Original Research Article

A REVIEW OF ANTI – DIARRHEAL ACTIVITY OF *AEGLE MARMELOS*

Abstract

The aim of this study was review the anti – diarrheal activity of *Aegle marmelos* . Siddha literatures were obtained from the library of Unit of Siddha Medicine, University of Jaffna. Data was collected from books and internet and tabulated for the analysis. Beal Fruit Tree (*Aegle marmelos*) (Tamil name *Vilvam, Kuvilam*, Sinhala name Belli), belongs to the family of Rutaceae. It is the most valuable medicinal plant in Siddha system of Medicine due to its various medicinal properties. It is a small or medium sized deciduous tree. It has alternate leave arrangement, Its flowers are greenish white, Fruit globose, grey or yellowish colour, Seeds Numerous. Found all over the Sri Lanka. Fruit (both unripe & ripe), root – bark, leaves, rind of the ripe fruit & flowers are used in drug preparations. Un-ripe fruit is astringent, digestive & stomachic & a little constipative. According to Siddha, *Aegle marmelos* has bitter, astringent taste, hot potency, pungent bio availability and reduce *Vatha, Pitha* and *Kapha dosha*. Diarrhoeal diseases are amongst the most common infectious diseases worldwide resulting in 3.2% of all deaths killing about 1.8 million people globally each year. It is quite evident from this review that *Aegle marmelos* is an important medicinal herb and extensively used in Ayurveda, Siddha, unani and traditional medicine. Historically, *Aegle marmelos* has been used for the number of ethonobotanical purposes. The collected information suggests that *Aegle marmelos* has anti-diarrheal activity.

Key words: *Aegle marmelos*, antidiarrheal activity, Unripe fruit, Beal, Siddha

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1.0 INTRODUCTION

Beal Fruit Tree (*Aegle marmelos*) (Tamil name *Vilvam, Kuvilam*, Sinhala name Belli), belongs to the family of Rutaceae. It is the most valuable medicinal plant in Siddha system of Medicine due to its various medicinal properties. It is a small or medium sized deciduous tree. It has alternate leave arrangement, Its flowers are greenish white, Fruit globose, grey or yellowish colour, Seeds Numerous. Found all over the Sri Lanka. Fruit (both unripe & ripe), root – bark, leaves, rind of the ripe fruit & flowers are used in drug preparations. Un-ripe fruit is astringent, digestive & stomachic & a little constipative. According to Siddha, *Aegle marmelos* has bitter, astringent taste, hot potency, pungent bio availability and reduce *Vatha, Pitha* and *Kapha dosha*. Diarrhoeal diseases are amongst the most common infectious diseases worldwide resulting in 3.2% of all deaths killing about 1.8 million people globally each year. This study was review the anti – diarrheal activity of *Aegle marmelos*

Aegle marmelos

English Name: Beal fruit, Bengal quince, Golden apple
Tamil Name: Vilvam, Vilva-pazham, Bilvam
Telugu: Bilvamu
Kingdom: Plantae
Order: Sapindales
Family: Rutaceae
Sub family: Aurantioideae
Genus: Aegle
Species: *A. marmelos*
Habitat: All over the Sri Lanka, specially seen in surrounding the Hindu Temples in Jaffna district and Matuvil, Kaithady areas commonly seen.

It extensively planted near Hindu temples for its leaves and wood which are used for worship, and for its edible fruits which are valued in indigenous medicine [43].

Description

A moderate- sized slender, aromatic tree, 6 – 7.5m height & 90 – 120cm in girth, with a somewhat fluted ble of 3 – 4.5m [43]. Branches armed with straight sharp axillary throns, 2.5 cm long. Leaves alternate, 3 – foliate, rarely 5- foliate; petiole 2.5 – 6.3cm long, terete, 2.5 cm long. Leaflets 5-10 by 2.5 – 6.3cm, ovate or ovate – lanceolates, crenate, acuminate, membranous, pellucid-punctate, the lateral opposite, subsessile, the terminal long petioluled. Flowers greenish white, sweet- scented about 2.5cm across, 2-sexual in short axillary panicles. Clayx flat, pubescent, 4 lobed; lobes rounded, sometimes obscure. Petals 4, spreading, oblong, thick, gland-dotted, much exceeding the sepals,imbricate. Stamens numerous, anthers elongate, apiculate; filaments free or fascicled inserted round an inconspiocuous disk [21][30].

