

Aegle marmelos (L.): An underutilized plant with incredible pharmaceutical and nutritional potential

Meena Yadav^{a,*}, Anshu Rana^b

^a Department of Zoology, Maitreyi College, University of Delhi, Delhi, India

^b Department of Nutrition Biology, Central University of Haryana, Mahendergarh, India

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ABSTRACT

Aegle marmelos (L.) or bael has a long history of use in traditional medicine across Southeast Asia, with roots in the ancient Indian traditional medicinal system- *Ayurveda*. It has therapeutic characteristics in all of its parts, notably the fruits, leaves, roots, stem, and bark. The plant has a plethora of bioactive compounds which account for its medicinal properties such as antibacterial, anti-inflammatory, antioxidant, antidiabetic, antidiarrheal, anticancer, diuretic and antiulcer activity. In this review, comprehensive information about the plant like its therapeutic properties, with focus on the mechanisms of action of bioactive components and their pharmacological efficacy towards variety of chronic diseases is provided. Its nutritional value along with its potential to be used as a food supplement and a source of nutraceuticals to address nutritional deficiencies is also discussed. Given its underutilization and limited research, there is an urgent need to increase its awareness among masses and propagate its ethnopharmacological significance to people, especially in low-income countries, as it has huge potential to provide pharmacological drugs and nutraceuticals. Conservation efforts are required as it has been listed as 'near threatened' in the IUCN Red list, and also it needs to be propagated for benefit of larger population.

1. Introduction

Plethora of plants has been used in traditional medicinal practices in India and other Asian countries. Among medicinal plants, *Aegle marmelos* (L.) Correa (Family Rutaceae), commonly known as bael in northern India, has been used in traditional medicinal practices for >5000 years in India (Baliga et al., 2011) (Fig. 1). It is native to India, Bangladesh, Nepal and Pakistan, but is also found in Thailand, Malaysia, Sri Lanka, Cambodia, the Philippines, Myanmar, Java, and other southeast Asian countries (Asghar et al., 2016; Plummer, 2020). Bael has various names in different Indian languages, such as Bilva, Shivaphala in Sanskrit; Bel, Beli, and Belgiri in Hindi; Belo in Oriya; Bel in Assamese and Marathi; and Vilva marum in Tamil in India. Other names for bael include Be Li in Sinhalese, Matoom in Thai, and Bela in Spanish. Many more vernacular names exist for *A. marmelos* (L.) in different countries (Rasool & Dehghan, 2022).

A. marmelos (L.) (AM) has mythological significance in Hindu religion. The leaves of this sacred plant, vernacularly known as 'Tripatra', have been an essential component of the offerings to Lord Shiva (Ladaniya, 2023), hence, it is extensively planted in temples, which could be a reason for its use in traditional medicinal practices in India.

The therapeutic potential of bael is mentioned in ancient Hindu sacred texts - Rig Veda (ऋग्वेदः), Charak Samhita (चरक संहिता), and Yajur Veda (यजुर्वेदः) (Singh et al., 2019; Tiwari et al., 2023). According to Charaka (1500 BCE), bael is considered to be one of the oldest and most significant medicinal plants in Ayurveda, which has been in existence for a long time and has been widely used by Indian inhabitants (Mujeeb et al., 2014). Bael is known to balance three doshas in Ayurveda i.e., 'vata', 'pitta' and 'kapha' (Tiwari et al., 2023). Thus, bael has been known since ancient times for its therapeutic and nutritional properties.

Recent studies have reported the useful phytochemicals isolated from bael having pharmaceutical properties (Baliga et al., 2013; Hazra et al., 2017; Bhar et al., 2019; Poonkodi et al., 2019; Hazra et al., 2020; Sarkar et al., 2020; Pathirana et al., 2020; Monika et al., 2023), and have tried to bridge the gap between its known functions and constituents. In addition to this, bael fruit can be used as a functional food and can also be used to produce nutraceuticals. Studies have reported some other useful functions also, like it acts as an adsorbent to remove heavy metals from contaminated samples, it can be used to produce biodiesel in future, its exudate gum can have multiple industrial applications, it can be used in reforestation drives to support wildlife and other key species, in dryer regions it contributes to nutrient recycling and it can be

* Corresponding author.

E-mail address: drmeena.yadav@gmail.com (M. Yadav).

