope of the invention should be determined by the plain text of the appended claims, rather than limited to the particular examples provided in the description.

CLAIMS:

1. A method for preparing a compound morusin, comprising:
extracting a plant with an organic solvent; and
isolating the extract by using column chromatography.

2. The method as claimed in claim 1, wherein the plant is Cortex Mori.

3. A pharmaceutical composition for treating or preventing oral diseases, comprising an amount of compound morusin effective for treating or preventing oral diseases and a pharmaceutically acceptable carrier.

4. An oral care product, comprising an amount of compound morusin effective for oral care and an oral care acceptable adjuvant.

5. A pharmaceutical composition for treating or preventing oral diseases or a product for oral care as claimed in claim 3 or 4, wherein the content of the compound morusin is 0.0005-20% (mass percentage).

6. A pharmaceutical composition for treating or preventing oral diseases or a product for oral care as claimed in claim 5, wherein the content of the compound morusin is 0.001-10% (mass percentage).

7. A pharmaceutical composition for treating or preventing oral diseases or a product for oral care as claimed in claim 5, wherein the content of the compound morusin is 0.025-5% (mass percentage).

8. A pharmaceutical composition for treating or preventing oral diseases or a product for oral care as claimed in claim 6, wherein the content of the compound morusin is 0.05-0.5% (mass percentage).

9. Use of a compound morusin in manufacturing medicaments for treating or preventing oral diseases.

10. Use of a compound morusin in manufacturing oral care products.