Folium Guavae

Definition
Folium Guavae consists of the dried and/or young leaves of *Psidium guajava* L. (Myrtaceae) (*1*).

Synonyms
Psidium aromaticum L. *P. cujavillus* Burm. f, *P. pomiferum* L., *P. pyriferum* L., *P. pumilum* Vahl (*2*).

Selected vernacular names
Abas, aduoba, aguoba, amba, amrood, amrud, amrut, amruta-phalam, araca-goiba, arasa, banjiro, banziro, bidji, bihi, bilauti, borimak, bugoyab, buyaki, dijamboé, coloc, djambu bidji, djambu klutuk, eguabe, fa-rang, goavy, goejaba, goiaba, goiabeira, goiabeira-vermelha, goiabeiro, gouyav, gouyavier, goyav, goyavier, goyya, grosse gelbe, gua, guafa, guajave, guava, guava tree, Guave, guayaba, guayaba cak, guayaba colorada, guayaba cotorrera, guayaba de gusano, guayaba de venado, guayaba del Peru, guayaba peruana, guayabe, guayabero, guayabo, guayabo agrio, guayabo blanco, guayava, Guayave, guega, guyaba, gwaabaa, gwawa, hind armudu, ipera, jaama, jamba, jambu biji, kautonga, Kiswahili, koyya, krue, ku'ava, kuabas, kuava, kuawa, kuiaba, kuliabas, mabera, maduriam, manssla, motiram, mpera, mugwavha, ngoaba, nulu, oguawa, pat'a, perala, pero delle Indie, peyara, posh, psidio, psidium, punjo, quwawa, sari guafa, sigra, sikra, tuava, warakel-guafa, wariafa, woba, xalxoctl (*1*, *3–10*).

Geographical distribution
Native to tropical America, but now pantropical (*7*, *8*, *11*).

Description
A large shrub or small tree up to 10 m high. Stem slender, usually not exceeding 30 cm in width; bark brownish, thin, smooth, and often flaking off in scaly patches. Leaves opposite, oblong, slightly oval shaped, 5–15 cm in length, light green on the upper surface, and downy and pale green on

the underside. They display prominent veins on the underside of the leaf. Flowers white, occur either singly or a few in a cluster in axils of the leaves. About 2.5 cm in diameter, with numerous stamens arranged in groups. Fruits are globose or pyriform, yellow, usually 2.5–10 cm long and 2.5–5 cm in diameter, horticulture varieties with larger fruits with an edible pink mesocarp are common. They contain many seeds, and the calyx persists in fruit (*7*, *8*).

Plant material of interest: dried or young leaves

General appearance

Oblong, slightly oval, apex acute, round or acuminate; base symmetrical, cordate; margin smooth or dentate; venation reticulate; green (*1*).

Organoleptic properties

Odour: slight; taste: astringent (*1*).

Microscopic characteristics

The surface view shows nearly straight anticlinal epidermal cell walls on both surfaces, those on upper surface thickened; abundant stomata and covering trichomes on lower surface; oil glands on both surfaces, but more frequent on lower surface. Transverse section shows small epidermal cells with straight anticlinal walls, upper epidermal layer 2–3 cells thick with a few oil glands (schizogeneous); palisade tissue multi-layered; numerous oil glands in the mesophyll region; midrib region shows collenchymatous cells; bicollateral vascular bundle is distinctly horse-shoe shaped and surrounded by lignified pericyclic fibres; xylem elements are generally lignified; uniseriate trichomes smooth-walled and abundant on lower epidermis (*1*).

Powdered plant material

Light green; taste astringent; lamina fragments show abundant stomata, punctate, numerous covering trichomes; rosette crystals; lignified vascular elements (*1*).

General identity tests

Macroscopic and microscopic examinations (*1*).

Purity tests

Microbiological

Tests for specific microorganisms and microbial contamination limits are as described in the WHO guidelines on assessing quality of herbal medicines with reference to contaminants and residues (*12*).

Foreign organic matter
To be established in accordance with national requirements.

Total ash
To be established in accordance with national requirements.

Acid-insoluble ash
To be established in accordance with national requirements.

Water-soluble extractive
To be established in accordance with national requirements.

Loss on drying
To be established in accordance with national requirements.

