For reprint orders, please contact: reprints@future-science.com



Phytochemical and biological review of Aegle marmelos Linn

S Monika¹, M Thirumal^{*,1} & PR Kumar¹

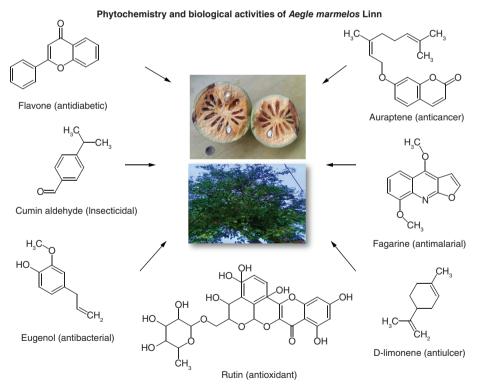
¹Department of Pharmacognosy, SRM College of Pharmacy, SRM Institute of Science & Technology, Kattankulathur, Chengalpet Dt, Tamilnadu, 603203, India

*Author for correspondence: Tel.: +91 98946 40595; thirumam@srmist.edu.in

India has one of the most expanded plant-origin medical traditions in the world. Researchers have evaluated molecules obtained from plants to treat a variety of ailments. Literature review shows that fundamental parts of the plant are used to treat different diseases. The related data is retrieved from Google scholar, PubMed, Science Direct and Scopus. The keywords include Bael, *A. marmelos*, Vilvam, and Marmelosin. Extensive studies show that *A. marmelos* has antidiarrhoeal, antimicrobial, antiviral, anticancer, chemopreventive, antipyretic, ulcer healing, antigenotoxic, diuretic, antifertility, and anti-inflammatory properties. In this work, an updated literature review is presented to clarify the current state of research on *A. marmelos* elucidating its constituents and their most relevant biological activities.

Plain language summary: India has one of the most expanded plant-origin medical traditions in the world. *A. marmelos* Linn, also familiar as bael, belongs to Rutaceae and is widely grown worldwide. *A. marmelos* is a fruit with various medicinal advantages. We searched various databases, studied elaborately, and understood the importance of this fruit. Thus, its constituents can help mitigate various diseases.

Graphical abstract:



First draft submitted: 25 October 2022; Accepted for publication: 2 March 2023; Published online: 23 March 2023

Keywords: Aegle marmelos • Marmelosin • phytochemistry • Rutaceae • Vilvam



The medicinal plant performs an essential role in the lives of underprivileged populations worldwide [1], likewise for primary medical care. Approximately 80 percent of countries worldwide rely on these conventional treatments, which frequently involve plant extracts [2]. India has one of the most expanded plant-origin medical traditions in the world. In India, rural communities know around 25,000 potent plant-based remedies employed in traditional medicine. Plants, especially those with ethno pharmacological uses, have been the primary sources of medicine for early drug discovery [3]. Anciently most medications have been developed via natural ingredients or ingredients derived from natural compounds [4,5].

However, a significant amount of basic and applied research is required to validate and use plants in phytopharmaceutical chemistry, and the potential use of higher plants as a source of new medications is still underutilized, with this resource ranking on par with conventional pharmaceutical products in terms of importance [6]. Only a small portion of the approximated 250,000–500,000 plant genera have been thoroughly explored in terms of their pharmacological qualities, and only a small portion have been investigated phytochemically [7]. By supporting the conscious exploration of biodiversity as a source of bioactive molecules and their application in the production of new therapeutic medications, it also aims to encourage the developing and disseminating of this plant-based medicine. The main aim of this review is to know the phytochemical parameters, Traditional uses, and innovative applications of *A. marmelos* Linn.

Research method

The search is done in Google scholar, PubMed, Science Direct and Web of Science. The databases are collected by the following keywords: Bael, *A. marmelos*, Vilvam, and Marmelosin.

Inclusion & exclusion criteria

The language of this study is English. It included chemical, and pharmacological data and specific animal trials using isolated chemicals and extracts from *A. marmelos*. Finally, to ensure dependability, only peer-reviewed academic publications are selected. This study excluded the clinical trials and computational and characterization studies. 350 articles were selected; from that, 79 articles were included.

Rutaceae family

The most recent phylogeny for Rutaceae, with 135 genera representing 87.7% of the recognized genera for Rutaceae and subfamilies of the family are Haplophylloideae, Amyridoideae, Aurantioideae, Cneoroideae, Rutoideae, and Zanthoxyloideae. The physiologically active essential oils produced by the Rutaceae family are widely known and found in many family members, as well as its ornamental and culinary herbs, which include orange, lime, lemon, grapes, and satinwood [8]. Several studies have found various plant substances, including alkaloids, terpenoids, flavonoids and coumarins [9]. Plants in the Rutaceae family contain high amounts of coumarins, like Marmelosin and Luvangetin, which have antihelminthic, antiulcer, antibacterial and antispasmodic activity.

Aegle marmelos Linn

Aegle marmelos Linn, also familiar as Bael as shown in Figure 1 and belonging to the family Rutaceae, has been frequently utilized in the indigenous Indian system of medicine because of its diverse medicinal properties. India holds high regard for the critical medicinal herb *A. marmelos* Linn (Rutaceae), also called Bengal quince, Bilva, Indian quince, Golden apple, Holy fruit, Bel, Belwa, Sriphal, Stone apple, and Maredo in India [10]. It has been utilized for over 5000 years by numerous ethnic populations living in the Indian subcontinent. In the ayurveda Indian traditional medicine system, it is used to treat various ailments [11]. The phytochemicals of *A. marmelos* were discovered in various sections of the same plant.

Indian medicinal plant known as bael has been used traditionally to treat several ailments, and numerous bioactive chemicals have been extracted [12,13]. *A. marmelos*, native to Northern India, are also widely dispersed over the Indian Peninsula, Burma, Bangladesh, Ceylon, Thailand and Indo–China [14]. The medium-sized, slow-growing *A. marmelos* tree can grow to 12–15 meters. It spreads with spiky branches and has a small trunk and thick, soft, peeling bark. Fractured branches, a transparent, viscous liquid that resembles gum arabic, oozes out, hangs down in long strands, and gradually solidifies. It starts tasting sweet but soon becomes unpleasant to the throat [15,16].

The biologically active chemicals and essential oil were extracted from Bael plants, and phytoconstituents characterization was carried out. Extraction techniques are used on the most active parts of the plant (roots,



Figure 1. Bael fruit and tree.

