J Herbmed Pharmacol. 2017; 6(4): 141-147.

Journal of Herbmed Pharmacology

Journal homepage: http://www.herbmedpharmacol.com

Aegle marmelos (L.) Correa as a potential candidate for treatment of diabetes mellitus: A review

L.D.A. Menuka Arawwawala[1*] and D.L.S. Madushani Jayaratne[1]

[1]Industrial Technology Institute, Bauddhaloka Mawatha, Colombo7, Sri Lanka

ARTICLEINFO

Article Type:
Review

Article History:
Received: 10 April 2017
Accepted: 20 August 2017

Keywords:
Aegle marmelos
Diabetes mellitus
Clinical
Toxicity

ABSTRACT

Introduction: *Aegle marmelos* (L.) Correa is an important medicinal plant, commonly known as Bael which is belonged to family Rutaceae. It is widely distributed in Asian countries. According to the literature, various chemical constituents and pharmacological effects have been reported for this plant. In Ayurvedic and traditional medicinal systems, different parts of *A. marmelos* are used for diabetes mellitus. In the present review, an attempt was made to summarize the in vivo and in vitro studies and clinical trials conducted to evaluate or validate the anti-diabetic activity and toxicity of *A. marmelos*.
Methods: PubMed, Science Direct, Google Scholar, Directory of open access journals (DOAJ), EMBASE, and Web of Science were searched using the keywords *Aegle marmelos* and diabetes.
Results: Anti-diabetic potential, clinical applications of different parts of *A. marmelos* and possible toxic effects have been revealed in *A. marmelos* extract.
Conclusion: *Aegle marmelos* can be used as a potential candidate for diabetes mellitus.

Implication for health policy/practice/research/medical education:
Different parts of *A. marmelos* are used to control diabetes mellitus. Therefore, isolation of active compounds which exhibit anti-diabetic activity may lead to development of new anti-diabetic drugs.
Please cite this paper as: Arawwawala LDAM, Jayaratne DLSM. *Aegle marmelos* (L.) Correa as a potential candidate for treatment of diabetes mellitus: A review. J Herbmed Pharmacol. 2017;6(4):141-147.

Introduction

Diabetes mellitus has been recognized as one of the emerging health problems worldwide because of its high prevalence, adverse clinical outcomes, marked reduction in the quality of life of patients and high healthcare costs (1-3). It is characterized by abnormalities in carbohydrate, lipid and lipoprotein metabolism. The disease not only leads to hyperglycemia but also causes many complications such as hyperlipidemia, hyperinsulinemia, hypertension and atherosclerosis (4,5). Global projections suggest that more than 350 million people will have diabetes by 2030 and the cost of treating diabetes and its complications could reach more than trillion dollars annually. Accordingly, it has become an adverse public health crisis in most of the South Asian countries including Sri Lanka with a prevalence of 8.5% in the general population (6,7). Before the discovery of insulin in 1922, the only treatment options for diabetes were those based on the traditional practices. Ethno-botanical knowledge has played a particularly important role in historical diabetes therapies, with over 1200 species of medicinal plants recognized throughout the world for their ability to treat diabetic indications (8,9). *Aegle marmelos* (L.) Correa (Figure 1) is one of the medicinal plants used in Asian countries to treat diabetes mellitus. This article aimed to review (*a*) chemical composition (*b*) the anti-diabetic properties (in vivo, in vitro experiments and clinical trials) and (*c*) toxicities of different parts of *A. marmelos*.

Taxonomy of *Aegle marmelos* L.

Kingdom: Plantae
Order: Sapindales
Family: Rutaceae
Sub family: Aurantioideae

***Corresponding author**: L.D.A.M. Arawwawala, Ph.D, Industrial Technology Institute, Bauddhaloka Mawatha, Colombo 07, Sri Lanka. Tele/Fax: (94) - 11- 2379848, Email: menuka@iti.lk

Figure 1. Fruits (A), flowers (B) and seeds (C) of *Aegle marmelos* L.