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developed as a functional food (Reviewed by Pathirana et al., 2020). However, the tree remains underutilized as its presence is limited, and the lack of large-scale cultivation of the tree hinders its widespread utilization as a functional food and as source of therapeutic ingredients, despite its huge potential. The purpose of this review is to comprehend necessary facts about latest research on therapeutic and nutritional potential of *A. marmelos*, which might give directions for future research.

2. Methodology

Research papers were searched using different keywords such as 'Aegle marmelos', 'traditional medicines', 'phytochemicals', 'bioactive compounds', 'therapeutic', 'pharmacological', 'bael', 'nutritional value', 'nutraceuticals', 'anticancer', 'antidiabetic', and 'antimicrobial' in different combinations, on a variety of databases such as Google Scholar, Scopus, Google, Springer Link, and Web of Science. The papers considered for the review included those discussing therapeutic potential of bael, phytochemical composition of different plant parts, and its nutritional potential. The papers published during the last decade, in reputed journals such as those published by Springer, ScienceDirect, Taylor & Francis, Wiley Online Library, and Societies were included in the discussion, while those published by other lesser-known publishers were preferably not considered. However, some important papers that were published before the considered period, but were essential for our discussion, were also included. Information from original papers was extracted to comprehend the research in this field, however, some notable review papers were also included. Only the most appropriate papers, that met the objective of this article, were considered for discussion.

3. Current status of aegle marmelos (L.)

A. marmelos (L.) is found in tropical, arid and semi-arid regions, but it grows best in fertile and well-drained soils. Although, the plant is indigenous to India and is found in Southeast Asian countries, it has been introduced in Florida, Hawaii (Sikka et al., 2018) and China (Plummer, 2020). It has been planted extensively in wastelands as it can adapt to acidic and alkaline soils (Vasava et al., 2018). The changing land use as well as changing global climate may put a pressure on its population. The population of *A. marmelos* is decreasing due to various human activities, primarily for residential and commercial development, and also commercial exploitation of its various parts in Pakistan (Waheed et al., 2023). In India too, it is in high commercial demand (>100MT/year) (Gowthami et al., 2021). Habitat loss and limited cultivation of the plant may also contribute to its lower population in future.

According to the IUCN Red List of Threatened Species, *A. marmelos* has been assessed as Near Threatened A2acd (Plummer, 2020). The Government of India constituted the National Medicinal Plant Board (NMPB) under the Ministry of AYUSH in 2000, with one of the aims being to conserve medicinal plants. NMPB listed 32 plants on priority list for conservation, which included *A. marmelos* (Kala, 2006; Gowthami et al., 2021).

4. Phytochemical characterization of A. marmelos

The recent research on crude extracts of different parts of AM shows that it has many therapeutic properties such as antimicrobial, antiviral, anti-diarrhoeal, anticancer, antipyretic, anti-inflammatory, anti-ulcerative, diuretic, and anti-ulcerative. Despite many useful applications of the plant and its popularity for a very long time, especially in Hindu religion, the thorough analysis of its bioactive compounds (phytochemicals) has been done only recently (Tiwari et al., 2023). >100 bioactive compounds have been identified and documented in AM, and the major ones include alkaloids, coumarins, terpenoids, flavonoids, phenolic acids, polyphenols, carotenoids, organic acids, fatty acids and amino acids (Khanal et al., 2023). Rasool and Dehghan (2022) have reviewed *A. marmelos* for its phytochemical composition, nutritional value and therapeutic properties, however, the review lacks certain aspects such as mechanisms of the therapeutic properties, which we have tried to include in our review.

A high concentration of phytochemicals in *A. marmelos* accounts for its multiple health advantages. The total amount of polyphenols in AM varies according to its maturation stage (Gurjar et al., 2019). These phytochemicals have enormous health advantages, from having antioxidant features to minimizing cholesterol absorption. Caffeic acid, arbutin, chlorogenic acid, p-coumaric acid, p-coumaroyl, quinic acid, and protocatechuic acid are some handful of phenolic compounds that are present in fruit juice (Gurjar et al., 2019). The fruit also contains terpenoids, saponins, flavonoids, glycosides and tannins (Rajan et al., 2011). Leaves retain therapeutic phytochemicals in a significant proportion. Phytochemicals such as 7, 8- dimethoxy-1- hydroxyl-2-methyl anthraquinone and 6-hydroxy-1-methoxy-3-methyl anthraquinone (Srivastava et al., 1996) and skimmiaepin A and skimmiaepin C have also been isolated from AM (Samarasekera et al., 2004). A list of common phytochemicals having medicinal properties, isolated from *A. marmelos*, is available as Annexure 1.