Pesticide residues
The recommended maximum limit of aldrin and dieldrin is not more than 0.05 mg/kg (*13*). For other pesticides, see the *European pharmacopoeia* (*13*) and the WHO guidelines on assessing quality of herbal medicines with reference to contaminants and residues (*12*) and pesticide residues (*14*).

Heavy metals
For maximum limits and analysis of heavy metals, consult the WHO guidelines on assessing quality of herbal medicines with reference to contaminants and residues (*12*).

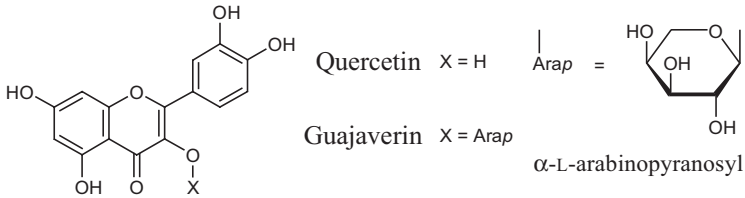
Radioactive residues
Where applicable, consult the WHO guidelines on assessing quality of herbal medicines with reference to contaminants and residues (*12*).

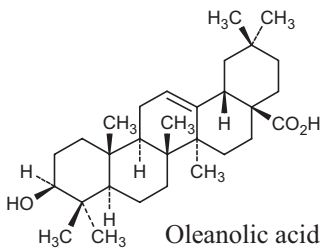
Chemical assays
Not less than 14% (w/w) tannins and not less than 0.6% (v/w) essential oil (*1*).

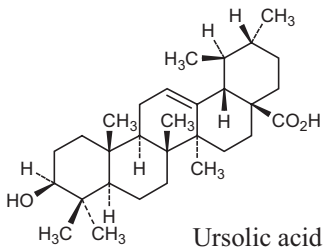
Major chemical constituents
Contains hydrolysable tannins, essential oils, flavonoids, and terpenes (*1*, *6*, *15*). New leaves contain the flavonols quercetin, guajaverin (= quercetin-3-*O*-arabinoside) and other quercetin glycosides; gallocatechin and the tannins ellagic acid and guavins A, C and D. Several triterpene acids are present, including ursolic and oleanolic acids and their 20-hydroxy-derivatives, crataegoic and guaijavolic acids. The leaf oil contains several mono- and sesquiterpenes, among which 1,8-cineol and α-pinene are the

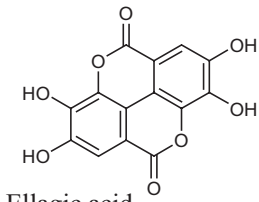
principal monoterpenes, and caryophyllene and γ-bisbolene are representative of the sesquiterpenes (*16–24*).

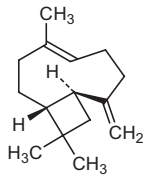
Structures of quercetin, guajaverin (= quercetin-3-*O*-arabinoside), ursolic oleanolic acids, ellagic acid, α-pinene and caryophyllene are presented below.

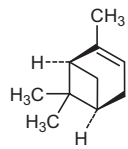



Oleanolic acid


Ursolic acid


Ellagic acid


Caryophyllene



α-Pinene

Medicinal uses

Uses supported by clinical data

Oral treatment of acute diarrhoea, gingivitis and rotaviral enteritis (*25–28*).

Uses described in pharmacopoeias and well established documents

No information was found.

Uses described in traditional medicine

Treatment of abdominal pain, bleeding gums, cough, gastritis, headache, ringworm, vaginitis, wounds and worms. Also used as an astringent, an antiemetic and an emmenagogue (*4*, *15*).

Pharmacology

Experimental pharmacology

Analgesic activity

Intragastric administration of 100.0, 200.0 or 400.0 mg/kg body weight (bw) of the essential oil of the leaves produced an antinociceptive effect in mice as assessed in the formalin test (*29*). A dose of 200.0 mg/kg bw of the essential oil to mice reduced pain as measured in the acetic acid-induced writhing test. One of the major constituents, α-pinene, also showed an antinociceptive effect in the formalin test, and when administered intragastrically at doses of 100 mg/kg and 200 mg/kg, a reduction of paw licking of 72% and 76%, respectively was observed. At a dose of 400.0 mg/kg bw, paw licking was reduced by 37% in the first (acute) phase and 81% in the second (chronic) phase (*29*).