Table 1. Taxonomical classification .			
Kingdom	Plantae		
Sub-kingdom	Tracheobionta		
Super division	Spermatophyta		
Division	Magnoliophyta		
Class	Magnoliopsida		
Subclass	Rosidae		
Order	Sapindales		
Family	Rutaceae		
Genus	Aegle		
Species	marmelos		

Table 2. Ethno medicinal uses of Aegle marmelos .				
Parts	Uses			
Leaves	The leaves are most effective in treating fever, nausea, vomiting, swellings, dysentery, dyspepsia, seminal weakness, and intermittent fever.			
Root	The roots of bael are thought to be effective in treating urinary problems, preventing heart palpitations, and curing fevers. They are also said to relieve abdominal pain. The medical properties of dashamula lie in its root to treat fever, diarrhea, and flatulence.			
Bark	The villagers use a decoction of the bark to treat fever and cough.			
Flower	An anti-dysenteric, antidiabetic, diaphorectic, and local anesthetic medication can be produced by distilling flowers. It is utilized as a tonic for the stomach and intestine. Along with being used as an expectorant, it is also helpful in epilepsy.			
Fruit	Bael fruits are edible. The pulp used to make delicious items like murabba, puddings, and juice. Apart from their laxative use and curing respiratory ailments, also used in several traditional medications to treat chronic diarrhea, peptic ulcers, inhibit lipid peroxidation, free radicals scavenging, antioxidants, anti-ulcerative colitis, gastroprotective, hepatoprotective, antidiabetic, cardioprotective, radioprotective, antibacterial, antidiarrheal and antiviral properties.			
Seed	Seed extract possesses antidiabetic and hypolipidemic effects in diabetic rats.			

fruit, leaves, flowers, or stem), using selective solvents and standard operating procedures [17]. The taxonomical classification of *A. marmelos* is discussed in Table 1 [18].

In traditional medicine, *A. marmelos* are used based on their radio protective [19], antidiabetic, and anticancer activities [20,21]. The various components of bael are used for its medicinal properties, such as managing asthma, fractures, anemia, wound healing, high blood pressure, jaundice, swollen joints, diarrhoea, and issues with typhoid during pregnancy [22]. The medicinal importance of *A. marmelos* has been discussed in Table 2 [23–28] focusing on each part of the plant.

A. marmelos is reported to contain chemical composition like alkaloids (aegeline, fragrine, aegelenine), coumarins (Marmin, Marmelide, Psoralen, Imperatonin), and terpenoids (cineol, Caryophyllene), etc [29–36].

Table 3.	Table 3. Compound isolated from various parts of Aegle marmelos.				
S. no	Parts	Chemical compound	Ref.		
i)	Leaves	α and β sitosterol, Rutin, Flavone, Cineol Glycoside, O- Halfordiol, Marmeline, Lupeol, Citronellal, Marmesinin, Aeglin, Cuminaldehyde, Phenylethyl cinnamamides, Citral, Skimmianine, Eugenol, Isopentenyl.	[44]		
ii)	Fruit	Aurapten, Imperatorin, Psoralen, Tannin, Luvangetin	[45]		
iii)	Bark	Fagarine, Marmin	[37]		
iv)	Seed	Citral, A-D-phellandrene, Cineol, P-cymene, D-limonene, Cumin aldehyde, Citronellal	[46]		

Reported phytochemical & its activity

The pulp of the bael fruit is rich in bioactive substances such as carotenoids, phenolics, alkaloids, pectins, tannins, coumarins, flavonoids, and terpenoids, according to studies. Methanol and water are the best solvents for extracting the metabolites of this plant, followed by ethanol [37–40]. The phytochemistry of *A. marmelos* has been extensively studied, and the plant has been found to contain a variety of biologically active compounds.

Some of the key phytochemicals found in *A. marmelos* include: Alkaloids are nitrogen-containing compounds that are found in many plants and are known for their pharmacological activity. Several alkaloids have been identified in the leaves and roots of *A. marmelos*, including marmesin, marmelosin, and aegeline [25].

Tannins are a group of compounds that are widely distributed in the plant kingdom and are known for their astringent and antioxidant properties. The fruit of *A. marmelos* contains high levels of tannins, which have been shown to have strong antioxidant and anti-inflammatory activities. Flavonoids are a group of compounds that are widely distributed in the plant kingdom and are known for their anti-inflammatory, anti-cancer, and antioxidant activities.

Flavonoids have been identified in the leaves and roots of *A. marmelos*, and some of these compounds have been shown to have antinociceptive (pain-relieving) and antipyretic (fever-reducing) activities [41].

Terpenoids are a group of compounds that are widely distributed in the plant kingdom and are known for their medicinal properties. Terpenoids have been identified in *A. marmelos*, and some of these compounds have been shown to have antifungal and antibacterial activities.

Saponins are a group of compounds that are widely distributed in the plant kingdom and are known for their foaming and emulsifying properties. Saponins have been identified in the fruit and leaves of *A. marmelos*, and some of these compounds have been shown to have antinociceptive and anti-inflammatory activities [33].

Glycosides are a group of compounds that are widely distributed in the plant kingdom and are known for their medicinal properties. Glycosides have been identified in the fruit and leaves of *A. marmelos*, and some of these compounds have been shown to have antinociceptive and anti-inflammatory activities [42]. The most widely investigated compounds from *A. marmelos* were determined by reviewing and evaluating the items from the obtained bibliographic data. The isolated phytochemicals from different parts of *A. marmelos* are discussed in Table 3, and the chemical structure of the compounds is shown in Table 4 [43].

Pharmacological activity

Pharmacological activity is essential in herbal plants. The various acts of *A. marmelos*, which have been reported scientifically and investigated, have been illustrated in Figure 2.