5. Traditional uses of A. marmelos

All parts of *A. marmelos* plant such as fruits, stem, bark, and leaves, are useful as they have therapeutic and nutritional properties as well as

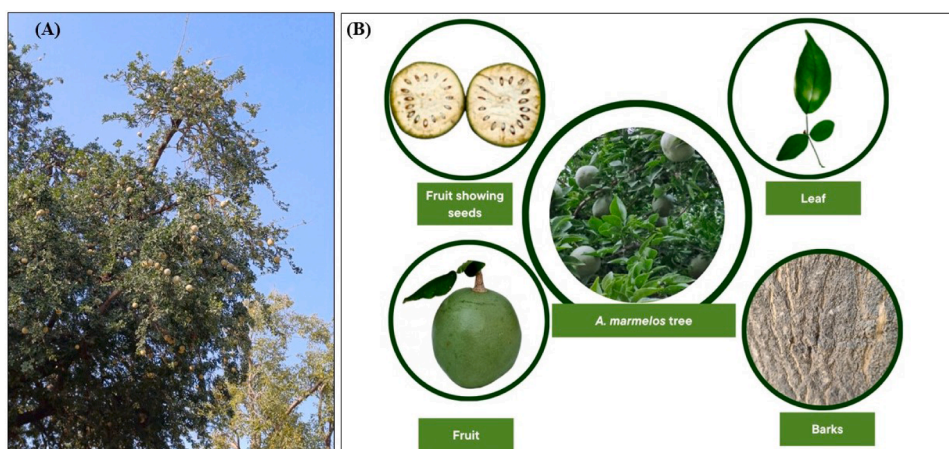


Fig. 1. *Aegle marmelos*: (A) Tree with fruits; and (B) Different parts of the tree used traditionally.

commercial importance. Its fruit, bark, leaves, flower, root and seed are capable of treating a broad spectrum of diseases in humans (Table 1). Many different kinds of tablets, pastes, and powders are produced from the plant. Bael is a key component in the creation of *dashmula* (meaning 'ten roots'; which heals colitis, dysentery, diarrhea, flatulence, and fever), chyawanprash, etc. (Kala, 2006). The unripe fruit and leaves are key components of treatments in Ayurveda for conditions like constant diarrhea, dysentery, diabetes etc. Bael leaves juice is taken in empty stomach early in the morning by diabetic patients, and it is said to reduce sugar levels in about a month (Kumar et al., 2012).

A potent cure for several mental illnesses can be found in a well-balanced mixture of the five components of AM i.e., the leaf, flower, fruit, root and bark. Fruit powder has anti-proliferative and anti-cancer properties also (Bhar et al., 2019). Unripe mature fruits are astringent, and as they become ripened, the edible pulp inside the fruit changes its coloring to yellowish/orange and develops a considerably sweeter taste, with a floral aroma and a pleasant flavor, and is consumed raw (Venthodika et al., 2021). In south India, fruit juice is given to patients for relieving wheezing and respiratory spasm. Ripened fruit is used to make sharbat (Kumar et al., 2012).

AM has several commercial uses. The fruit is a rich source of pectin known as bael fruit pectin (BFP), which is a good gelling substance and has better emulsification properties. Also, since BFP is stable and better than the commercial citrus pectin (CP), it can be exploited as an additive in pharmaceuticals and food (Jindal et al., 2013). The unripe fruit of the plant yields yellow dye which is used for tanning calico and silk fabrics by the textile industry (Mali et al., 2020). *A. marmelos* plant acts as an air purifier also by absorbing hazardous toxic gasses from the atmosphere, making them inert/neutral, and thus removing toxic pollutants. The plant is considered a 'fragrant' plant as it can neutralize bad odors (Venthodika et al., 2021).