Antidiarrhoeal activity

A decoction of the leaves inhibited Microlax-induced diarrhoea when administered by gastric lavage to rats at a dose of 10.0 ml/kg bw (*30*). Intragastric administration of a methanol extract of the leaves to mice at a dose of 200.0 mg/kg bw prevented castor oil-induced diarrhoea (*31*). Intragastric administration of an aqueous or methanol extract of the leaves to rats at a dose of 400.0 mg/kg bw prevented castor oil-induced diarrhoea, reduced gastric motility and prostaglandin E2-induced enteropooling (*32*). A dried 70% methanol extract of the leaves inhibited the electrically-induced peristaltic reflex of isolated guinea-pig ileum at a concentration of 100 µg/ml (*22*). The main active constituent of the extract was quercetin 1.4×10^{-5} (72.1%), with isoquercetin and hyperin being weakly active (*22*).

Antihyperglycaemic activity

Intragastric administration of a 50% ethanol extract of the leaves to rats, at a dose of 200.0 mg/kg bw, prevented alloxan-induced hyperglycaemia. A butanol fraction of the 50% ethanol extract reduced alloxan-induced hyperglycaemia in rats when administered at a dose of 25.0 mg/kg bw by gastric lavage (*33*). Intragastric administration of a 50% ethanol extract to rats at a dose of 200.0 mg/kg bw did not stimulate insulin biosynthesis (*33*).

Antiinflammatory and antipyretic activity

Intragastric administration of 0.8 ml/kg bw of the leaf essential oil to rats reduced inflammation in the carrageenan-induced oedema of the hind paw test and the cotton pellet granuloma test (*34*). Intragastric administration of a dried methanol extract of the leaves to mice at a dose of 200.0 mg/kg bw reduced carrageenan-induced pedal oedema (*31*). Intra-

gastric administration of a dried methanol extract of the leaves to mice at a dose of 200.0 mg/kg bw reduced yeast-induced pyrexia (*31*).

Antimalarial activity

The following extracts of the crude drug had activity against *Plasmodium falciparum* in vitro with a median inhibitory concentration as follows: ethyl acetate,10.0 µg/ml; 95% ethanol, 36.0 µg/ml; aqueous, 80.0 µg/ml; and petroleum ether, 13.0 µg/ml (*35*, *36*).

Antimicrobial activity

A decoction of the crude drug inhibited the growth of *Carnobacterium gallirarum*, *Escherichia coli*, *Salmonella enteritidis* and *Staphylococcus aureus* with a median inhibitory concentration of 31.25 µg/ml and *Klebsiella pneumoniae*, *Pseudomonas aeruginosa,* and *Shigella flexneri* at a concentration of 62.5 µg/ml (*37*). A tannin fraction separated from an extract of the crude drug had antibacterial activity against *Escherichia coli*, *Citrobacter diversus*, *Klebsiella pneumoniae, Shigella flexneri*, *Salmonella enteritidis* and *Staphylococcus aureus* at concentrations of 60.0–95.0 µg/ml in vitro (*38*). An aqueous extract of the leaves had anti-adhesion activity in *Streptomyces mitis* (70%); these bacteria are involved in the development of dental plaque (*39*).

Antioxidant activity

The antioxidant activity of an aqueous and a 50% ethanol extract of the leaves was assessed using 1,1-diphenyl-2-picrylhydrazyl radical colorimetry. Compared to ascorbic acid, the extracts of the crude drug had a significantly lower antioxidant effect (*40*).

Antispasmodic activity

A dried methanol extract of the leaves reduced spontaneous contractions of isolated rat and guinea-pig ileum when added to the bath media at concentrations of 20.0 ml/l and 80.0 µg/ml, respectively (*30*, *37*, *41*). An aqueous, methanol, or hexane extract of the leaves had smooth muscle relaxant activity in guinea-pig ileum in vitro, at a concentration of 250.0–1000.0 µg/ml (*41*, *42*). A butanol extract of the leaves at a concentration of 0.2 mg/ml reduced acetylcholine-induced contractions in guinea-pig ileum by 95–100% (*43*).

Antitussive activity

Intragastric administration of an aqueous extract of the leaves to rats and guinea-pigs at a dose of 5.0 g/kg bw reduced capsaicin-induced coughing (*44*).

