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The Potential Treatment of Guava Leaf (*Psidium guajava* Linn.) For Diarrhea in Children

Extin Faulinza[1*]

[1] Department of Pediatric, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

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***Corresponding author:**
Extin Faulinza

E-mail address:
extin1989@gmail.com

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A B S T R A C T

Diarrhea is one of the common health problems which is causes death in children, especially in developed countries. Not everybody can access the diarrhea treatment suggested by WHO. Some people decided to utilize alternative treatment, such as medicinal plants in their environment. It is cheaper and easier to get. One of herb plant that uses is guava leaf (*Psidium guajava* Linn.). It contains some active ingredients such as quercetin, tannins, flavonoids, and phenols which have the potential for antidiarrheal activity. To date no death or unusual behavior reported. Guava leaf (*Psidium guajava* Linn.) extract can be provided as potential antidiarrheal in children.

1. Introduction

Diarrhea is a condition that watery stools and loose three or more times daily. It is a common problem in almost every part of the world.[1] Based on United Nations International Children's Emergency Fund 2015 data, diarrhea and pneumonia are causes of death in children.[2,3] In Indonesia, based on the statistics of Primary Health Research 2018, the incidence of diarrhea based on diagnosis by health workers is about 6,8 % and the highest incidence of diarrhea based on age group occurs in 1-4 years old (11,5%).[4]

Rotavirus and *Escherichia coli* are the two most common causes of diarrhea in developed countries.[5] According to the World Health Organization 2013, therapy for diarrhea in children is rehydration by (*Andrographis paniculata*) considered can be used to give more fluid, zinc supplementation, and continue breastfeeding.[2] Some studies about using alternative treatments were revealed in Indonesia.[6,7] Supa et al., presented a high prevalence of traditional medicine use in Indonesian children.[8] In Tegal regency some parents use initial diarrhea treatment for their children such as turmeric, guava leaves, and tea.[3] It is similar to ethnic groups in South Sulawesi, which used medicinal plants to treat diarrhea in children.[9]

Some plants can be used to treat diarrhea in children such as Zingiber officinale, and *Psidium guajava* Linn. Cyperus rotundus and Aegle marmelos.[9] In Indonesian Traditional Medicine Compound Formulary 2017, Psidium guajava Linn.,

Sambiloto (*Andrographis paniculata*) considered can be used to treat diarrhea. Psidium guajava Linn. especially its leaf has more effectiveness than other anti-diarrhea plants.[10,13] It is related to some compounds of guava leaf. It may assist in developing cost-effective approaches for the treatment of diarrhea.[11]

Definition and etiology of diarrhea

Diarrhea is a condition that watery stools and loose three or more times daily. It is one of the infection symptoms caused by viruses, bacteria, and other parasite microorganisms. Infections of diarrhea are classified into three groups secretory, exudative-secretory, and osmotic-secretory.[1] Pathogenic rotavirus, Shigella spp, Escherichia coli, and Vibrio cholera, are suspected to be the most common causative agent of diarrhea in humans.[1,4,7,12]

Characteristic of psidium guajava Linn.

There is some term for *Psidium guajava* Linn. (Family myrtaceae) that is commonly used in this part of the world. It called guave, goyave or goyavier In French; guave, Guavenbaum, Guayave in German; goiaba, goiabeiro in Portugal; banjiro in Japanese; guavenbaum, guayaba in Spanish; goiaba in Portuguese and guava in English. In Indonesia there is some terms are used such as "kulutuk; bayawas; tetokal; tokal" in Java and "bender" in Madura.[13]

Parts of Psidium guajava Linn. which potentially as anti-diarrhea is its leaf.[3,10,11,12.] It contains flavonoids, saponins, tannins, and alkaloids.[14,15] In addition, the effects of the leaf have been related to individual compounds such as catechin, quercetin, gallic acid, vescalagin, pentaoxide, guaijaverin isoquercitrin, and hyperoside.[16]

Biological activity of P*sidium guajava* Linn. Leaf as antidiarrhea.