Fruit is globose, grey or yellowish, rind woody. *Aegle marmelos* is mostly prized for its fruit. The fruit is a pyriform, may vary from oval to round, and size varies from 10-20 cm in diameter. The fruit has a hard, woody exocarp and inside it is a thick, fleshy and aromatic, slightly sweet pulp. The colour of the pulp may vary from bright orange to sunset yellow and the pulp contains seeds that are present in grooves and is surrounded by thick, clear mucilage. It is greenish when unripe and upon ripening it turns into yellowish colour. Both ripe and unripe fruits are used for their medicinal values [21][29].

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2.0 DIARRHOEAL DISEASES

Diarrhoeal diseases are amongst the most common infectious diseases worldwide resulting in 3.2% of all deaths killing about 1.8 million people globally each year [45]. Annually, diarrhoeal diseases kill over 1.5 million children globally [25]. Even though economic development and progress in health care delivery are expected to catalyze substantial improvements in infectious disease related morbidity and mortality by the year 2020, it is predicted that diarrhea will remain a leading health problem [27]. It affects mostly children in developing countries and can lead to dehydration and death in survivors to impaired growth and malnutrition [2]. In adults, while the impact is less severe, it nevertheless can lead to nutritional deficiencies especially in the case of persistent diarrhea [12].

2.1 PATHOGENESIS OF INFECTIOUS DIARRHOEA

The pathogenesis of infectious diarrhea has been widely studied. Enteric pathogens have evolved a remarkable array of virulence traits that enable them to colonize the intestinal tract. These organisms colonize and disrupt intestinal function to cause mal-absorption or diarrhea by mechanisms that involve microbial adherence and localized effacement of the epithelium, production of toxin(s) and direct epithelial cell invasion [13]. Adherence which is a means of colonizing the appropriate ecological niche enables the organism to resist being swept away by mucosal secretions. Adherence also aids in subsequent proliferation and colonization of the gut and may be followed by toxin production or invasion [3].

The importance of using colonization and production and action of enter toxins as specific parameters reflecting the pathogenesis has been earlier used by us as an approach towards understanding the varied mechanism(s) of action of anti-diarrheal medicinal plants against infectious diarrhea [4-5][8-9][31].

3.0 CHARACTERISTICS OF AEGLE MARMELOS

3.1 CHEMICAL CONSTITUENTS

The pulp contains mucilage, pectin, ugar, tannin (tannic acid), volatile oil, bitter principle, ash 2 percent & a balsamic principle resembling balsam of peru. According to Fluckiger & Hanbury the dry pulp contains chiefly mucilage & probably pectin. The dried pulp was exhausted by Henry & Brown, with boiling alcohol, the extract concentrated in vacua & the thick syrup diluted with water to precipitate fatty & resinous matters. The liquor from this precipitate after concentration in vacua to remove all alcohol, was tested by them on free living protozoan glaucoma [29].

3.2 PHARMACOLOGICAL ACTION

Ripe fruit is sweet, aromatic, cooling alterative & nutritive. When taken fresh it possess laxative properties. Un-ripe fruit is astringent, digestive & stomachic & a little constipative. Pulp is stimulant, anti pyretic & anti-scorbutic [29]. Fresh juice is bitter & pungent. Root is Anti inflammatory [43].

3.3 NUTRITIONAL PROPERTIES

Aegle marmelos is one of the most valuable medicinal plants; it has numerous uses in day to day life. Chemical studies prove that Bael fruit is rich in nutritional value, and this is being used from several years ago. Fruit is rich source of mineral, vitamin and fiber. Nutritional value of the Bael fruit

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(*Aegle marmelos*) (% per 100 g pulp) The Bael fruit is highly nutritious. It contains 61.5 g water, 1.8 g protein, 0.39 g fat, 1.7 g minerals, 31.8 g carbohydrates, 55 mg carotene, 0.13 mg thiamine, 1.19mg riboflavin, 1.1 mg niacin, and 8 mg per 100 g of edible portion vitamin C [38]. No other fruit has such a high content of riboflavin [26]. The riboflavin content of ripe fruit was very high. Bael fruit is highly nutritive with the richest source of riboflavin. Marmelosin ($C_{13}H_{12}O_3$) a resinous substance is most probably the therapeutically active principle of Bael fruits [26][35][38].