Genus: *Aegle*
Species: *A. marmelos*

Morphology

Aegle marmelos tree is a slow-growing of medium size up to 25 or 30 feet tall with short trunk, thick, soft, flaking bark, and spreading, sometimes spiny branches, the lower ones drooping. Young suckers bear many stiff, straight spines. There are sharp, axial one inch long spikes on this tree. The leaflets are oval or lancet shaped 4-10 cm long, 2-5 cm wide. Leaves composed of 3 to 5 leaflet in it. The lateral leaflets are without petiole and the terminal one has a long one. The petiole is 1 to 2.5 inch long. Mature leaves emit a peculiar fragrance when bruised. Flowers occurs in clusters of 4 to 7 along the young branchlets, have 4 recurved, fleshy petals. The flowers are greenish white in color with a peculiar fragrant. Flowering occurs during the month of May and June (10). Fruit is spherical or oval in shape with a diameter of 2 to 4 inch. Shell is thin, hard and woody in nature. It is greenish when unripe and upon ripening it turns into yellowish color. The pulp of the fruit has 8 to 15 segments. The pulp is yellow, soft, pasty, sweet, resinous and fragrant. Fruition occurs in the month of May and June. The seeds are embedded in the pulp. The seeds are small (nearly 1 cm in length), hard, flattened-oblong, bearing woolly hairs and each enclosed in a sac of adhesive (10,11).

Distribution

Aegle marmelos is a subtropical plant growing well in the dry forests on hilly and plain regions. It is a widely distributed plant and found in India, China, Nepal, Sri Lanka, Myanmar, Vietnam, Laos, Cambodia, Pakistan, Bangladesh, Thailand, Indonesia, Java, Philippines Malaysia, Tibet, and Fiji. In India it found in sub-Himalayan tracts from Jhelum eastwards to West Bengal, in central and south India (10-12). *A. marmelos* is known by different names in different parts of world, some of them are mentioned in Table 1 (13).

Table 1. Names of *Aegle marmelos* L. in different languages

Name	Language
Aegle marmelos	Latin
Wood/Stone apple, Bengal Quince, Indian Quince	English
MbauNau, Trai Mam	Vietnamese
Bel, Gudu	Nepali
Toum	Lao (Sino-Tibetan)
Bnau	Khmer
Modjo	Javanese
Oranger du Malabar	French
Ohshit, opesheet	Burmese
Mojo tree	Indonesian
PokokMajaBatu	Malay
Mapin, Matum, Tum	Thai
Shreephal, Bilva, Bilwa	Sanskrit
Sir Phal	Old Hindi
Bel, Shreefal	Bengali
Kaveeth	Marathi
VilvaMaram, VilvaPazham	Tamil
Maredu	Telugu
Bel	Urdu
Belli	Sinhala

Propagation

Usually seeds are used for propagation. At first, ripe fruits are collected. Then seeds are squeezed out, washed thoroughly, dried in shade and stored in airtight containers. Seeds are pretreated by soaking in cold water for 24 hours and sown on sandy beds. The beds should be regularly watered. Germination commences on the ninth day onwards and completed within 20 days. The percentage of germination is around 90%. Four leaved seedlings are transplanted to containers.

Sprouted root cuttings are also used for propagation. These are obtained by making incision on lateral roots and taking root cuttings with sprouted portions, usually 9-12 months after making incision (14).

Phytochemical constituents

Several research groups have isolated and identified various chemical constituents present in different parts of *A. marmelos* (Table 2).

Anti-diabetic activity

In vivo experiments

In vivo experiments on anti-diabetic activity of *A. marmelos* are summarized in Table 3.

Table 2. Phytochemical constituents of different parts of *Aegle marmelos* L.