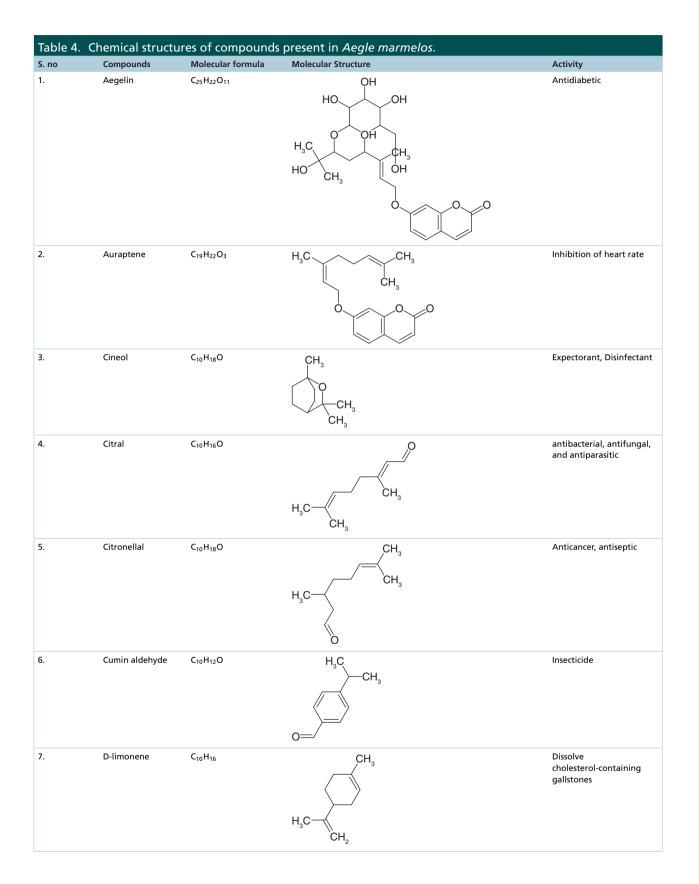
Anticancer activity

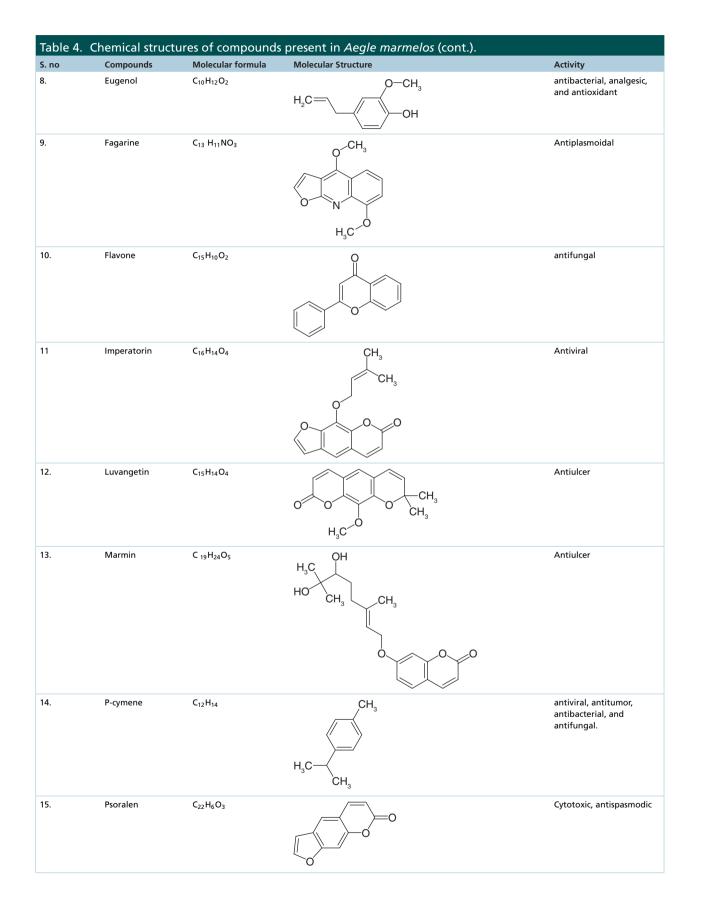
The *A. marmelos* of methanol and acetone extract of cytotoxicity against HEp-2, MDA-MB-231, and Vero cells were investigated. The IC₅₀ for the methanol extract of *A. marmelos* was 47.08 g/ml, whereas the IC₅₀ for the acetone extract of *A. marmelos* was 79.62 g/ml, making HEp-2 cells more sensitive to it. Both extracts of *A. marmelos* are toxic to cancer cells; however, Vero cells can survive 24 hours [47].

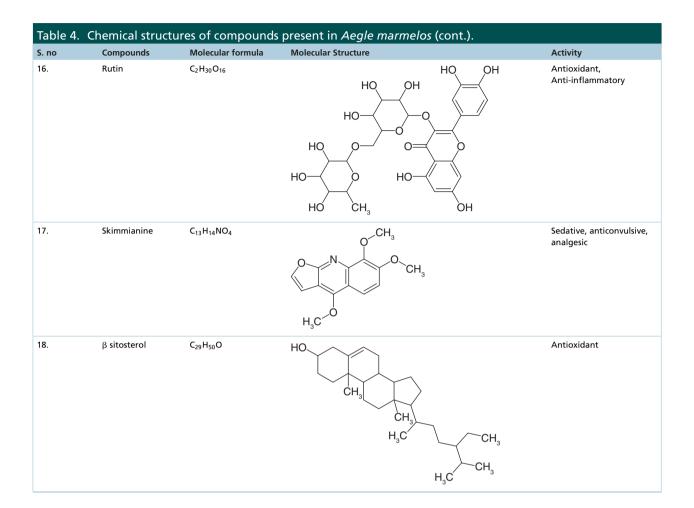
MTT assays on the human breast cancer cell line MCF-7 at various concentrations confirmed the *in vitro* anticancer activity. The flavonoids in fruit extracts act as a potential reducing agent and are reasonable for forming gold nanoparticles [48].

The aqueous fruit pulp extract from *A. marmelos* caused the most excellent MCF7 cell death at 100 g/ml and the _{IC50} at 47.92 g/ml concentrations [49].

In an *in-vivo* study, Swiss albino mice with Ehrlich ascites carcinoma received an intraperitoneal injection of a 400 mg/kg hydroalcoholic extract of *A. marmelos*. That significantly increased median survival time up to 28 days







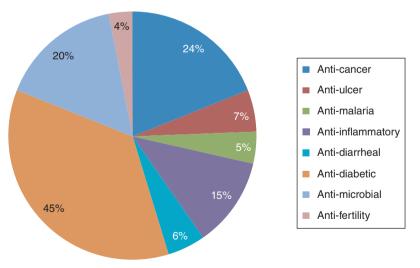


Figure 2. Percentage of reported biological activity of *Aegle marmelos* linked with each compound, from all investigated articles.

after tumor inoculation compared with the saline-injected control group [21]. The *A. marmelos* fruit pulp's ethanolic extract has anti-proliferative effect by inhibiting the proliferation of breast cancers in a rat model. Both the breast tumour volume (p < 0.05) and the different blood biomarkers (p < 0.0001) significantly decreased after *A. marmelos* treatment [50].