Mineral contents of unripe fruit of Aegle marmelos (ppm) are Na-55.6, Ca-78.9, K-1356, Mg- 142, Zn- 0.66, Cu-0.67 and Fe-19.3 [32].

3.4 BIOACTIVE COMPOUND

The Bael fruit is a good source of many functional and bioactive compounds and indigenous natural antioxidants containing relatively high content of dietary fiber, carotenoids, phenolics, flavonoids, ascorbic acid, alkaloids, and also strong antioxidant activities. Additionally, it also has the attractive yellowish-orange pulp appearance as well as a fragrant and pleasant flavour. The main volatile compounds are monoterpenes and sesquiterpenes [6]. Phytoconstituents isolated from of Aegle marmelos Fruit (Marmelosin, Luvangetin, Aurapten, Psoralen, Marmelide, Tannin). Bael gets its medicinal values on basis of the various bioactive compound present in it like alkaloids, coumarins, polysaccharides, essential oils etc.

3.4.1 Alkaloids

Aegelin, aegelinine, fragine, o-methylhal forodinine, oisopentanylhalfordinol, N-2-[4-(3',3'- dimethylallyloxy) phenyl] ethyl cinnamide, o-(3,3- dimethylallyl) halofodinol, Ethyl cinnamide [39].

3.4.2 Carotenoids

Carotenoids are Principle pigment responsible for imparting pale yellow colour to fruit [39].

3.4.3 Coumarins

The coumarins present in Bael fruit includes marmelosin, marmesin, imperatorin, marmin, alloimperatorin, methyl ether, xanthotoxol, scoparone, scopoletin, umbeliferone, marmelide and marmenol [39].

Minor constituents Ascorbic acid, sitosterol, crude fibers, α-amyrin, crude proteins [11].

3.4.4 Polysaccharides

Galactose, arabinose, uronic acid, L-rhamanose [39].

3.4.5 Tannins

There is as much as 9% tannin in the pulp of wild fruits, less in cultivated type. Tannin is also present in leaves as skimmianine. It is also named as 4, 7, 8-trimethoxyfuroquinoline [7] .

4.0 TRADITIONAL USES

The unripe fruit is oily bitter, acrid, sour, tasty but difficult to digest, appetizer, binding cures dysentery, removes pain. The oil is hot & cures vatha.

According to Siddha, *Aegle marmelos* has bitter, astringent taste, hot potency, pungent bio availability and reduce *Vatha, Pitha* and *Kapha dosha*. Ayurveda said that the ripe fruit is acrid, bitter, sweet; appetizer binding, tonic, febrifuge; cases biliousness & *tridosha*; removes *vatha* & *kapha*; good

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for the heart. *Unani* said that The ripe fruit is hot & dry; tonic, restorative, astringent, laxative; good for the heart & the brain; bad for the liver & chest [21][28].

An unripe beal fruit is taken (in which the starch is on point of being converted into sugar). It cracked in two or three places & roasted when the inside of the fruit is a little softened by the heat & starch is further converted into sugar. This is mixed with hot water to which a little fried & pulverized Anesi (Foeniculum vulgare) is added & the whole mixture is strained so that the starch – water containing Beal – sugar, the active anti – dysenteric principle of beal fruit & the fine particles of the carminative anesi, are taken as when cold 3 or 4 times a day. No other food is given when this food prescription is in force. Extract of beal made from fresh unripe fruit is also given in the alternative, in half to one drachm does several times a day [29].

Fruit is very valuable in habitual constipation, chronic dysentery & dyspepsia. It is one of the ingredients in the "Dasamul" or ten roots used in ayurveda.

Unripe or half ripe fruit owing to the presence of tannins or mucilageous substances which act as demulcent, cut up in slices & sun-dried or roasted & made into comfiture (conserve) or a powder, is prescribed in chronic diarrhea & dysentery with debility of the mucous membrane, intestinal condition specially useful in chronic diarrhea & dysentery of children where there is no fever. Dried pulp of the fresh ripe fruit is made into a pleasant orange coloured morning sherbet by mixing with sugar & cream or with curds two ounces of the pulp in three or four ounces of water or syrub, by straining all these through a piece of muslin to remove seeds & mucilage.