Effects on the central nervous system

Intragastric administration of a dried methanol extract of the leaves to mice at a dose of 200 mg/kg bw reduced acetic acid-induced writhing, thereby demonstrating analgesic activity (*31*). Intragastric administration of a dried methanol extract of the leaves to mice at a dose of 200 mg/kg bw also potentiated phenobarbitone-induced sleeping time (*31*). Intraperitoneal administration of a dried hexane extract of the leaves to mice at a dose of 100 mg/kg bw potentiated sodium pentobarbital-induced hypnosis and increased the latency of leptazol-induced convulsions (*42*). Intragastric or intraperitoneal administration of a dried methanol extract of the leaves at a dose of 3.3 mg/kg bw reduced spontaneous motor activity in mice (*45*). Intragastric administration of dried hexane, ethyl acetate or methanol extracts of the crude drug, at doses of 100.0–1250.0 mg/kg bw produced dose-dependent antinociceptive effects in mice, and prolonged pentobarbitone-induced sleep (*46*).

Haemostatic effects

The effects of an aqueous leaf extract on the bleeding time and the three main mechanisms of haemostasis: vasoconstriction, platelet aggregation and blood coagulation, were investigated. Topical application of the aqueous extract at a concentration of 0.05 µg/ml did not reduce bleeding times in wounded rats. However, the extract (2–6 µg/ml) potentiated the vascular muscle contraction induced by phenylephrine (4.0 µg/ml) in isolated aortic strips from rabbits. The extract also significantly prolonged blood coagulation time in normal plasma treated with 6.0 mg/ml extract in the activated partial thromboplastin time test ($p < 0.05$) (*47*).

Inotropic effects

In guinea-pig atria, an ethanol extract of the leaves reduced atrial contractions by depressing the myocardial force in a concentration-dependent manner (median effective concentration (EC_{50}) = 1.4 g/l). Concentrations higher than 2.5 g/l completely abolished the myocardial contractility. Furthermore, an acetic acid fraction (EC_{50} = 0.07 g/l) of the extract increased the relaxation time measured at 20 and 50% of the force curve by 30 and 15%, respectively, but did not change the contraction time. The negative inotropic effect of the extract was abolished by atropine sulfate, suggesting that either the active substance acts as a cholinergic agonist or that it could release acetylcholine from parasympathetic synapses (*48*).

Toxicity

Intragastric administration of an aqueous extract of the leaves to rats exhibited a median lethal dose of 50.0 g/kg bw (*47*). In chronic toxicity tests,

an aqueous extract of the leaves was administered by gavage to 128 rats of both sexes at doses of 0.2, 2.0 and 20.0 g/day (1, 10 and 100 times the normal therapeutic dose for the treatment of diarrhoea) for 6 months.

The results showed that the body weight gains in male rats were lower in all treated animals. Significant increases in white blood cell count, alkaline phosphatase, serum glutamate pyruvate transaminase and serum blood urea nitrogen levels were observed ($p < 0.05$). Serum sodium and cholesterol levels were significantly reduced ($p < 0.05$) indicating signs of hepatotoxicity. In female rats, serum sodium, potassium and albumin levels increased significantly ($p < 0.05$), while levels of platelets and serum globulin were significantly decreased ($p < 0.05$). Histopathological assessment showed a mild degree of fatty change and hydronephrosis in male rats and nephrocalcinosis and pyelonephritis in female rats (*49*).

Clinical pharmacology

Seventy subjects with gingivitis were enrolled in a 3-week placebo-controlled, double-blind clinical trial to assess the efficacy of a mouthwash containing a decoction of the dried leaves (3 kg in 30 l water boiled for 20 minutes). The placebo mouthwash contained the same ingredients with the exception of the decoction of the leaves. The subjects were stratified into two balanced groups according to their baseline pre-prophylaxis gingivitis scores calculated using the Loe-Silness Gingival Scoring Index. The subjects rinsed their mouth three times daily for 1 minute with 15 ml of their assigned mouthwash. Patients who used the mouthwash containing the leaf extract had less inflammation of the gingiva (19.8%) and fewer sites of severe gingival disease (40.5%) than those using the placebo mouthwash (*26*).