Table 5. Antidiabetic activities of Aegle marmelos.					
Part	Extract	Animal used	Standard	Inference	
Fruit	Aqueous	Mice	Glibenclamide	lowers blood sugar and boosts insulin secretion	
Fruit	Lectin	Glucose uptake by yeast cells	Metformin	IC_{50} of 3.36 $\mu g/ml$ had greater efficiency than the usual medication	
Various parts	Petroleum ether, methanol, chloroform, Benzene, aqueous	Streptozotocin diabetic Rabbit	-	Methanol extract showed maximum antidiabetic effect	
Seed	Aqueous	Albino Wistar rats	Tolbutamide	reduces the blood glucose level	
Leaves	Ethanol	α -amylase and α -glycosidase HepG2 cells	Acarbose	$\alpha\text{-amylase}$ and $\alpha\text{-glucosidase}$ were found to be IC_{50} 123.65 $\mu\text{g/ml}$ and IC_{50} 141.56 $\mu\text{g/ml}.$	
				Reduced ROS levels and enhanced glucose consumption (p $<$ 0.05).	
Leaves	Chloroform, butanol, and water	Streptozotocin induced Male albino rats	Metformin	Lowering the blood glucose levels	

Antidiabetic activity

The aqueous extract of A. marmelos fruits lowers blood sugar in streptozotocin-induced diabetes rat model. It boosts insulin secretion by partial regeneration from the β -cells of pancreatic islets [51]. The effects seen in the fruit extracttreated mice were better when compared with animals treated with glibenclamide. The present study's in-vitro assay demonstrated a potent antidiabetic effect from lectin extract, as measured by glucose uptake in yeast cells [52]. A fruit lectin extract with an IC₅₀ of 3.36 μ g/ml had greater efficiency than the usual medication metformin at increasing glucose uptake by yeast cells. This study found that A. marmelos fruit extract had hypoglycemic activity, which could be attributed to its antioxidant activity and high content of active constituents [53]. As a result, the various parts of A. marmelos plant could be beneficial as a portion of healthy food and in developing antidiabetic drugs. The active components in the leaf and callus materials reduce blood sugar levels in STZ-diabetic rabbits, and A. marmelos callus powder methanol extract is as powerful as the leaf extract in treating diabetes, as discussed in Table 5 [54]. This study indicates the aqueous seed extract of A. marmelos reduces the blood glucose level in normal as well as in severely diabetic rats and improves glucose tolerance in sub and mild diabetic animals and is referred to standard as tolbutamide [26]. The alcoholic extract of A. marmelos leaves significantly inhibited the enzymes α -amylase and α -glycosidase with IC₅₀ values of 46.21 and 42.07 µg/ml, respectively. A. marmelos significantly reduced ROS levels that were elevated due to high glucose and enhanced glucose consumption in HepG2 cells (p < 0.05) [9].

Anti-inflammatory & antipyretic activity

The study examined the potential anti-inflammatory activities of the repeated extracts from *A. marmelos* leaves. An apparent analgesic effect was demonstrated in mouse models of carrageenan-induced paw edema and cotton-pellet granuloma to establish the antipyretic and analgesic activities of the leaf extracts. Additionally, the early and late phases of paw licking were diminished, and hyperpyrexia decreased [55]. In another study, the anti-inflammatory properties of the aqueous extract of *A. marmelos* dried flowers are investigated in Wistar rats. The anti-inflammatory effects of water extract were most effective at 200 mg/kg two hours after administration [56]. Aqueous extract from unripe *A. marmelos* fruit was found to have a dose-dependent impact in a different investigation focused on inflammatory bowel disease in albino Wistar rats. With much higher SOD and lower MDA levels and defense against mast cell degranulation, *A. marmelos* fruit had anti-inflammatory, antioxidant, and mast cell stabilizing properties [57].

Antimalarial activity

In vitro antimalarial activity of A. marmelos leaf methanol extract, which showed the highest activity against *Plasmodium falciparum*, elicited low cytotoxicity, and the promising antiplasmodial activity of A. marmelos of IC50 is found to be 7 g/ml [58]. Infected mice with a suppressive effect on the parasite did not respond to C. longa treatment; however, A. marmelos at 20 and 40 mg/kg body weight inhibited parasite infection. Finally, A. marmelos, demonstrated strong antioxidant and antiplasmodial properties; it could be one of the traditional plants used to treat malaria [59]. With an IC₅₀ of 500.06 ppm, standard *Temephos* has better larvicidal activity toward Anopheles stephensi when compared with crude leaf extracts of A. marmelos Correa [60].

Table 6. Antimicrobial activity of Aegle marmelos.						
Plant part	Extract	Method	Organism	Standard		
Leaves	Ethyl acetate	Disc-diffusion method	E. coli, S. typhii, and P. aeroginosa	Streptomycin		
Fruit pulp	Aqueous, Ethanolic, and petroleum	Standard tube dilution technique	Staphylococcus aureus	Ampicillin		
Leaves	Pet ether	Disc-diffusion method	Multi-resistant strains of bacteria	Streptomycin		

Antimicrobial activity

The antimicrobial activity of *A. marmelos* is discussed briefly in Table 6 respectively. *Candida albicans, Aspergillus niger, Aspergillus fumigatus*, and *Staphylococcus aureus* all had MIC (Minimum inhibitory concentrations) values of 19.5 g/ml, 39 g/ml, 625 g/ml, and 1.25 g/ml, respectively [61]. When used against *Candida albicans* and *Aspergillus niger*, it showed practical MFC (Minimum fungicidal Concentration) values of 2.5 mg ml⁻¹ and 5 mg ml⁻¹, respectively. In the present review, the decoction was more effective against fungi than food-pathogen bacteria. The control drug ampicillin was identified to be effective as similar to the ethanolic extract of *A. marmelos* fruit pulp by inhibiting the growth of pathogenic bacterial strains [62]. The antibacterial activity of the different *A. marmelos* leaf extracts was tested using the disc diffusion method on multi-resistant strains of bacteria. From there, it can be shown that the pet ether extract exhibits greater action than regular streptomycin [63]. In the ethyl acetate extract of *A. marmelos* leaf, the quinine compound was identified and possessed good antibacterial activity against gram-positive and negative bacteria [64].