Liquid extract of beal prepared from dried slices of unripe fruit is also prescribed in doses of one to two drachms. The sherbet has mild astringent properties, is laxative & is a good simple cure for dyspepsia. Beal fruit is eaten during convalescence after diarrhea. Beal marmalade or a romatized confection is useful at the breakfast during convalescence from chronic dysentery or diarrhea for daily use as a preventive during chronic epidemics. It is also given to prevent the growth of piles.

The astringent rind of the ripe fruit is employed by kavirajas in acute dysentery & its usefulness in enhanced by the combination of opium. Powder of the dried pulp, kept in airtight bottles is given in doses if ½ to 1 drachm with treacle in recent dysentery with gripping pain in the loins & costiveness. Does as tonic is from 12 to 15 grains of the powdered pulp as a febrifuge & anti-scorbutic it is from 16 to 20 grains & as nauseant & anti-dysenteric it is from 20 grains to 2 drachms.

Powder is more useful in acute diseases & the syrup in the chronic. The beneficial effects of the beal fruit are however most evident when the condition in amoebic dysentery has become sub acute or chronic. After its administration in these conditions, the blood gradually disappears & the stools assume a more foeculent & solid form. If beal is continued for sometimes, the mucus is also decreased & may disappear. It is very useful in patients suffering from chronic dysenteric condition characterized by alternative constipation & diarrhea.

Claims have also been made that it relieves flatulent colic in patients suffering from a

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condition of chronic gastro-intestinal catarrh. In the after treatment of bacillary dysentery, beal is useful adjuvant. According to action & Knowledge the chief trouble with such patients, as a rule, is constipation which if not relieved does not allow the ulcerated surfaces to heal firmly. Beal sherbet is a useful addition to the dietary at this stage & acts chiefly as a demulcent.

In cases of spure also, the beal fruit has been spoken of highly by Manson-Bahr. In many patients, especially those in the pre- spure or early stages of the disease, it is undoubtedly helpful. The fresh fruit is best taken raw mixed with sugar through dried fruit has also been recommended. For a child the following is an excellent prescription in cases of chronic diarrhea. Powder of unripefruit six grains, compound powder of kino one grain & pure white sugar in fine powder one grain, mixed together dose is to be given two or three times a day. The small unripe fruit is given with fennel seeds & ginger in decoction for piles [29].

5.0 HOME REMEDY

Beal fruit 1, *Holarrhena antidysentrica* 2, Indian sweet fennel seeds 1, *Chebulic myrobalan*1, & sugar 3 parts, are mixed & reduce the whole to a powder, then add plantago, Ispaghula. Dose is to be 1-3 drachms (drs) for sub acute & chronic dysentery.

Beal fruit 4 drs, *Scindapsus officinalis* 1 dr, *Andropogon muricatus* 1 dr, *Symplocos racemosa* 1 dr, Mixed together & used in chronic diarrhea & dysentery.

Beal (dried pulp) 21/2 drs, dried ginger ½ dr, Indian sweet funnel seeds 21/2drs, silk cotton tree's gum 1 dr, honey 2drs & sugar 3drs mixed together & reduce the whole to the fine powder. Dise is to be ½ - 1 drachm for chronic dysentery & dysenteric diarrhea of hot climate.

Beal pulp 1dr, catechu 1dr, pomegranate bark 1 dr are mixed & make a powder. Dose is to be ½ to 1 drachm for dysentery & chronic diarrhea [29].

6.0 TOXICITY STUDIES

Dried fruit pulp of *Aegle marmelos* was screened for its topical profile. Ethanolic extract of *Aegle marmelos* dried fruit pulp was screened for the acute oral toxicity test in swiss albino mice at 550 and 1250 mg/kg body weight. At these concentrations test should be extract did not show any sign of toxicity. No change in the behavior and physiological activity was recorded in mice during the experiment (14 days). The results concluded that LD50 of the test extract is more than 1250 mg/kg body weight [1].