Some studies presented that *Psidium guajava* Linn. is used in many parts of the world for the treatment of some diseases such as antihypertension, antidiabetic, anti-diarrhea, antibiotic, anti-inflammatory, and also cure of wounds. It is related to the compounds of *Psidium Guajava* Linn. leaf. Rosa Martha et al summarized the advantages of Psidium guajava Linn. based on using of part guajava leaf and the countries (Table. 1).[17]

Table. 1. Ethnomedical uses *Psidium guajava* Linn.

Place, country	Part(s) used	Ethanol medical uses
Colombia, Mexico	Leaves	Gastroenteritis, diarrhea, dysentery, rheumatic pain, wounds, ulcers, and toothache
Indigenous Maya, Nahuatl, Zapotec and Popoluca of the region Tuxtlas, Veracruz, Mexico	Leaves	Cough, diarrhea
Latin America, Mozambique	Leaves	Diarrhea, stomach ache
Mexico	Shoots, leaves, bark, and leaves mixed, ripe fruits	Febrifuge, expel the placenta after childbirth, cold, cough hypoglycaemic, affections of the skin, caries, vagina l hemorrhage, wounds, fever, dehydration, respiratory disturbances
Panama, Cuba, Costa Rica, Mexico, ´ Nicaragua, Panama,´ Peru, Venezuela, ´ Mozambique, Guatemala, Argentina	Leaves	Anti-inflammatory
South Africa	Leaves	Diabetes mellitus, hypertensio
Caribbean	Leaves	Diabetes mellitus
China	Leaves	Diarrhea, antiseptic, Diabetes mellitus
Philippines	Leaf, bark, unripe fruit, roots	Astringent, ulcers, wounds, diarrhea
India	Leaves,	Febrifuge, antispasmodic, rheumatism
Ghana	shoots	Convulsions, astringent

Place, country	Part(s) used	Ethanol medical uses
Peru	Flower buds, leaves	Heart and constipation, conjunctivitis, cough, diarrhea, digestive problems, dysentery, edema, gout, hemorrhages, gastroenteritis, gastritis, lung problems, shock, vaginal discharge, vertigo, vomiting, worms
Kinshasa, Congo	Leaves, bark	Diarrhea, antiamoebic
Senegal	Shoots, roots	Diarrhea, dysentery
Uruguay	Leaves	Vaginal and uterine wash, especially in leucorrhoea
Fiji	Leaves, roots, ripe fruit	Diarrhea, coughs, stomach-ache, dysentery, toothaches, indigestion, constipation
Tahiti, Samoa	The whole plant, shoots	Skin tonic, painful menstruation, miscarriages, uterine bleeding, premature labor in women, wounds
New Guinea, Samoa, Tonga, Niue, Futuna, Tahit	Leaves	Itchy rashes caused by scabies
Cook Islands	Leaves	Sores, boils, cuts, sprains
Trinidad	Leaves	Bacterial infections, blood cleansing, diarrhea, dysentery
Latin America, Central, and West Africa, and Southeast Asia	Leaves	Gargle for sore throats, laryngitis, and swelling of the mouth, and it is used externally for skin ulcers, vagina l irritation and discharge
Panama, Bolivia, and Venezuela	Bark and leaves	Dysentery, astringent, used as a bath to treat skin ailments
Brazil	Ripe fruit, flowers, and leaves	Anorexia, cholera, diarrhea, digestive problems, dysentery, gastric insufficiency, inflamed mucous membranes, laryngitis, mouth (swelling), skin problems, sore throat, ulcers, vaginal discharge
USA	Leaf	Antibiotic and diarrhea

Most of the research reported the relation of Psidium guajava Linn. leaf compounds as antidiarrheal activity. A study by Jayshri R. Hirudkar, et, al. demonstrated significant antidiarrheal activity of quercetin (50 mg/kg), Psidium guajava Linn. alcoholic leaf extract at 200 and 400 mg/kg, p.o. to reduce the total number of diarrheal stools, the weight of stools and mean defecation rate of stools taken after 6th and 24th h of treatment. It is attributed to inhibition in intestinal secretion, reduced nitric oxide production, and inflammatory expression along with reactivation of Na+/K–ATPase.[12]