Type of the part plant	Chemical constituents	References
Fruit	Hexanal, isoamyl acetate, limonene, β-phellandrene, p-cymene, acetoin, (E)-2-octenal, (E,E)-2,4-heptadienal, dehydro-p-cymene, linalool, 3,5-octadiene-2-one, α-cubebene, trans-p-mentha-2,8-dienol, citronellal, cineole, p-cymene, citronella, citral, cuminaldehyde, β-cubebene, β-caryophyl-lene, hexadecane, pulegone, α-humulene, verbenone, carvone, carvylacetate, dihydro-β-ionone, (E)-6,10-dimethyl-5,9-undecadien-2-one, β-ionone, caryophyllene oxide, humulene oxide and hexadecanoic acid	(15)
Fruit	Coumarins like aegeline, aegelenine, marmelin, o-mtheylhalfordinol, alloimperatorin, furocoumarins, psoralen, o-isopentenylhalfordinol, marmelosin, tartaric acid, linoleic acid, tannins, phlobatannins, leucoanthocyanins, anthocyanins, flavonoid glycosides	(16-19)
Fruit Pulp	Carotenoids, phenolics, alkaloids, pectins, tannins, coumarins, flavonoids, terpenoids	(15,17-19)
Bark	Isomeric lignan-glucosides: glucoside, (-) – lyoniresinol 2α-O-β-D glucopyranoside, (-) 4 - epi-lyoniresinol, 3α -O -β -D-glucopyranoside, glucosides, (+)- lyoniresinol. 3α-O-β-D-glucopyranoside, (-)-lyoniresinol 3α-O-β-D-D-glucopyranoside	(20)
Stem Bark	Marmesin – 1"- α -L – rhamnopyranoside, 1,5 -dihydroxy - 6 - methoxy -2 -methyl anthraquinone, lupeol, β-sitosterol	(21)
Leaves	Aegeline, lupeol, rutin, marmesinine, β-sitosterol, flavone, glycoside, oisopentenyl halforidol and phenylethyl cinnamamides, N-2-[4-(3', 3'-dimethylallyloxy) phenyl] ethylcinnamide,N-2-hydroxy-2-(4-hydroxyphenyl) ethylcinnamide, marceline, shahidine	(22-24)

In vitro experiments

In an experiment lectin extract of *A. marmelos* increased the glucose uptake in yeast cell by 71.1% at the highest concentration (5 µg/mL) and 2.6% at the lowest concentration used (0.313 µg/mL) whereas the standard drug, metformin increased the glucose uptake in yeast cell by 4.6 % at the highest concentration (5 µg/mL). This result indicates that lectin extract of *A. marmelos* has high efficiency in increasing the glucose uptake by yeast cells as compared to standard drug i.e. metformin.

Two groups of researchers have carried out alpha amylase inhibition assay to evaluate in vitro anti-diabetic activity of *A. marmelos*. According to Saha and Verma (35), aqueous methanol extracts (50% and 100%) were prepared using leaves of *A. marmelos*.

Both extracts obtained were subjected to an in vitro amylase inhibitory assay using starch as a substrate and pancreatic amylase as the enzyme. The plant leaves methanol extract (50%) at doses of 50 to 500 µg/mL decreased amylase activity. However, the 100% methanol extract showed the least inhibitory activity. According to Soneji et al (36), petroleum ether and ethanol extracts were prepared using leaves of *A. marmelos*. Petroleum ether and ethanol extracts of *A. marmelos* revealed a significant inhibitory action of alpha amylase enzyme (36). As a concentration of 20 ug/mL of *A. marmelos* petroleum ether and ethanol extracts showed a 90.3% and 96.6% inhibition respectively and for 100 ug/mL extracts showed 94.5% and 99.3% inhibition respectively.

In a non-enzymatic glycosylation of hemoglobin (Hb) assay the petroleum ether and ethanol extracts of *A. marmelos* showed higher inhibition of glycosylation for the concentrations of 20 ug/mL and 40 ug/mL as compared to the reference drug (36).

Clinical trials on anti-diabetic activity of different parts of *Aegle marmelos L.*

A study was conducted to evaluate the hypoglycemic effect of the *A. marmelos* flower extract in diabetic patients (37). In diabetic patients, daily administration of *A. marmelos* flower extract significantly reduced the fasting glucose levels and oral glucose tolerance test (OGTT) values, while the post glucose load plasma insulin levels were significantly increased by 62%. Serum levels of tested enzymes, creatinine and Glycated hemoglobin (HbA1c) were not significantly altered at the end of one month. The *A. marmelos* flower extract exerted a significant hypoglycemic effect and increased insulin secretion in type II diabetic patients with no adverse effects.

In another study *A. marmelos* leaves were evaluated on non-insulin dependent diabetes mellitus patients. It caused significant changes in postprandial blood glucose level (PPBGL) of patients who were receiving *A. marmelos* leaves in comparison to patients who were on their standard oral hypoglycemic therapy (38).