7.0 PHARMACOLOGICAL ACTIVITES

7.1 Antiulcer activity

Ulcer develops when there is imbalance between the defensive and aggressive factors on the mucosa resulting from either potentiation of aggressive factors and/or lowering of mucosal protection [44]. Stress, non-steroidal anti-inflammatory drugs (NSAIDs) and Helicobacter pylori are the most common causes of ulceration. Cigarette smoking and alcohol ingestion are other inducers of this disease [24]. Bael is an Indian indigenous plant which also has prominent gastroprotective effect. Pretreatment of rats with unripe bael fruit extract produced a significant inhibition of absolute ethanol induced gastric mucosal damage [10]. This activity may be due to the compound Luvangetin present in the fruit.

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Gastric ulcer is basically mediated by the development of oxidative stress and the compounds preventing ulcer formation may act through inhibition of oxidative stress in the gastro duodenal mucosa. The phenolic compounds are potent antioxidants [22] and have powerful antiulcer activities.

7.2 Antibacterial activity

Various extracts of Bael leaves, roots and fruits have been reported to be active against many bacterial strains. Leaf extract have shown activity against *Escherichia coli* [18]. The ethanolic extract of the root has shown activity against *Vibrio cholerae, Salmonella typhimurium, E. coli, Bacillus subtilis* and *Staphylococcus aureus* [33]. The ethyl acetate extract of the plant has exhibited activity against *Vibrio cholerae, S. typhi, S. aureus* and *Bacillus anthracis* [36][37].

Methanol and aqueous extract of Bael fruit have shown strong activity against multidrug resistant *S. typhimurium* [23]. The in vitro anti-diarrheal activity of dried fruit pulps of *Aegle marmelos* was reported. Anti-diarrheal activity was performed by MIC method against the causative organisms of diarrhea. The ethanolic extract showed good activity against *Shigella boydii, S.sonnei* and *S.flexneri* moderate against *S.dysenteriae* [1][40].

Bael has antibacterial activity and the mechanism of action may be the blockage of protein synthesis either at transcription or translation level and /or peptide-glycan synthesis at membrane level [14]. The antibacterial activity of leaf extract may be due to the presence of Cuminaldehyde and Eugenol because these compounds have already shown their activities against various bacterial strains .

7.3 Anti-diarrhoeal and anti-dysentric activities

The unripe or half riped fruit is the most effective remedy for chronic diarrhea and dysentery without fever. The *Aegle marmelos* fruit pulp has been shown to possess anti-protozoal activity in chronic dysentery condition accompanied by loose stool alternately with occasional constipation. The unripe fruit used in different formulations for treatment of chronic diarrhea. After the use of the fruit powder in these conditions, the blood gradually disappears and the stool resume a more feculent and solid form. The mucous also disappears after continued use for sometimes [3][41][42].

The crude aqueous extract of *Aegle marmelos* fruit has been reported to be non mutagenic to *Salmonella typhimurium* strain TA 100 in the Ames assay [28]. In addition, acute toxicity studies have reported that a hydroalcoholic extract of *Aegle marmelos* fruit is non-toxic up to a dose of 6 g/kg body weight in mice [15]. Pharmacological studies on animal models involving repeated doses of *Aegle marmelos* fruit extract over a period of up to 30 days have not reported any adverse effect up to a maximum dose of 250 mg/kg body weight [15][19-20]. The decoction of *Aegle marmelos* showed no cytotoxic activity on HEp-2 cells in the present study even at the highest concentration tested (1:10) [3].

The decoction of unripe fruit of Aegle marmelos exhibited antigiardial and antirotaviral activity. The antidiarrhoeal effect of this plant is possibly due to its ability to affect other bacterial virulence parameters [3].

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Aegle marmelos prevented the colonization by *E. coli* B170, *E. coli* E134 and *S. flexneri*. The reduction in colonization is probably due to its effect on the metabolism of HEp-2 cells and/or modification of cell receptors to prevent adherence or bacterial entry as seen on the pre-incubation of HEp-2 with the decoction. The decoction exhibited greater inhibition of invasion of *E. coli* E134 and *S. flexneri* as compared to adherence of E. coli B170 in both protocols. The adherence of the pathogen to the gut epithelium is the foremost stage of the disease process, inhibition of adherence could be a very important aspect in the antidiarrhoeal activity of the plant [3].