A randomized, controlled clinical trial assessed the efficacy of a decoction of the crude drug for the treatment of infantile rotaviral enteritis. Sixty-two patients with rotaviral enteritis were randomly assigned either to the group treated with the decoction or to the control group. The time until cessation of diarrhoea, the content of sodium in blood, the content of sodium and glucose in stools, and the rate of negative conversion of human rotavirus antigen were recorded. After 3 days, 87% of the subjects in the treated group had recovered, significantly more than the number in the control group (58.1%, $p < 0.05$). The time elapsed until cessation of diarrhoea in the treated group (25.1 ± 9.5 h) was significantly shorter than that for the control group (38.7 ± 15.2 h, $p < 0.01$). The content of sodium and glucose in stools was reduced in the treated group ($p < 0.05$), while the reduction in the control group was insignificant. The rate of negative conversion of human rotavirus in the faeces of the treated group was 87.1%, significantly better than that of the control group (58.1%, $p < 0.05$) (*28*).

An aqueous extract of the crude drug was tested in a clinical study involving small groups of patients aged 5 years and younger or 20–40 years. Patients with acute diarrhoea received the extract, while a comparison group received a kaolin or pectin suspension. The results were similar in all three groups with an efficacy of treatment above 70% (*25*).

A randomized, double-blind, clinical study was performed to evaluate the safety and efficacy of an extract of the crude drug with a standardized content of quercetin. The extract was administered orally to a group of adult patients with acute diarrhoeic disease. Adult patients of both sexes between 20 and 59 years of age suffering from non-complicated acute diarrhoea were included. Acute diarrhoeic disease was defined as a clinical condition characterized by the passing of at least three liquid stools during the previous 24 h and abdominal pain or cramps. Pregnant women and patients with systemic diseases concomitant to acute diarrhoeic disease (such as immunodeficiency and intestinal syndrome), were excluded. The capsules containing 500 mg of the extract were administered every 8 h for 3 days to the treatment group (n = 50), while the control group (n = 50) received capsules of the same size, taste and colour, containing 500 mg of placebo every 8 h for 3 days. Oral rehydration therapy was administered to all patients according to conventional procedures followed in the medical institution for treatment of acute diarrhoeic disease. The results showed that the guava product decreased the duration of abdominal pain in these patients (*27*).

A randomized, double-blind, clinical trial involving 122 patients (64 men and 58 women) was conducted to compare the efficacy of the powdered crude drug with that of tetracycline for the treatment of acute diarrhoea (*50*). The patients were treated with 500 mg of the powdered crude drug (2 capsules of 250 mg each) or matching tetracycline capsules (2 capsules of 250 mg each) every 6 hours for 3 days. The results of the study demonstrated that the powdered drug decreased the stool output, fluid intake and the duration of diarrhoea. The differences between the results from the group treated with tetracycline and the group that received the powdered crude drug were not statistically significant (*50*).

Adverse reactions

One report of allergic dermatitis has been recorded after external application of a tea prepared from the crude drug (*51*).

Contraindications

Hypersensitivity or allergy to the plant material.

Warnings
Do not exceed the recommended dose or duration of treatment (*49*).

Precautions
Carcinogenesis, mutagenesis, impairment of fertility
No information was found.

Pregnancy: teratogenic effects
No information was found.

Pregnancy: non-teratogenic effects
Due to the lack of safety data, the use of the crude drug during pregnancy is not recommended.

Nursing mothers
Due to the lack of safety data, the use of the crude drug during breastfeeding is not recommended.

Paediatric use
Due to the lack of safety data, the use of the crude drug in children aged under 12 years is not recommended.

Other precautions
No information was found.

Dosage forms
Crude drug, decoctions, extracts and teas.

Posology
(Unless otherwise indicated)
As a mouthwash: 15 ml of aqueous extract three times daily for at least 1 minute per session (*26*).

For diarrhoea: 500 mg of the powdered leaf three or four times daily (*50*).

References
1. *Ghana herbal pharmacopoeia*. Accra, Policy Research and Strategic Planning Institute, 1992.
2. National Genetic Resources Program. *Germplasm Resources Information Network (GRIN)* [Online Database]. National Germplasm Resources Laboratory, Beltsville, MD (available at: http://www.ars-grin.gov/cgi-bin/npgs/html/tax_search.pl?psidium+guajava).