6. Therapeutic potential of *A. marmelos*

A. marmelos is one of the primary medicinal and nutritious plants. Studies also shown many of its ethnomedicinal uses such as antibacterial, antiviral, antidiarrheal, anti-ulcerative, antioxidative, gastro-protective, hepatoprotective, antidiabetic, cardioprotective, anticancer, and radioprotective effects (Gurjar et al., 2019; Rasool & Dehghan, 2022; Jagetia et al., 2023; Khanal et al., 2023). Usage of medicinal plants like AM in traditional medicine is guided by its safety factor. AM leaf extracts do not induce toxicity with a range of doses i.e., 50, 70, 90, and 100 mg/kg body weight, so it has a high margin of drug safety (Veerappan et al., 2007). Even a dose of 250mg/kg did not show any adverse effect in animal models (Jagetia et al., 2003; Dhankhar et al., 2011). The therapeutic properties of the plant are a function of diverse phytochemicals present in different plant parts (Mujeeb et al., 2014). Some novel phytochemicals isolated from the plant and their activities have been listed in Table 2. AM holds huge potential in treatment of various medical conditions. Fig. 2 summarizes these functions and their mechanisms of actions.

6.1. Antimicrobial activity

Bacteria are one of the leading causes of diseases in humans. Several antibacterial drugs are available in the market, however, due to adverse side effects and generation of drug-resistance in bacteria, alternative treatment strategies are being explored. *A. marmelos* is known to have antimicrobial properties due to its rich phytochemical constituents. For example, AM methanolic leaf extracts show potent antimicrobial activity against Gram positive (eg. *Bacillus cereus*, *Staphylococcus aureus* and *Staphylococcus epidermidis*) and Gram negative (eg. *Enterobacter aerogenes*) bacteria (Mujeeb et al., 2014; Rejiniemon et al., 2014; Jamal et al., 2017). Petroleum ether extracts of AM show antimicrobial activity against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Streptococcus haemolyticus* group A, whereas chloroform extract is

Table 1

Some traditional uses of different parts of *Aegles marmelos*.

Plant part	Used for treating	Reference
Leaf	Jaundice, asthma	Bhar et al. (2019)
	Remove mucilage from bronchial tubes; conjunctivitis, deafness; constipation, bowel syndrome, leucorrhoea	Patkar et al. (2012); Sharma et al. (2010)
	Beri-beri	Kumar et al. (2012)
Flower	Essential oil (EO) of AM inhibits certain enzymes of clinical significance such as those linked with skin disorders, diabetes and neurodegenerative disorders.	Mahomoodally et al. (2018)
	Additionally, EO has antioxidant and antibacterial activities also	
	Cough in infants is cured by giving fresh leaf juice with black pepper; leaf decoction for treating fever;	Sharma et al. (2010)
	Fever, swellings, dysentery, vomiting, dyspepsia, seminal weakness, intermittent fever, nausea	Monika et al. (2023)
	Used for epilepsy treatment as it has astringent and antiseptic properties	Gautam et al. (2014)
Fruit	Conjunctivitis treatment using Marmala water (obtained by distillation from flower)	Mani et al. (2017)
	Wound healing	Gautam et al. (2014)
	Flowers are distilled to prepare local medicine which is an anti-dysenteric, antidiabetic, diaphoretic, and anesthetic medication; used as a tonic for the stomach and intestine; useful as an expectorant and also helpful in epilepsy	Monika et al. (2023)
	Used for treating thyroid problems; cures vomiting during pregnancy if taken with boiled rice water; abscess treatment	Kala (2006)
	Useful in treating dysentery, urinogenital disorders, intestinal ulcers, indigestion, chronic constipation,	Kumar et al. (2012)
Bark and root	Treatment of gonorrhoea, epilepsy, piles, chronic gastrointestinal disorders, rectum inflammation; lowers blood sugar levels	Dhankhar et al. (2011)
	Fruit, consumed as sherbet, can clear long accumulated fecal matter	Bhar et al. (2019); Sharma et al. (2007)
	Powdered fruit and mustard oil in a ratio of 1:2 is a good ointment for burns	Sharma et al. (2007)
	Fruit pulp used to make delicious items like murabba, puddings, and juice; used as laxative and for curing respiratory ailments; treatment for chronic diarrhea, peptic ulcers, inhibit lipid peroxidation, free radicals scavenging; has antioxidants, anti-ulcerative colitis, hepatoprotective, gastroprotective, antidiabetic, cardioprotective, radioprotective, antidiarrheal, antibacterial, and antiviral properties	Monika et al. (2023)
	Decoction of root and bark helpful in treating heart palpitation, intermittent fever and melancholia; root used in preparation of ' <i>dashmula</i> ' - an ayurvedic medicine; treatment of secretions from ear (root extract, onion and turmeric in 1:1:1 ratio)	Kala (2006)
Root	Bark decoction or leaf extract with honey is used for treatment of fever, cough, febrile and intermittent fever; bark paste applied on burns/boils	Sharma et al. (2010); Monika et al. (2023)
	Preventing heart palpitations, urinary problems, and curing fevers; relieve abdominal pain; used in preparing ' <i>dashmula</i> ' to treat fever, diarrhea, and flatulence	Monika et al. (2023)
Seed	Antidiabetic and hypolipidemic in rats	Monika et al. (2023)