The decoction also reduced the binding of both LT (*E.coli* heat liable toxin) and CT (Cholera toxin) to the GM1 (Ganglioside monosialic acid) thereby inhibiting their action. LT and CT are known to be antigenically similar. Hence, the effect of the decoction on their binding suggest that it may contain some compound(s), which either bind to the common antigenic moiety of these toxins or may directly block the GM1 on the cell membrane thereby inhibiting their binding to the receptor. In addition, though the decoction had no effect on production of LT it inhibited the production of CT. Since the decoction had no cidal activity against *V. cholerae*, suppression of CT production suggests that the decoction affected the bacterial metabolism [3].

The effect of aqueous extract of unripe fruit of *Aegle marmelos* was observed on the experimental animal models of Inflammatory Bowel Disease (IBD), in albino rats. The results showed a decrease in severity of intestinal inflammation following treatment with AMFE (*Aegle marmelos* unripe fruit aqueous extract). This effect may be due to inhibition of inflammatory mediators like IL1, IL6, IL8, and TNF-α [17].

The phytochemical constituents of AMFE like flavinoids, phenolic compounds, and steroids may be responsible for this anti-inflammatory effect. AMFE showed increase in superoxide dismutase (SOD) activity and decrease in malonaldehyde (MDA) levels in the tissue homogenate. This effect may be due to presence of antioxidants like carotene, thiamine, riboflavin, niacin, and vitamin C in the A. marmelos fruit [17].

Tannins and flavonoids in general have been reported to have antidiarrhoeal activity through inhibition of intestinal motility, antimicrobial action and antisecretory effects [3].

The anti diarrhoeal effect of unripe fruit extract of *Aegle marmelos* is inhibiting the intestinal mortality and secretion [10].

8.0 DISCUSSION

Diarrhoeal diseases are the most common infectious diseases worldwide. *Aegle marmelos* has been used for centuries in Sri Lanka not only for its dietary purposes but also for its various medicinal properties [21][29]. The fruit is widely consumed as sherbet, murbha (jam) and unripe fruit is highly recommended for diarrhea and is especially for chronic diarrhea [3][29].

Aegle marmelos is effective in chronic cases of diarrhea due to the presence of large quantities of mucilage, which act as a demulcent [3]. It has been shown to be effective in experimental models of irritable bowel syndrome and physiological diarrhea [10][16][42].

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AMFE has anti-inflammatory, antioxidant, and mast cell stabilizing effects. *Aegle marmelos* contains a number of polar and nonpolar phytoconstituents, which are the key factors in the medicinal value of this plant. Therefore, aqueous extract of unripe fruit of *Aegle marmelos* has protective effect against IBD [17].

The decoction of A. marmelos can control several forms of infectious diarrhoeal diseases caused by EPEC (Enteropathogenic *Escherichia coli*), EIEC (Enterotoxigenic *Escherichia coli*), LT producing ETEC, *Vibrio cholerae*, *Shigella flexneri* and to some extent it can also control giardiasis and rotaviral infections. However, it may not be effective against diarrhoea caused by ST producing ETEC [3].

9.0 CONCLUSION

It is quite evident from this review that *Aegle marmelos* is an important medicinal herb and extensively used in Ayurveda, Siddha, unani and traditional medicine. Fruit (both unripe & ripe), root – bark, leaves, rind of the ripe fruit & flowers are used in drug preparations. Historically, *Aegle marmelos* has been used for the number of ethonobotanical purposes. The collected information suggests that *Aegle marmelos* has anti-diarrheal activity.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

Bibliography

1. Bhaskar Rao, V.K., *et al,* A review on pharmacological and phytochemical properties of *Aegle marmelos* (L.) Corr. Serr. (Rutaceae), Asian Journal of Plant Science and Research, 2011, 1 (2): 8-17.
2. Briend A: Is diarrhea a major cause of malnutrition among the under-fives in developing countries? A review of available evidence. Eur J Clin Nutr 1990, 44:611-628 [http://horizon.documentation.ird.fr/exl-doc/pleins_textes/pleins_textes_5/b_fdi_2231115.pdf].
3. Brijesh, S. Poonam Daswani, Pundarikakshudu Tetali, Noshir Antia, Tannaz Birdi, Studies on the antidiarrhoeal activity of Aegle marmelos unripe fruit: Validating its traditional usage,BMC Complementary and Alternative Medicine 2009, 9:47
4. Brijesh S, Daswani PG, Tetali P, Antia NH, Birdi TJ: Studies on Dalbergia sissoo Roxb. leaves: Possible mechanism(s) of action in infectious diarrhoea. Indian J Pharmacol 2006, 38:120-124.
5. Brijesh S, Daswani PG, Tetali P, Rojatkar SR, Antia NH, Birdi TJ: Studies on Pongamia pinnata (L.) Pierre leaves: Understanding the mechanism(s) of action in infectious diarrhea. J Zhejiang Univ Sci B 2006, 7:665-674.