Toxicity on different parts of *Aegle marmelos L.*

Herbal medicines are regarded by the public and some health care providers to be gentle and safe, but there is no scientific basis for this belief. The active components of plants have potential to cause serious adverse effects (39). The usefulness of drugs depends greatly on their lack of toxicities or adverse side effects. Therefore, many attempts have been taken by researches to assess any toxic effects of *A. marmelos* using different parts of the plant.

A single dose of 500 mg/kg *A. marmelos* flower extract was used for 42 consecutive days to evaluate any toxic effects on the levels of blood aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), Hb, creatinine and gamma GT on rats (40).

Table 3. In vivo experiments on anti-diabetic activity of different parts *Aegle marmelos* L.

Preparation of the extract	Experimental procedure	Results	Ref
Seeds were extracted with boiling water for 10 h and filtered. The filtrate was evaporated in a vacuum to give a residue.	The anti-diabetic property was evaluated in diabetic rats by following methods: (*a*) Evaluating the effect of different doses of *A. marmelos* seed extract on blood glucose levels in rat. (*b*) Evaluating by giving the most effective dose of the extract (250 mg/kg) once a day for 14 consecutive days and observing the changes in FBG level, body weight, urine sugar and lipid profile.	A significant ($P \leq 0.05$) reduction in blood glucose level was observed after 6 h of administration. Highest hypoglycemic activity was observed with 250 mg/kg. The mid dose (250 mg/kg) of *A. marmelos* produced a maximum anti-diabetic activity after 2 h of glucose administration. The FBG levels of rats were decreased by 37.4% and 60.8% respectively, after 1 h and 2 weeks of treatment. Furthermore, decreased the levels of TC (by 25.4%), LDL (by 53.9%), TG (by 45.7%) and urine sugar levels (75%) while increased the levels of HDL (by 33.3%) and body weights after continuous treatment of 14 days.	(25)
Aqueous fruit extract (brown dry powder) was suspended in distilled water	Evaluating by giving 125, 250 mg/kg doses twice a day for 28 consecutive days to STZ-induced diabetic rats	A significant reductions in blood glucose, plasma thiobarbituric acid, hydroperoxides α-tocopherol and ceruloplasmin as well as an elevation in plasma glutathione and vitamin C in diabetic rats. At dose of 250 mg/kg was more effective than the reference drug, glibenclamide in restoring the values of these parameters.	(26)
Aqueous fruit extract was suspended in distilled water	Experimentation design was similar to the previous study (25). After 30 days of treatment blood was collected to determine FBG level and removed the heart and pancreas (to assess the antioxidant activities) after the rats were sacrificed.	A significant reduction blood glucose was observed in rats treated with extracts The lowered glutathione content in the heart and pancreas of diabetic rats was found to increase on treatment with extracts. The effect of 250 mg/kg dose was more than that of the reference drug, glibenclamide.	(27)
Aqueous fruit extract was suspended in distilled water	By evaluating anti-lipid peroxidative activity in hepatic and renal tissues in diabetic rats. Experimentation design was similar to the previous study (26).	*A. marmelos* fruit extracts prevented STZ-induced hyperglycaemia and hypoinsulinemia. A significant decrease in peroxidation products and hydroperoxides in diabetic rats. Antioxidant enzymes such as superoxide dismutase, catalase and glutathione peroxidase increased in the hepatic and renal tissues of diabetic animals treated with extracts. *A. marmelo*s fruit extract at a dose of 250 mg/kg, was more effective than glibenclamide.	(28)
Aqueous fruit extract was suspended in distilled water	Positive effects on heart and pancreas antioxidants in STZ-induced diabetic rats. Experimentation design was similar to the previous study (25).	A significant reduction was observed in rats treated in the elevated levels of peroxidation products, viz. thiobarbituric acid reactive substances and hydroperoxides in the tissues of diabetic rats. The depressed activities of superoxide dismutase, catalase and glutathione peroxidase and lowered glutathione content in the heart and pancreas of diabetic rats increased. However, effect of 250 mg/kg dose of *A. marmelos* on tested parameters was found to be more than that of the reference drug, glibenclamide.	(27)
Aqueous fruit extract was suspended in distilled water	Effects in normal and STZ- induced diabetic rats and anti-lipid peroxidative activity was studied in hepatic and renal tissues in diabetic rats (26)	The fruit extracts prevented STZ-induced hyperglycemia and hypoinsulinemia and produced significant decrease in peroxidation products and hydroperoxides in diabetic rats. The activity of antioxidant enzymes such as superoxide dismutase, catalase and glutathione peroxidase increased in the hepatic and renal tissues of diabetic animals treated with extracts. However, *A. marmelos* fruit extract at a dose of 250 mg/kg, was more effective than glibenclamide.	(28)
Aqueous fruit extract was suspended in distilled water	Effects in normal and STZ- induced diabetic rats and serum and tissue (e.g. Liver, kidney and heart) lipids such as total cholesterol, triglycerides, free fatty acids and phospholipids were evaluated	The fruit extract at doses of 125 and 250 mg/kg to diabetic rats twice daily for 1 month significant lowered these lipids in diabetic rats. The fruit extract at a dose of 250 mg/kg had greater effect than that of glibenclamide (300 µg/kg). The results of this study demonstrate that an aqueous *A. marmelos* fruit extract exhibits an antihyperlipidemic effect in STZ-induced diabetic rats.	(29)