Antioxidant activity

Antioxidants are organic complexes that can safely interplay with free radicals and stop the chain reaction before harming fundamental molecules. Free radicals are highly reactive molecular species containing one or more unpaired electrons. They are generated from regular metabolism while using O_2 to burn food for energy [65]. It is generally known that reactive oxygen species (ROS) play a role in developing several illnesses, including cancer and cardiovascular disease. Plants include antioxidants or polyphenols that can successfully neutralize these ROS and prevent the spread of disease [66]. Oxidative stress is produced during normal metabolic processes in the body and induced by various environmental and chemical factors, which causes the generation of various reactive free radicals and subsequent damage to macromolecules like DNA, proteins, and lipids. In comparison to standard - gallic acid (IC₅₀ 1.1 ± 0.08 µM), marmelosin exhibited potent antioxidant activity with an IC₅₀ of ~15.4 ± 0.32 µM in ethyl acetate extract of bael fruit. Marmelosin was discovered to have better antioxidant properties than standard gallic acid [67]. In this investigation, the *A. marmelos* fruit decoction showed good antioxidant activity with an IC₅₀ of 17.37 ± 2.71 mg/ml and 379.9 ± 28.28 mg AEAC/100 g for standard ascorbic acid [61].

Antispermatogenic activity

In *A. marmelos* bark extract, marmin and fagarine are high, reducing male fertility [68]. The ethanolic extract of *A. marmelos* bark on sperm motility was reported to have a beneficial effect on sperm locomotor activity. It has also been reported that increasing the concentration of extracts reduces sperm motility. The alkaloids isolated from *A. marmelos* leaf were significantly decreased the fertility in male albino rats in dose dependent manner [69]. *A. marmelos* extract is an excellent choice for male contraception, the extract has the ability to completely suppress pregnancy and restore fertility rapidly after treatment cessation [68]. The male albino rats reproductive systems were subjected to three various doses of a 50% ethanolic extract from *A. marmelos* leaves: 100, 200, and 300 mg\kg 1 day 1 for each rat for 60 days. All of the significant accessory sex organs shrunk after ingesting the extract [70]. The cauda epididymis of the treated animals produced considerably less sperm, both in terms of motility and density. Male rat fecundity was completely decreased by *A. marmelos* at 300 mg.

Antiulcer activity

Methanolic and aqueous extracts of *A. marmelos* seeds were tested for antiulcer activity in indomethacin-induced ulceration, stress-induced ulceration, and pylorus ligation-induced ulceration by using ranitidine as standard (50 mg/kg) [71]. Peptic ulcers are caused by the bacteria *H. pylori*. There is little or no literature on the effect of *A. marmelos* on Helicobacter pylori, so more research is required to determine its effect on H. pylori. If it

positively reduces AMR, it will be an excellent herbal drug to treat abscesses with no adverse effects [72]. *A. marmelos* is frequently used to heal ulcers and related illnesses in Ayurveda and observed for the oral administration of methanolic extract of *A. marmelos* for affected rats with stomach ulcers induced by lipopolysaccharide caused by Helicobacter pylori [73]. A dose of 500 mg/kg of methanolic extract was shown in the trial to reduce stomach ulcers by 93.98%. Gastric secretory parameters, such as free and total acidity, acid output, stomach juice volume, and pepsin concentration, were inhibited, resulting in decreased gastric ulcers.

Antiviral activity

Different portions of the *A. marmelos* are observed against human coxsackie viruses B1-B6 for *in-vitro* antiviral activity with ribavirin as a standard antiviral drug. Thus Marmelide possessed 32-times more potent inhibitory activity than ribavirin [74]. *A. marmelos* extracts were shown to be effective against the white spot syndrome virus in shrimp at a dose of 150 mg/kg of animal body weight [75]. The isolated volatile oil from *A. marmelos* is examined for its ability to inhibit the growth of eight different types of fungi. At 0.05% concentration, the essential oil completely prevented all fungi from producing spores. The majority of the fungus is significantly inhibited at around 75% and 90% at 0.03% and 0.04%, respectively. At concentrations of 0.03% and 0.04% of the oil, the most resistant strain, *Fudum*, showed 65% and 80% inhibition rates, respectively [76].

Toxicity studies

A. marmelos dried fruit pulp is examined for its topical characteristics. Swiss albino mice were tested for acute oral toxicity with an ethanol extract of the dried fruit pulp from *A. marmelos* at 550 and 1250 mg/kg. Test results should indicate that the extract is not hazardous at these doses. Mice's behavior and physiological activity remained unchanged (14 days) throughout the trial [43]. The findings showed that the test extract's LD₅₀ is highly significant. The oral acute toxicity study did not show any toxic symptoms, changes in behavior, or mortality at 1250 mg/kg doses. Thus, the ethanolic extract of *A. marmelos* dried fruit pulp extract has no discernable biologically significant toxic effect on the mice below LD₅₀.

Discussion

The biological actions of isolated compounds from *A. marmelos* that are being investigated using extracts can be connected to this review. This investigation concludes that *A. marmelos* has a promising future in treating and preventing different ailments, including cancer, infectious disorders and diabetic conditions. Reviews on spermatogenic, analgesic and antipyretic, inflammatory, antiulcer, and malaria treatment drugs are only a few topics covered in these reviews. For this reason, it is essential to develop clinical research on this medicinal plant and learn from traditional healers who have gathered knowledge through many generations of trial and error. The use of bael has gained popularity worldwide as its beneficial characteristics are being researched to develop new treatments potentially. As a result, the demand for novel therapeutic drugs with focused action and limited adverse effects justifies further clinical and preclinical research on *A. marmelos*.

Conclusion

These investigations have shown that *A. marmelos* has therapeutic potential and contains elements that could be used to make new medications for the prevention, mitigation, or treatment of diabetes, cancer, and a variety of pathogenic illnesses. *A. marmelos* has been historically used for a variety of ethno botanical purposes. Unfortunately, most compounds still need to be thoroughly assessed to investigate novel lead molecules or pharmacophores. Furthermore, the mechanisms of a few bioactive chemicals have been discovered so far. Comprehensive research is necessary to ascertain the mechanisms of action, the bioactivity of numerous phytochemicals, and the effectiveness of *A. marmelos* medicinal characteristics.