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6. Charoensiddhi S, Anprung P. Bioactive compounds and volatile compounds of Thai bae
7. Daniel M. Medicinal Plants-Chemistry and properties of Medicinal Plants, IBH publication, 2006, 147. 6.
8. Daswani PG, Birdi TJ, Antia NH: Study of the action of Cyperus rotundus root decoction on the adherence and enterotoxin production of diarrhoeagenic Escherichia coli. Indian J Pharmacol 2001, 33:116-117 [http://medind.nic.in/ibi/t01/i2/ibit01i2p116.pdf].
9. Daswani PG, Birdi TJ, Antarkar DS, Antia NH: Investigation of the antidiarrhoeal activity of Holarrhena antidysenterica. Indian J Pharm Sci 2002, 64:164-167 [http://www.ijpsonline.coartie.asp?issn=025474X;year=2002;vole=64;issue=2;spage=164;epa;aulast=Daswani;type=0].
10. Dhuley, J.N. Investigation on the gastroprotective and antidiarrhoeal properties of Aegle marmelos unripe fruit extract, Hindustan Antibiotic Bulletin, 45:41-46, 2003.
11. Farooq S. Medicinal plants: field and laboratory manual. International book distributor, 2005, 40-42.
12. Guerrant RL, Lima AAM, Davidson F: Diarrhea as a cause and effect of malnutrition: diarrhea prevents catch-up growth and malnutrition increases diarrhea frequency and duration. Am J Trop Med Hyg 1992, 47:28-35
13. Guerrant RL, Steiner TS, Lima AAM, Bobak DA: How intestinal bacteria cause disease. J Infect Dis 1999, 179:S331-337. 13. Ashkenazi S, Pickering LK: Pathogenesis and diagnosis of bacterial diarrhoea. Eur J Clin Microbiol Infect Dis 1989, 8:203-206.
14. Gupta, D. John, P. P. Kumar Pankaj, Kaushik, R. Yadav, R. PHARMACOLOGICAL REVIEW OF AEGLE MARMELOS CORR. FRUITS, IJPSR (2011), Vol. 2, Issue 8 original
15. Jagetia GC, Venkatesh P, Baliga MS: Fruit extract of Aegle marmelos protects mice against radiation-induced lethality. Integr Cancer Ther 2004, 3:323-332.
16. Jagtap AG, Shirke SS, Phadke AS: Effect of a polyherbal formulation on experimental models of inflammatory bowel diseases. J Ethnopharmacol 2004, 90:195-204.
17. Jayanti, P. Bisweswar, M. Roja Ramani. Y, Bandana Rath, and Supriya Pradhan Effect of aqueous extract of Aegle marmelos unripe fruit on inflammatory bowel disease. Indian J Pharmacol. 2012 Sep-Oct; 44(5): 614–618.
18. Joshi CG, Magar NG (1952). Antibiotic activity of some Indian medicinal plants. J. Sci. Ind. Res., 11: 261.
19. Kamalakkannan N, Mainzen S, Prince P: Effect of Aegle marmelos Correa. (Bael) fruit extract on tissue antioxidants in streptozotocin diabetic rats. Indian J Exp Biol 2003, 41:1285-1288.
20. Kamalakkannan N, Prince PS: The effect of Aegle marmelos fruit extract in streptozotocin diabetes: a