Table 2Novel phytochemicals isolated from *Aegles marmelos* and their activities.

Novel Phytochemicals	Activity	Mechanism of action	Reference
Aegelin	Cardioprotective substance; antidiabetic	Antihyperglycemic activity	Monika et al. (2023)
Anthraquinone: 1-methyl-2-(3'-methyl-but-2'-enyloxy)-anthraquinone (1) (Obtained from seed)	Antifungal activity against <i>Aspergillus</i> sp. and <i>Candida albicans</i>	–	Mishra et al. (2010a)
Auraptene	Inhibits heart rate	–	Monika et al. (2023)
Cineol	Disinfectant, expectorant	–	Monika et al. (2023)
Citral	Antibacterial, antiparasitic and antifungal	Inhibits cell proliferation (G2/M phase); induces apoptosis and decreases prostaglandin synthesis	Chaouki et al. (2009)
Citronellal	Antiseptic, anticancer	–	Monika et al. (2023)
Cumin aldehyde	Insecticide	–	Monika et al. (2023)
D-limonene	Dissolves cholesterol containing gallstones; antineoplastic	–	Monika et al. (2023)
Fagarine	Antiplasmodial	–	Monika et al. (2023)
Eugenol	Cytotoxic activity against tumor cells; Antioxidant, antibacterial, analgesic	–	Slameňová et al. (2009); Monika et al. (2023)
	Antibacterial and antioxidant activity	Hepatoprotective activity against CCl ₄ induced liver damage	Kumaravelu et al. (1995); Shoba and Thomas (2001)
Flavone	Antifungal	–	Monika et al. (2023)
Imperatorin (Fucocoumarin) (Isolated from fruit)	Antibacterial (<i>Shigella dysenteriae</i>); antiviral	Inhibits copper, zinc superoxide dismutase (SOD) of <i>Shigella</i> , and causes oxidative stress	Raja et al. (2011b); Monika et al. (2023)
Lupeol	Antineoplastic effects	Cell cycle arrest at G1-S phase; decrease in <i>cyclin D1</i> , <i>D2</i> and <i>cdk2</i> expression; increase in <i>p21</i> expression; Induces apoptosis by downregulating <i>Bcl2</i> and upregulating <i>Bax</i> , <i>caspase-3</i> , <i>caspase-9</i> and <i>apaf1</i> genes	Baliga et al. (2013)
Luvangetin	Anti-ulcer	–	Monika et al. (2023)
Marmelin (1-hydroxy-5,7-dimethoxy-2-naphthalene-carboxaldehyde)	Inhibits cell proliferation in epithelial cancer cells: reduced cell survival, proliferation, and invasiveness	Cell cycle arrest at G1 phase leading to apoptosis via activated caspase-3: Activation of TNF- α , TNFR1, and TRADD mRNA and protein; activation of caspase-8 and Bid, with release of cytochrome C, a possible cross-talk between death receptor and the mitochondrial pathways; inhibition of AKT and extracellular signal regulated kinase phosphorylation	Subramaniam et al. (2008); Baliga et al. (2013)
Marmesiline (alkaloid); 6-(4-acetoxy-3-methyl-2-butenyl)-7-hydroxycoumarin and 6-(2-hydroxy-3-hydroxymethyl-3-butenyl)-7-hydroxycoumarin (coumarins); Marmelonine and 8-hydroxysmyrindiol (dihydrofuranocoumarins) (Obtained from green fruits of <i>A. marmelos</i>)	Marmelonine and 8-hydroxysmyrindiol did not show any antifungal or antibacterial activity, rest were not tested	–	Chakthong et al. (2012)
Marmin	Anti-ulcer	–	Monika et al. (2023)
Novel lectin (a dimeric protein with N-acetylgalactosamine, mannose and sialic acid binding specificity) (Isolated from fruit pulp)	Antibacterial	–	Raja et al. (2011a)
Novel phenanthrenequinone	Antibacterial and antifungal	–	Rejiniemon et al. (2014)
Polyphenols	Antigenotoxic activity	Inhibit cytochrome P 450 dependent enzymes that help in activating aflatoxin B1	Kaur et al. (2009)
Scopoletin	Inhibits thyroid functions without hepatotoxicity; Antioxidant activity	Decreases levels of thyroid hormones and glucose in serum, and glucose-6-phosphatase in liver; Inhibits lipid peroxidation in the liver; increases activity of antioxidant enzymes – SOD and catalase (CAT);	Panda & Kar (2006)
Shahidine (alkaloid)	Antibacterial	–	Jamal et al. (2017); Sarkar et al. (2020)
Skimmianine	Anticancer, antipyretic, hypothermic, antimetham; sedative, analgesic, anticonvulsive	–	Monika et al. (2023)
Xylorhamnoarabinogalactan I pectic polysaccharide - BAPP1	Anticancer	Inhibits galectin-3, immunoregulatory cytokines (interleukin 10/17 i.e., IL10/IL17) and tyrosinase	Pynam and Dharmesh (2019)
β - sitosterol	Antioxidant	–	Monika et al. (2023)
2-isopropenyl-4-methyl-1-oxa-cyclopenta[b]anthracene-5,10-dione; (+)-4-(2'-hydroxy-3'-methylbut-3'-enyloxy)-8H-[1,3]dioxolo[4,5-h]chromen-8-one;	Antimicrobial activity (isolated from seed)	Other phytochemicals isolated were: Imperatorin, β -sitosterol, Plumbagin, 1-methyl-2-(3'-methyl-but-2'-enyloxy)-anthraquinone, β -sitosterol glucoside, Stigmaterol, vanillin and Salicin	Mishra et al. (2010b)