Future perspective

This study concludes the various parts of *A. marmelos*; preclinical studies are performed for different activities. Many chemical compounds are isolated, but fewer studies are conducted. In the future, clinical trials will be conducted for those activities. The demand for Bael fruit is likely to increase due to its growing popularity as a health food and ingredient in various food and beverage products. Additionally, the growing interest in traditional and natural remedies for various health conditions is likely to drive demand for Bael fruit.

Executive summary

Rutaceae

- Aegle marmelos (Indian bael or bael fruit), Rutaceae family, tree species native to India and Southeast Asia. Aegle marmelos Linn
- Traditionally used for the treatment of various ailments, including diarrhoea, dysentery, and fever.
- Reported phytochemical & its activity
- Phytoconstituents, including alkaloids, coumarins, tannins, flavonoids, terpenoids, saponins, and glycosides. Pharmacological activity
- Antibacterial, antifungal, antiviral, antimalarial, and antiparasitic activities.

Author contributions

Literature research and writing have been done by S Monika and M Thirumal. Actualization has been done by PR Kumar. English vocabulary as well as phrase structure revision of the whole document have been done by S Monika. M Thirumal was the supervisor of all work.

Acknowledgments

The authors express sincere gratitude to all the supervisors and professors of SRM College of Pharmacy, SRM Institute of Science and Technology, Kattankulathur (Tamil Nadu, India), who extended their contribution and support in this work.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Open access

This work is licensed under the Creative Commons Attribution 4.0 License. To view a copy of this license, visit http://creativecommons.org/licenses/by/4.0/

References

Papers of special note have been highlighted as: • of interest

- 1. Shinwari ZK, Qaiser M. Efforts on conservation and sustainable use of medicinal plants of Pakistan. Pak. J. Bot. 43(1), 5–10 (2011).
- Li R-J, Gao C-Y, Guo C, Zhou M-M, Luo J, Kong L-Y. The anti-inflammatory activities of two major withanolides from *Physalis minima* via acting on NF-κB, STAT3, and HO-1 in LPS-stimulated RAW264.7 cells. *Inflammation* 40(2), 401–413 (2017).
- Süntar I. Importance of ethnopharmacological studies in drug discovery: role of medicinal plants. *Phytochem. Rev.* 19(5), 1199–1209 (2020).
- There is an reference addressing the drug discovery and drug development in traditional medicine.
- 4. Katiyar C, Kanjilal S, Gupta A, Katiyar S. Drug discovery from plant sources: an integrated approach. *AYU (An Int. Q. J. Res. Ayurveda)* 33(1), 10 (2012).
- 5. Lahlou M. The success of natural products in drug discovery. *Pharmacol. Pharm.* 4(3A), 15 (2013).
- 6. Vuorela P, Leinonen M, Saikku P *et al.* Natural Products in the Process of Finding New Drug Candidates. *Curr. Med. Chem.* 11(11), 1375–1389 (2004).
- 7. Rates SM. Plants as source of drugs. Toxicon 39(5), 603-613 (2001).
- Appelhans MS, Bayly MJ, Heslewood MM, et al. A new subfamily classification of the Citrus family (Rutaceae) based on six nuclear and plastid markers. Taxon 70(5), 1035–1061 (2021).
- Ahmad W, Amir M, Ahmad A et al. Aegle marmelos leaf extract phytochemical analysis, cytotoxicity, in vitro antioxidant and antidiabetic activities. Plants 10(12), 2573 (2021).
- 10. Vinita Bisht N, Johar V. Bael (*Aegle marmelos*) extraordinary species of India: a Review. Int. J. Curr. Microbiol. Appl. Sci. 6(3), 1870–1887 (2017).
- 11. Rahman S, Parvin R. Therapeutic potential of Aegle marmelos (L.)-An overview. Asian Pacific J. Trop. Dis. 4(1), 71-77 (2014).
- 12. Badam L, Bedekar S, Sonavane KB, Joshi SP. *In vitro* antiviral activity of bael (*Aegle marmelos* Corr) upon human coxsackieviruses B1-B6. *J. commun. Dis.* 34(2), 88 (2002).