Table 3. Continued.

Aqueous fruit extract was suspended in distilled water	Effects in histopathological examinations of the pancreas of STZ- induced diabetic rats	*A. marmelos* fruit extract improved functional state of the pancreatic β-cells and partially reversed the damage caused by STZ to the pancreatic islets.	(30)
Methanolic extract of the bark	Effects in hypoglycemic and β-cells regenerative effects of STZ- induced diabetic rats	At 200 and 400 mg/kg doses showed significant reduction in blood glucose level by 19.1% and 47.3%, respectively in diabetic rats. *A. marmelos* bark extract treatment significantly increased insulin level, and produced similar effects on other biochemical parameters. Histological studies showed the regenerative effect of *A. marmelos* bark extract on the β-cells of diabetic rats. The extract increased insulin immunoreactive β-cells.	(31)
Hot aqueous flower extract	Effects in hypoglycemic effects of alloxan monohydrate - induced diabetic rats	500 mg/kg for continuous 42 days increased hypoglycemic effect and decreased the HbA1c level in diabetic rats.	(32)
Methanolic extract of the leaves	Hypoglycemic effects and antioxidant activity of alloxan monohydrate - induced diabetic rats	Reduce blood sugar in alloxan diabetic rats. Decrease the lipid peroxidation, conjugated diene and hydroperoxide levels in serum as well as in liver induced by alloxan. Catalase and glutathione peroxidase activities in blood and liver were found to be increased from 9th day onwards after drug administration. Superoxide dismutase and glutathione levels were found to be increased only on 12th day.	(33)

Abbreviations: FBG, fasting blood glucose; $HbA1_C$, glycated hemoglobin; Hb, hemoglobin; HDL, high density lipoprotein; LDL, low density lipoprotein; TC, total cholesterol; TG, triglyceride; STZ, streptozotocin.

There was no statistically significant ($P>0.05$) difference between the values of above parameters of test group compared to the control group. The results of the present study showed that the water extract of dried flowers of *A. marmelos* does not exert any adverse effects as judged by the parameters studied (40).

Acute, sub acute toxicities and LD_{50} values of total alcoholic, total aqueous and methanolic extracts prepared from leaves of *A. marmelos* were evaluated. There were no remarkable changes noticed in the histopathological studies after 50 mg/kg body weight of the extracts of *A. marmelos* when administered intraperitoneally for 14 days successively. Pathologically, neither gross abnormalities nor histopathological changes were observed. After calculation of LD_{50} values using graphical methods, we found a broad therapeutic window and a high therapeutic index value for *A. marmelos* extracts. Intraperitoneal administration of different doses of the leaves extracts of the plant (50, 70, 90 and 100 mg/kg for 14 consecutive days) to male and female Wistar rats did not induce any short term toxicity (41).

Conclusion

Aegle marmelos has been evaluated for its anti-diabetic activity by using in vivo, in vitro and clinical researches. According to the promising anti-diabetic properties and non toxicity, *A. marmelos* can be used as a potential candidate for treatment of diabetes mellitus. Therefore, necessary researches should be undertaken for the development of functional foods, nutraceuticals and herbal medicine for better therapeutic utilization of the plant.