effective against *Klebsiella pneumonia*, *Proteus mirabilis*, and methanolic extract against fungi such as *Candida albicans*, *C. tropicalis* and *Aspergillus flavus* (Kothari et al., 2010). Essential oils (EO) extracted from AM

inhibit the growth of a range of bacterial species viz. *Arthrobacter citreus*, *Salmonella typhi*, *Streptococcus aureus*, *Corynebacterium diphtheria*, *B. cereus*, *Bacillus subtilis*, *P. mirabilis*, *P. aeruginosa*, *Streptococcus faecalis*, *E.*

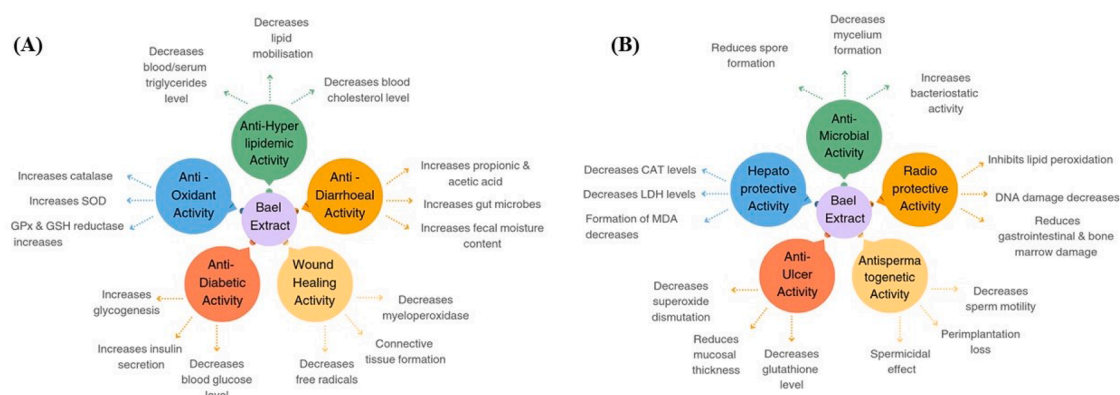


Fig. 2. (A) Mechanisms of antioxidant, anti-diarrheal, antihyperlipidemic, wound healing and anti-diabetic activities of AM extracts (SOD: superoxide dismutase, GSH: reduced glutathione; GPx: Glutathione peroxidase). (B) Mechanisms of antimicrobial, antispermatic, anti-ulcer, radioprotective and hepatoprotective activities of *A. marmelos* extracts.