3. Ross IA. *Medicinal plants of the world*. Totowa, NJ, Humana Press, 1999.
4. Farnsworth NR, ed. *NAPRALERT database.* Chicago, University of Illinois at Chicago, IL (an online database available directly through the University of Illinois at Chicago or through the Scientific and Technical Network [STN] of Chemical Abstracts Services), 30 June 2005.
5. Nadkarni KM, Nadkarni AK, eds. *Indian materia medica*, reprint of 3rd revised and enlarged ed. Bombay, Popular Prakashan, 1976.
6. *Medicinal plants of India. Vol. 2.* New Delhi, Indian Council of Medical Research, 1987.
7. *Medicinal plants in the South Pacific.* Manila, World Health Organization Regional Office for the Western Pacific, 1998 (WHO Regional Publications, Western Pacific Series, No. 19).
8. Iwu MM. *Handbook of African medicinal plants*. Boca Raton, FL, CRC Press, 1993.
9. Matos FJA. *Plantas medicinais Brasileiras*, 2nd ed. Lima, Universidade Federal do Ceará Edições, 2004.
10. Mejía K, Rengifo E. *Plantas Medicinales de Uso Popular en la Amazonia Peruana.* Lima, Agencia Española de Cooperación Internacional, 2000 [in Spanish].
11. Perry LM, Metzger J. *Medicinal plants of east and southeast Asia: attributed properties and uses*. Cambridge, MA, MIT Press, 1980.
12. *WHO guidelines on assessing quality of herbal medicines with reference to contaminants and residues.* Geneva, World Health Organization, 2007.
13. *European pharmacopoeia*, 5th ed. Strasbourg, Directorate for the Quality of Medicines of the Council of Europe (EDQM), 2005.
14. *Guidelines for predicting dietary intake of pesticide residues*, 2nd rev. ed. Geneva, World Health Organization, 1997 (WHO/FSF/FOS/97.7).
15. Farnsworth NR, Bunyapraphatsara N, eds. *Psidium guajava. Thai medicinal plants: recommended for primary health care system*. Bangkok, Mahidol University, 1992:202–207.
16. Okuda T et al. Guavin B, an ellagitannin of novel type. *Chemical and Pharmaceutical Bulletin*, 1984, 32:3787–3788.
17. Okuda T et al. Guavin A, C and D, complex tannins from *Psidium guajava*. *Chemical and Pharmaceutical Bulletin*, 1987, 35:443–446.
18. Soliman G, Farid MK. Constituents of the leaves of *Psidium guajava* L. Part I. Psidiolic acid. *Journal of the Chemical Society*, 1952, 1952:134–136.
19. Osman AM, Younes ME, Sheta AE. Triterpenoids of the leaves of *Psidium guajava. Phytochemistry*, 1974, 13:2015–2016.
20. Arthur HR, Hui WH. Triterpene acids from the leaves of *Psidium guajava* L. *Journal of the Chemical Society*, 1954, 1954:1403–1406.
21. Begum S et al. Triterpenoids from the leaves of *Psidium guajava. Phytochemistry*, 2002, 61:399–403.
22. Lozoya X et al. Quercetine glycosides in *Psidium guajava* L. leaves and determination of a spasmolytic principle. *Archives of Medical Research*, 1994, 25:11–15.