UNDER PEER REVIEW

histopathological study. J Herb Pharmacother 2005, 5:87-96

21. Kirutikar, Basu, Indian Medicinal plants. 2nd edition, 2012. Pg no: 499-502
22. Karakaya S (2004). Bioavailability of phenolic compounds. Crit. Rev. Food Sci. Nutr., 44:453.
23. Kruawan K, Kangsadalampai K: Antioxidant activity, phenolic compound contents and antimutagenic activity of some water extract of herbs. Thai J Pharma Sci 2006, 30:1-47.
24. Liu ES, Cho CH (2000). Relationship between ethanol-induced gastritis ulcer and gastric ulcer formation in rats. Digestion, 62: 232.
25. Lopez AD, Mathers CD: Measuring the global burden of disease and epidemiological transitions: 2002-2030. Annals Trop Med Parasitol 2006, 100:481-499.
26. Mukharjee B, Ahmad K. Riboflavin. Pakistan J Bio l Agr Sci. 1957; 4:47-51.
27. Murray CJL, Lopez AD: Alternative projections of mortality and disability by cause 1990-2020: Global burden of disease study. Lancet 1997, 349:1498-1504.
28. Muruhesa muthaliyar, S. K., Gunapadam (Part I), Pg no: 819 - 823
29. Nadkarni, M.K., Indian Materia Medica Vol I, 3rd edition, 2009. Pg no: 45- 49
30. Pakkar Atul, N. Desai Nilesh, V. Ranage Akkatai, A. A review of Aegle marmelos: A potential medicinal tree. International research journal 2012; 3(8): 2230-8407
31. Pandey DK, Asthana A, Tripathi NN and Dixit SN (1981). Volatile plant products vis-à-vis potato pathogenic bacteria. Ind. Perfum., 10: 25.
32. Paras Porwal,DEVELOPMENT AND OPTIMIZATION OF SPRAY DRIED BAEL (Aegle marmelos Correa.) POWDER TO DEVELOP VALUE ADDED PRODUCT
33. Pitre S, Srivastava SK (1987). Pharmacological, microbiological and phytochemical studies on the roots of Aegle marmelos. Fitoterapia., 58: 197.
34. Rajan S, Gokila M, Jency P, Brindha P, Sujatha RK. Antioxidant and phytochemical properties of Aegle marmelos fruit pulp. Int J Curr Pharm Res. 2011;3:65–70.
35. Roy SK, Singh RN. Studies on utilization of bael fruit (Aegle marmelos Correa) for processing-III. Preparation and preservation of bael fruit products. Indian Food packer. 1979a; 34:9-14.
36. Rusia K, Srivastva SK (1988). Antimicrobial activity of some Indian medicinal plants. Ind. J. Pharmaceut. Sci., 50: 57
37. Sandeep Dhankhar1 , S. Ruhil1 , M. Balhara1 , Seema Dhankhar 2 and A. K. Chhillar1, Aegle marmelos (Linn.) Correa: A potential source of Phytomedicine , Journal of Medicinal Plants Research Vol. 5(9), pp. 1497-1507, 4 May, 2011
38. Sawale, KR. Deshpande, HW. Kulkarni, DB. Bael (Aegle marmelos) a super fruit of an hour: A review, International Journal of Chemical Studies 2018; 6(3): 1720-1723

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39. Sharma PC, Bhatia V, Bansal N, Sharma A. A review on bael tree. Natural Product Radiance. 2007; 6(2):171-178.
40. Singh KV, Bhatt SK, Sthapak JK (1983). Antimicrobial and anthelmintic properties of the seeds of Aegle marmelos. Fitoterapia., 54: 261.
41. Subramaniya BR, Malliga RM, Malathi GK, Anbarasu K, Devaraj SN: Effect of aqueous extract of Aegle marmelos fruit on adherence and β-lactam resistance of Enteropathogenic Escherichia coli by down regulating outer membrane Protein C. American Journal of Infectious Diseases 2009; 5(2); 161-169. 18.
42. Shoba FG, Thomas M: Study of antidiarrhoeal activity of four medicinal plants in castor-oil induced diarrhoea. J. Ethnopharmacol. 2001; 76; 73-76.
43. Vivian, S., Materia medica II, (Gunapadam II), 2008
44. Wallace JL, Granger DN (1996). The cellular and molecular basis of gastric mucosal defense. Faseb. J., 10: 731.
45. World Health Organization: World Health Report 2004:120-125 [http://www.who.int/whr/2004/annex/topic/en/annex_2_en.pdf]. Geneva:WHO

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