- 13. Gupta AK, Tandon N. Reviews on Indian medicinal plants. Indian Council of Medical Research, New Delhi, India 1, 312 (2004).
- 14. Brijesh S, Daswani P, Tetali P, Antia N, Birdi T. Studies on the antidiarrhoeal activity of *Aegle marmelos* unripe fruit: validating its traditional usage. *BMC Complement. Altern. Med.* 9, 47 (2009).
- 15. Kaur A, Kalia M. Physico chemical analysis of bael (*Aegle marmelos*) fruit pulp, seed and pericarp. *Chem. Sci. Rev. Lett.* 6(22), 1213–1218 (2017).
- 16. Aung HT, Zar T, Sein MM, Komori Y, Vidari G, Takaya Y. Constituents of *Aegle marmelos* from Myanmar. J. Asian Nat. Prod. Res. 23(9), 844–850 (2021).
- 17. Badal S, Delgoda R. Pharmacognosy fundamentals, applications and statergy. Academic Press, London, UK (2016).
- 18. Boy HIA, Rutilla AJH, Santos KA *et al.* Recommended medicinal plants as source of natural products: a Review. *Digit. Chinese Med.* 1(2), 131–142 (2018).
- Jagetia GC, Venkatesh P. Inhibition of radiation-induced clastogenicity by *Aegle marmelos* (L.) Correa in mice bone marrow exposed to different doses of γ-radiation. *Hum. Exp. Toxicol.* 26(2), 111–124 (2007).
- Subramaniam D, Giridharan P, Murmu N et al. Activation of Apoptosis by 1-Hydroxy-5,7-Dimethoxy-2-Naphthalene-Carboxaldehyde, a Novel Compound from Aegle marmelos. Cancer Res. 68(20), 8573–8581 (2008).
- 21. Jagetia GC, Venkatesh P, Baliga MS. *Aegle marmelos* (L.) Correa. Inhibits the Proliferation of Transplanted Ehrlich Ascites Carcinoma in Mice. *Biol. Pharm. Bull.* 28(1), 5864 (2005).
- 22. Sanghi SB, Mushtaq S. Aegle marmelos a potential medicinal tree: an overview. Int. J. Res. -Granthaalayah 5(8), 63-66 (2017).
- 23. Mazumder R, Bhattacharya S, Mazumder A, Pattnaik AK, Tiwary PM, Chaudhary S. Antidiarrhoeal evaluation of *Aegle marmelos* (Correa) Linn. root extract. *Phyther. Res.* 20(1), 82–84 (2006).
- Soumya Prakash Rout, Choudary KA, Kar DM, Das L, Jain A. Plants in traditional medicinal system future source of new drugs. International J. Pharm. Sci. 1(1), 1–23 (2009).
- Baliga MS, Bhat HP, Joseph N, Fazal F. Phytochemistry and medicinal uses of the bael fruit (*Aegle marmelos* Correa): a concise review. *Food Res. Int.* 44(7), 1768–1775 (2011).
- 26. 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.* 107(3), 374–379 (2006).
- 27. Nemkul CM, Bajracharya GB, Shrestha I. Phytochemical, antibacterial and DPPH free radical scavenging evaluations of the barks of *Aegle marmelos*(L.) Correa. *J. Pharmacogn. Phytochem.* 7(4), 1637–1641 (2018).
- Dhankhar S, Ruhil S, Balhara M, Dhankhar S, Chhillar AK. Aegle marmelos (Linn.) Correa: a potential source of Phytomedicine. J. Med. Plants Res. 5(9), 1497–1507 (2011).
- 29. Ali MS, Pervez MK. Marmenol: a 7-geranyloxycoumarin from the leaves of Aegle marmelos corr. Nat. Prod. Res. 18(2), 141-146 (2004).
- Takase H, Yamamoto K, Hirano H, Saito Y, Yamashita A. Pharmacological Profile of Gastric Mucosal Protection by Marmin and Nobiletin from a Traditional Herbal Medicine, *Aurantii fructus immaturus. Jpn J. Pharmacol.* 66(1), 139–148 (1994).
- 31. Sharma B, Sharma P. Constituents of Aegle marmelos. Planta Med. 43(09), 102-103 (1981).
- Reference addressing the ethanobotanical uses of Aegle marmelos.
- Gerardo Aguirre, Araceli Salgado-Rodríguez, Lucía Z Flores-López, MP-H y Ratnasamy Somanathan. Asymmetric Synthesis of Naturally Occurring β-Hydroxyamides (R)-Tembamide and (R)-Aegeline. J Mex. Chem Soc. 45, 21–24 (2001).
- 33. Wilzer KA, Fronczek FR, Urbatsch LE, Fischer NH. Coumarins from Aster praealtus. Phytochemistry 28(6), 1729–1735 (1989).
- 34. Goel RK, Maiti RN, Manickam M, Ray AB. Antiulcer activity of naturally occurring pyrano-coumarin and isocoumarins and their effect on prostanoid synthesis using human colonic mucosa. *Indian J. Exp. Biol.* 35(10), 1080–1083 (1997).
- 35. Masuda T, Takasugi M, Anetai M. Psoralen and other linear furanocoumarins as phytoalexins in *Glehnia littoralis*. *Phytochemistry* 47(1), 13–16 (1998).
- 36. Gautam M, Ramanathan M. Ameliorative potential of flavonoids of *Aegle marmelos* in vincristine-induced neuropathic pain and associated excitotoxicity. *Nutr. Neurosci.* 24(4), 296–306 (2021).
- Maity P, Hansda D, Bandyopadhyay U, Mishra D. Biological activities of crude extracts and chemical constituents of Bael, *Aegle marmelos* (L.) Corr. *Indian J. Exp. Biol.* 47, 849–861 (2009).
- Sharma GN, Dubey SK, Sati N, Sanadya J. Phytochemical screening and estimation of total phenolic content in *Aegle marmelos* seeds. Int. J. Pharm. Clin. Res. 2(3), 27–29 (2011).
- 39. Veer B, Singh R. Phytochemical Screening and Antioxidant Activities of Aegle marmelos Leaves. Anal. Chem. Lett. 9(4), 478-485 (2019).
- Venkatesan D, Karrunakarn CM, Kumar SS, Swamy P. Identification of phytochemical constituents of *Aegle marmelos* responsible for antimicrobial activity against selected pathogenic organisms. *Ethnobot. Leafl.* 11(4), 1362–1372 (2009).
- Choudhary Y, Saxena A, Kumar Y, Kumar S, Pratap V. Phytochemistry, pharmacological and traditional uses of *Aegle marmelos. Pharm. Biosci. Journal.* 20, 27–33 (2017).
- There is an reference addressing phytochemical present in Aegle marmelos.