23. Matsuo T et al. Identification of (+)-gallocatechin as a bio-antimutagenic compound in *Psidium guajava* leaves. *Phytochemistry*, 1994, 36:1027–1029.
24. Xiao DJ et al. The essential oil of the leaves of *Psidium guajava* L. *Journal of Essential Oil Research*, 1991, 3:187–189.
25. Caceres A. *Plantas de uso medicinal en Guatemala*. Guatemala City, Editorial Universitaria, Universidad San Carlos de Guatemala, 1996:194–197.
26. Kraivaphan V et al. The effect of a mouthrinse containing *Psidium guajava* leaves extract on gingivitis. *Journal of the Dental Association of Thailand*, 1991, 41:323–328.
27. Lozoya X et al. Intestinal anti-spasmodic effect of a phytodrug of *Psidium guajava folia* in the treatment of acute diarrheic disease. *Journal of Ethnopharmacology*, 2002, 83:19–24.
28. Wei L et al. Clinical study on treatment of infantile rotaviral enteritis with *Psidium guajava* L. *Zhongguo Zhong Xi Yi Jie He Za Zhi*, 2000, 20:893–895 [in Chinese].
29. Santos FA et al. Investigation on the antinociceptive effect of *Psidium guajava* leaf essential oil and its major constituents. *Phytotherapy Research*, 1998, 12:24–27.
30. Lutterodt GD. Inhibition of Microlax-induced experimental diarrhoea with narcotic-like extracts of *Psidium guajava* leaf in rats. *Journal of Ethnopharmacology*, 1992, 37:151–157.
31. Olajide OA, Awe SO, Makinde JM. Pharmacological studies on the leaf of *Psidium guajava. Fitoterapia*, 1999, 70:25–31.
32. Lin J, Puckree T, Mvelase TP. Anti-diarrhoeal evaluation of some medicinal plants used by Zulu traditional healers. *Journal of Ethnopharmacology*, 2002, 79:53–56.
33. Maruyama Y et al. Study on *Psidium guajava* L. (I). Anti-diabetic effect and effective components of the leaf of *Psidium guajava* L. *Shoyakugaku Zasshi*, 1985, 39:261–269 [in Japanese].
34. Kavimani S et al. Anti-inflammatory activity of volatile oil of *Psidium guajava. Indian Journal of Pharmaceutical Sciences*, 1997, 59:142–144.
35. Gessler MC et al. Screening Tanzanian medicinal plants for antimalarial activity. *Acta Tropica*, 1994, 56:65–77.
36. Weenen H et al. Antimalarial activity of Tanzanian medicinal plants. *Planta Medica*, 1990, 56:368–370.
37. Tona L et al. Biological screening of traditional preparations from some medicinal plants used as antidiarrhoeal in Kinshasa, Congo. *Phytomedicine*, 1999, 6:59–66.
38. Lutete T et al. Antimicrobial activity of tannins. *Fitoterapia*, 1994, 65:276–278.
39. Razak FA, Rahim ZH. The anti-adherence effect of *Piper betle* and *Psidium guajava* extracts on the adhesion of early settlers in dental plaque to saliva-coated glass surfaces. *Journal of Oral Science*, 2003, 45:201–206.
40. Qian H, Nihorimbere V. Antioxidant power of phytochemicals from *Psidium guajava* leaf. *Journal of Zhejiang University Science*, 2004, 5:676–683.

41. Lozoya X, Becerril G, Martinez M. Modelo de perfusión intraluminal del ileon del cobayo *in vitro* en el estudio de las propiedades antidiarréicas de la guayaba (*Psidium guajava*) [Intraluminal perfusion model of *in vitro* guinea pig's ileum as a model of study of the antidiarrheal properties of the guava (*Psidium guajava*)]. *Archivos de Investigacion Médica (México)*, 1990, 21:155–162 [in Spanish].
42. Meckes M et al. Terpenoids isolated from *Psidium guajava* hexane extract with depressant activity on central nervous system. *Phytotherapy Research*, 1996, 10:600–603.
43. Kambu K et al. Activité antispasmodique d'extraits à partir de plantes utilisées en préparations comme antidiarrhéiques à Kinshasa, Zaïre [Antispasmodic activity of extracts used in traditional plant antidiarrheic preparations in Kinshasa, Zaire]. *Annales Pharmaceutiques Françaises*, 1990, 48:200–208 [in French].
44. Jaiarj P et al. Anticough and antimicrobial activities of *Psidium guajava* Linn. leaf extract. *Journal of Ethnopharmacology*, 1999, 67:203–212.
45. Lutterodt GD, Maleque A. Effects on mice locomotor activity of a narcotic-like principle from *Psidium guajava* leaves. *Journal of Ethnopharmacology*, 1988, 24:219–231.
46. Shaheen HM et al. Effect of *Psidium guajava* leaves on some aspects of the central nervous system in mice. *Phytotherapy Research*, 2000, 14:107–111.
47. Jaiarj P et al. Guava leaf extract and topical haemostasis. *Phytotherapy Research*, 2000, 14:388–391.
48. Conde Garcia EA, Nascimento VT, Santiago Santos AB. Inotropic effects of extracts of *Psidium guajava* L. (guava) leaves on the guinea pig atrium. *Brazilian Journal of Medical and Biological Research*, 2003, 36:661–668.
49. Attawish A et al. Toxicity study of *Psidium guajava* Linn. leaves. *Bulletin of the Department of Medical Sciences*, 1995, 37:289–305.
50. Thanangkul B, Chaichantipayut C. Double-blind study of *Psidium guava* L. and tetracycline in acute diarrhea. *Siriraj Hospital Gazette*, 1987, 39:263–267.
51. Obi M et al. Allergic contact dermatitis due to guava tea. *Contact Dermatitis*, 2001, 44:116–117.