Authors' contributions

All the authors contributed to data collection and preparation of the manuscript equally. All read the final version and confirmed for publication.

Conflict of interests

The authors declared no competing interests.

Ethical considerations

Ethical issues have been completely observed by the authors.

Funding/Support

None.

References

1. Chen L, Magliano DJ, Zimmet PZ. The worldwide epidemiology of type 2 diabetes mellitus--present and future perspectives. Nat Rev Endocrinol. 2011;8(4):228-36.
2. Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. Global estimates of diabetes prevalence for 2013 and projections for 2035. Diabetes Res Clin Pract. 2014;103(2):137-49.
3. Ramachandran A, Snehalatha C, Ma RC. Diabetes in South-East Asia: an update. Diabetes Res Clin Pract. 2014;103(2):231-7.
4. Chait A, Brunzell JD. Diabetes, lipids and atherosclerosis. In: LeRoith D, Taylor SI, Olefsky JM, eds. Diabetes Mellitus. Philadelphia: Lippincott – Raven; 1996:467-9.
5. Watkins PJ. ABC of Diabetes. 5th ed. Tavistock Squre, UK; BMJ Publishing Group Ltd; 2003.
6. Forouhi NG, Wareham NJ. Epidemiology of diabetes. Medicine (Abingdon). 2014;42(12):698-702.
7. Somani R, Kasture S, Singhai AK. Antidiabetic potential of *Butea monosperma* in rats. Fitoterapia. 2006;77(2):86-90.
8. Marles RJ, Farnsworth NR. Antidiabetic plants and their active constituents. Phytomedicine. 1995;2(2):137-89.
9. Kim SH, Hyun SH, Choung SY. Anti-diabetic effect of cinnamon extract on blood glucose in db/db mice. J Ethnopharmacol. 2006;104(1-2):119-23.
10. Jayaweera DMA. Medicinal Plants (Indigenous and Exotic) Used in Ceylon. Colombo, Sri Lanka: National Science Council; 1980.
11. Lambole VB, Murti K, Kumar U, Sandipkumar PB, Gajera V. Phytopharmacological properties of *Aegle marmelos* as a potential medicinal tree: An Overview. Int J Pharm Sci Rev Rese. 2010;5(2):67-72.
12. Dhankhar S, Ruhil S, Balhara M, Dhankhar S, Chhillar AK. *Aegle marmelos* (Linn.) Correa: a potential source of phytomedicine. J Med Plants Res. 2011; 5(9): 1497-1507.
13. The Ayurvedic Pharmacopoeia of India Part 1, Vol 1. India: Government of India, Ministry of Health and Family Welfare, Department of Ayush; 1999:35-6.
14. Warrier PK, Nambiar VPK, Ganaoathy PM. Some Important Medicinal Plants of the Western Ghats, India: A Profile. India: Medicinal and Aromatic Plants Program in Asia (MAPPA); 2001.
15. Charoensiddhi S, Anprung P. Bioactive compounds and volatile compounds of Thai bael fruit (*Aegle marmelos* (L.) Correa) as a valuable source for functional food ingredients. Int Food Res J. 2008;15(3):287-295.
16. Rastogi RP, Mehrotra BN. Compendium of Indian medicinal plants. Lucknow India: Central Drug Research Institute; 1990.
17. Parmar C, Kaushal MK. Wild Fruits of the Sub-Himalayan Region. New Delhi, India: Kalyani; 1982.
18. Roy SK, Khurdiya DS. Other subtropical fruit. In: Alunkhe DK, Kadam SS, eds. Handbook of Fruit Science and Technology: Production, Composition, Storage and Processing. New York: Marcel Dekker; 1995.
19. Maity P, Hansda D, Bandyopadhyay U, Mishra DK. Biological activities of crude extracts and chemical constituents of Bael, *Aegle marmelos* (L.) Corr. Indian J Exp Biol. 2009;47(11):849-61.
20. Ohashi K. Isolation of some isomeric lignin glycosides from the bark of *A. marmelos*. Chem Lett. 1995; 10: 881-910.
21. Nema D, Srivastava SK. Isolation some pigment from stem bark of the *A. marmelos*. Physical Sci J. 1991;61:452-67.
22. Govindachari TR, Premila MS. Some alkaloids from aegle marmelos. Phytochemistry. 1983;22(3):755-7.
23. Pattnaik S, Subramanyam VR, Kole C. Antibacterial and antifungal activity of ten essential oils in vitro. Microbios. 1996;86(349):237-46.