- 42. Dhankhar S, Ruhil S, Balhara M, Dhankhar S, Chhillar AK. Aegle marmelos (Linn.) Correa: a potential source of Phytomedicine. J. Med. Plants Res. 5(9), 1497–1507 (2011).
- 43. Rakulini K. A Review of Anti-Diarrhoeal Activity of Aegle marmelos. J. Complement. Altern. Med. Res. 7(2), 1-10 (2019).
- 44. Shoeb A, Kapil RS, Popli SP. Coumarins and alkaloids of Aegle marmelos. Phytochemistry 12(8), 2071–2072 (1973).
- 45. Kim HJ, Seo YJ, Htwe KM, Yoon DK. Chemical Constituents from Aegle marmelos Fruits. Nat. Prod. Sci. 27(4), 240-244 (2021).
- Pathirana CK, Madhujith T, Eeswara J. Bael (Aegle marmelos L. Corrêa), a Medicinal Tree with Immense Economic Potentials. Adv. Agric. 2020, 1–13 (2020).
- Seemaisamy R, Faruck LH, Gattu S, et al. Anti Microbial and Anti Cancer activity of Aegle marmelos and Gas Chromatography Coupled Spectrometry Analysis of their Chemical Constituents. Int. J. Pharm. Sci. Res. 10(1), 373–380 (2019).
- 48. Vijayakumar S. Eco-friendly synthesis of gold nanoparticles using fruit extracts and *in vitro* anticancer studies. *J. Saudi Chem. Soc.* 23(6), 753–761 (2019).
- 49. Vardhini SP, Sivaraj C, Arumugam P, Ranjan H, Kumaran T, Baskar M. Antioxidant, anticancer, antibacterial activities and GCMS analysis of aqueous extract of pulps of *Aegle marmelos* (L.) Correa. J. Phytopharm. 7(1), 72–78 (2018).
- 50. Akhouri V, Kumari M, Kumar A. Therapeutic effect of *Aegle marmelos* fruit extract against DMBA induced breast cancer in rats. *Sci. reports.* 10(1), 18016 (2020).
- Kamalakkannan N, Prince PSM. The effect of Aegle marmelos fruit extract in streptozotocin diabetes: a histopathological study. J. Herb. Pharmacother. 5(3), 87–96 (2005).
- 52. Saha RK, Nesa A, Nahar K, Akter M. Anti-diabetic Activities of the Fruit Aegle mamelos. J. Mol. Biomark. Diagn. 7(2), 1-5 (2016).
- Abdallah IZA, Salem IS, Abd El-Salam NAS. Evaluation of Antidiabetic and Antioxidant Activity of Aegle marmelos L. Correa Fruit Extract in the Diabetic Rats. Egypt. J. Hosp. Med. 67(2), 731–741 (2017).
- 54. Arumugam S, Kavimani S, Kadalmani B, Ahmed AB, Akbarsha MA, Rao MV. Antidiabetic activity of leaf and callus extracts of *Aegle marmelos* in rabbit. *ScienceAsia* 34(3), 317–321 (2008).
- Arul V, Miyazaki S, Dhananjayan R. Studies on the anti-inflammatory, antipyretic and analgesic properties of the leaves of Aegle marmelos Corr. J. Ethnopharmacol. 96(1–2), 159–163 (2005).
- Kumari KDKP, Weerakoon TCS, Handunnetti SM, Samarasinghe K, Suresh TS. Anti-inflammatory activity of dried flower extracts of *Aegle marmelos* in Wistar rats. J. Ethnopharmacol. 151(3), 1202–1208 (2014).
- 57. Behera J, Mohanty B, Ramani Yr, Rath B, Pradhan S. Effect of aqueous extract of *Aegle marmelos* unripe fruit on inflammatory bowel disease. *Indian J. Pharmacol.* 44(5), 614 (2012).
- Kamaraj C, Kaushik NK, Rahuman AA, Mohanakrishnan D, Bagavan A, Elango G et al. Antimalarial activities of medicinal plants traditionally used in the villages of Dharmapuri regions of South India. J. Ethnopharmacol. 141(3), 796–802 (2012).
- Kettawan Aikkarach, Wongsansri Kanokkarn, Chompoopong Supin, Rungruang T. Antioxidant and antiplasmodial activities of *Curcuma longa* and *Aegle marmelos* on malaria infeced mice (*in vitro* and *in vivo*). Siriraj Med. J. 64, 78–81 (2012).
- 60. Angajala G, Pavan P, Subashini R. One-step biofabrication of copper nanoparticles from *Aegle marmelos* Correa aqueous leaf extract and evaluation of its anti-inflammatory and mosquito larvicidal efficacy. *RSC Adv.* 4(93), 51459–51470 (2014).
- Gheisari HR, Amiri F, Zolghadri Y. Antioxidant and antimicrobial activity of Iranian Bael (Aegle marmelos) fruit against some food pathogens. Int. J. Curr. Pharm. Res. 3(3), 85–88 (2011).
- Behera P, Raj VJ, Basavaraju R. Phytochemical and antimicrobial activity of fruit pulp of *Aegle marmelos. J. Chem. Pharm. Res.* 6(8), 319–326 (2014).
- 63. Gavimath CC, Ramachandra YL, Rai SP, Sudeep HV, Ganapathy PS, Kavitha BT. Antibacterial activity of *Aegle marmelos* Correa leaves extract. *Asian J. Bio Sci.* 3(2), 333–336 (2008).
- 64. Rejiniemon TS, Arasu MV, Duraipandiyan V, *et al.* In-vitro antimicrobial, antibiofilm, cytotoxic, antifeedant and larvicidal properties of novel quinone isolated from *Aegle marmelos*(Linn.) Correa. *Ann. Clin. Microbiol. Antimicrob.* 13(1), 1–9 (2014).
- Shrivastava V, Roy A. In vitro Antioxidant activity and phytochemical screening of Aegle marmelos extracts. Res. J. Pharmacogn. Phytochem. 4(2), 80 (2012).
- 66. Panth N, Paudel KR, Parajuli K. Reactive Oxygen Species: A Key Hallmark of Cardiovascular Disease. Adv. Med. 2016, 1–12 (2016).
- Pynam H, Dharmesh SM. Antioxidant and anti-inflammatory properties of marmelosin from Bael (*Aegle marmelos* L.); Inhibition of TNF-α mediated inflammatory/tumor markers. *Biomed. Pharmacother.* 106, 98–108 (2018).
- 68. Srivastava AK, Singh VK. Anti-Fertility Role of Aegle marmelos (Bael). J. Appl. Heal. Sci. Med. 2(2), 21-25 (2022).
- There is an reference addressing the spermatogenic activity.
- Kumar BS, Rao KM, Madhusudhan K, Reddy MK, Prasad MK. Isolation and evaluation of antifertility activity of total alkaloids from leaves of *Aegle marmelos* in male albino rats (rattus norvegicus). *International Journal of Applied Biology and Pharmaceutical Technology* 2(3), 178–183 (2011).

- Chauhan A, Agarwal M, Kushwaha S, Mutreja A. Suppression of fertility in male albino rats following the administration of 50% ethanolic extract of *Aegle marmelos. Contraception* 76(6), 474–481 (2007).
- 71. Sharma GN, Dubey SK, Sati N, Sanadya J. Ulcer healing potential of *Aegle marmelos* fruit seed. *Asian J Pharm Life Sci.* 1(2), 172–178 (2011).
- 72. Kumar TM. Exploring antibacterial & antiulcer activity of *Aegle marmelos* linn: a review. *Int. J. Pharm. Chem. Anal.* 7(3), 107–112 (2020).
- 73. Ramakrishna YG, Savithri K, Kist M, Devaraj SN. *Aegle marmelos* fruit extract attenuates Helicobacter pylori Lipopolysaccharide induced oxidative stress in Sprague Dawley rats. *BMC Complement. Altern. Med.* 15, 375 (2015).
- 74. Badam L, Bedekar SS, Sonawane KB, Joshi SP. *In vitro* antiviral activity of bael (*Aegle marmelos* Corr) upon human coxsackieviruses B1-B6. *J. Commun. Dis.* 34(2), 88–99 (2002).
- 75. Balasubramanian G, Sarathi M, Kumar SR, Hameed ASS. Screening the antiviral activity of Indian medicinal plants against white spot syndrome virus in shrimp. *Aquaculture* 263(1–4), 15–19 (2007).
- Rana BK, Singh UP, Taneja V. Antifungal activity and kinetics of inhibition by essential oil isolated from leaves of *Aegle marmelos. J. Ethnopharmacol.* 57(1), 29–34 (1997).