Quercetinalso showed significant anti-diarrheal activity on the contraction of guinea pig ileum in vitro and the peristaltic motion of mouse small intestine, and also reduced the permeability of abdominal capillaries. It is related to the inhibition of acetylcholine as a spasmogenic neurotransmitter.[17] Tannaz Birdi,et al presented a study with an animal model about antibacterial activity and its effect on virulence features of common diarrhea pathogens colonization of epithelial cells and action of enterotoxins. Colonization as measured by adherence of enteropathogenic Escherichia coli (EPEC) and invasion of enteroinvasive E. coli (EIEC) and Shigella flexneri was assessed using the HEp-2 cell line. The result is Psidium guajava Linn. showed antibacterial activity towards S. flexneri and Vibrio cholerae.10 in the other research by Jayshri R. et al, Psidium guajava Linn. leaf extract and its biomarker quercetin also recovering massive epithelial damage which caused by Shigella after 5th day of treatment.18 Tannins can inhibit the growth of bacteria E. coli, and Psudomonas aeruginous, S. aureus. It can form hydrogen bonds with the protein contained in bacterial cells, if the hydrogen bonds formed between tannins with proteins will be denatured proteins possible that bacterial metabolism becomes impaired.[14] Dingfa, et. al concluded that besides tannins and quercetin there are some active ingredients such as flavonoids, phenolics, and their derivatives have biological activity as antidiarrheal. In their study piglets challenged by ETEC has a higher diarrhea incidence than the piglets without ETEC challenge in the blank control group. The supplementation of 50 mg kg -1 quinocetone, or 50-200 mg kg-1 of guava leaf extract in diets reduced diarrhea incidence of piglets compared with the negative control group. The guava leaf extract is might

mainly attribute to its.[19]

Khaled, et.al also showed that in male albino diarrheal rats, kidney oxidative stress was observed. Treatment with Psidium guajava Linn. leaf extract inhibited oxidative status-associated kidney damage. This specific role of Psidium guajava Linn. leaf extract may be due to antioxidants present in the leaves. Similarly, Psidium guajava Linn. leaves have shown antioxidant effects which counteract the damaging effect of free radicals in different body organs.[20]

Toxicology of *Psidium guajava* Linn. Leaf

No mortality was observed throughout the trial which uses the supplementation of 50-200 mg kg-1 of guava leaf extract in diets reduced diarrhea incidence of piglets compared with the negative control group.[19] Maria Flaviana, et al. concluded the toxicity of Psidium guajava Linn. leaf assays indicate the safety for usage.[21] Shekins and Dorathy showed no sign of toxicity and mortality were observed after the analysis of the acute toxicity of the aqueous extract of Psidium guajava Linn. in rats using different concentrations of 50, 100, and 800 mg/kg body weight.[22] The work of Etuk and Francis demonstrated toxicity in male and female rats (200 a 250 g) with aqueous extracts from *Psidium guajava* Linn. leaves of 5 g/ 500 mL in concentrations ranging between 10 and 50 mg/100 g. No death or unusual behavior was reported after 72 hs observation.[23]

2. Conclusion

The leaf of Psidium guajava Linn. is commonly used as an antidiarrheal in children. Some studies demonstrated the usefulness of Psidium guajava L. leaf in different forms of infectious diarrhea. The mechanisms of antidiarrheal activity of Psidium guajava L. leaves such as antimicrobial activity, antispasmodic activity, and reduction in the total number of diarrheal stools. Most importantly, no serious adverse effects were reported or documented. Psidium guajava Linn. leaf study can provide newer insights into the varied possible antidiarrheal mechanisms which can use globally. Further study must be continued inhuman. It is a very important part of our biodiversity to respect and sustainably use for the next generations.

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