24. Baslas KK, Deshpandey SS. Edible Medicinal and Non-Medicinal Plants. Fruits J Indian Chem Soc. 1951;28:19-22.
25. Kesari AN, Gupta RK, Singh SK, Diwakar S, Watal G. Hypoglycemic and antihyperglycemic activity of *Aegle marmelos* seed extract in normal and diabetic rats. J Ethnopharmacol. 2006;107(3):374-9.
26. Kamalakkannan N, Prince PS. Hypoglycaemic effect of water extracts of *Aegle marmelos* fruits in streptozotocin diabetic rats. J Ethnopharmacol. 2003;87(2-3):207-10.
27. Kamalakkannan N, Stanely Mainzen Prince P. Effect of *Aegle marmelos* Correa. (Bael) fruit extract on tissue antioxidants in streptozotocin diabetic rats. Indian J Exp Biol. 2003;41(11):1285-8.
28. Kamalakkannan N, Prince PS. Antidiabetic and anti-oxidant activity of *Aegle marmelos* extract in streptozotocin-induced diabetic rats. Pharm Biol. 2004;42(2):125-30.
29. Kamalakkannan N, Prince PS. Antihyperlipidaemic effect of *Aegle marmelos* fruit extract in streptozotocin-induced diabetes in rats. J Sci Food Agric. 2005;85(4):569-73.
30. Kamalakkannan N, Prince PS. The effect of *Aegle marmelos* fruit extract in streptozotocin diabetes: a histopathological study. J Herb Pharmacother. 2005;5(3):87-96.
31. Gandhi GR, Ignacimuthu S, Paulraj MG. Hypoglycemic and beta-cells regenerative effects of *Aegle marmelos* (L.) Corr. bark extract in streptozotocin-induced diabetic rats. Food Chem Toxicol. 2012;50(5):1667-74.
32. Kumari KDKP, Samarasinghe K, Suresh TS. Hypoglycemic effect of the traditional drink, the water extract of dried flowers of *Aegle marmelos* (L) Correa (bael fruit) in Wister rats. Indian Journal of Traditional Knowledge. 2013;12(3):384-9.
33. Sabu MC, Kuttan R. Antidiabetic activity of *Aegle marmelos* and its relationship with its antioxidant properties. Indian J Physiol Pharmacol. 2004;48(1):81-8.
34. Saha RK, Nesa A, Nahar K, Akter M. Antidiabetic activities of the fruit *Aegle marmelos*. J Mol Biomark Diagn. 2016;7(2):272.
35. Saha S, Verma R. Inhibitory potential of traditional herbs on alpha-amylase activity. Pharm Biol. 2012;50(3):326-31.
36. Soneji IB, Thokal VN, Khan ZH. In vitro antidiabetic activity of *Aegle marmelos* leaves. Eur J Biom Pharm Sci. 2016;3(5):530-2.
37. Kumari KDKP, Suresh TS, Samarasinghe K, Handunnetti SM, Samaranayake TSP. Evaluation of a traditional Sri Lankan herbal beverage (water extract of dried flowers of *Aegle marmelos*, Bael fruit) in type II diabetic patients. 4th World Congress on Diabetes Metabolism; Holiday Inn, USA; August 14-16, 2013.
38. Yaheya M, Ismail M. Clinical evaluation of antidiabetic activity of *Trigonella* seeds and *Aegle marmelos* leaves. World Applied Sciences Journal. 2009;7(10):1231-4.
39. De Smet PA. Health risks of herbal remedies: an update. Clin Pharmacol Ther. 2004;76(1):1-17.
40. Kumari KD, Suresh TS, Samarasinghe K. Effect of long term feeding of the water extract of dried flowers on *Aegel marmelos* in Wistar rats. Planta Med. 2012;78:121.
41. Veerappan A, Miyazaki S, Kadarkaraisamy M, Ranganathan D. Acute and subacute toxicity studies of Aegle marmelos Corr., an Indian medicinal plant. Phytomedicine. 2007;14(2-3):209-15.