coli, *Fusarium oxysporum*, *Fusarium udum*, *Ciceris A. carthami*, *Alternaria brassicae*, *Alternaria alternate*, *Colletotrichum capsici*, *Sarcina lutea*, *Ustilago cynodontis*, and *Curvularia lunata* (Ibrahim et al., 2015; Mahomoodally et al., 2018). α -phellandrene and α -pinene, the two major phytochemicals in AM essential oil, account for its bacteriostatic and bactericidal activities (Ibrahim et al., 2015). Similarly, the methanol and hexane AM bark extracts too inhibit growth of several bacterial species viz. *B. subtilis*, *E. coli*, *Enterococcus faecalis*, *K. pneumonia*, *P. aeruginosa*, *Salmonella enterica* subsp. *serovar typhi* and *S. aureus* (Nemkul et al., 2018). It is noteworthy that methanol AM extracts are effective against multidrug resistant *S. typhi*, opening gates for new drug formulations (Rani & Khullar, 2004).

The AM fruit juice inhibits growth of *Enterococcus faecalis*, *S. faecalis*, *Micrococcus luteus* and *K. pneumonia* (Rani & Khullar, 2004; Chakthong et al., 2012). Raja et al. (2011a) isolated a novel lectin from AM fruit pulp which inhibited hemagglutination of *Shigella dysenteriae* (MIC = 0.625 μ g/well). The lectin has N-acetylgalactosamine, sialic acid and mannose binding specificity, and inhibited the adherence and invasion of *Shigella* to HT29 cells. Additionally, Raja et al. (2011b) isolated another novel compound imperatorin, a fucocoumarin, from aqueous extract. Imperatorin inhibited copper, zinc SOD in *Shigella* due to which the bacterium succumbed to oxidative stress. Antimicrobial activities of AM seeds and leaves have been documented against the NK 65 strain of *Plasmodium berghei* (Dhankhar et al., 2011). The antimicrobial effects of AM extract on microbes causing diarrhea have been discussed in Section 6.4.

AM extracts are useful in managing bacterial infections in aquaculture. AM leaf extract increased the chances of survival of the freshwater fish *Cyprinus carpio* infected with *Aeromonas hydrophila* Chester. The survival rate became extremely high with a dosage of 5g/kg body weight. This might be due to increase in phagocytic activity, lysosomal activity, white blood cells, red blood cell count, haemoglobin levels, and high pathogen clearance (Pratheepa et al., 2010).

In addition to bacteria, AM extracts also inhibit the growth of other organisms also such as viruses and fungi. Marmelide extracted from AM inhibited the growth of the virus coxsackieviruses B1–B6 by inhibiting its growth in early stages of replicative cycle i.e., during adsorption and penetration. In fact, marmelide has been found to be more effective than the antiviral drug ribavirin (Badam et al., 2002). The fruit juice has antiviral potential against Ranikhet disease virus (Dhar et al., 1968). Human immunodeficiency virus (HIV) is a dreaded virus, and AM extract showed potential anti-HIV activity. It reduced production of viral particles in CEM-GFP cells infected with HIV-1NL4.3 (Sabde et al., 2011).

Ethanol leaf extracts and leaf extract oil, reduced the production of the aflatoxin B1 by *Aspergillus flavus* (Patil et al., 2009; Singh et al., 2009). EO obtained from AM leaves shows fungistatic and fungicidal

activity against dermatophytes and *Fusarium* sp. (Rana et al., 1997). Surprisingly, the EO shows higher antifungal activity against *Aspergillus niger* and *C. albicans* than antifungal antibiotics, opening new avenues for better antimicrobial drugs. EO also inhibits spore formation in *A. niger* and *F. oxysporum* (Ibrahim et al., 2015). Aqueous extracts, and ethanol and methanol fractions show potential antifungal activities against five clinical isolates of dermatophytes i.e., *Trichophyton mentagrophytes*, *Trichophyton rubrum*, *Microsporum canis*, *Microsporum gypseum* and *Epidermophyton floccosum*. The antifungal activity of these extracts is due to presence of essential oils, and phytochemicals such as alkaloids, and condensed tannins, flavonoid glycosides, flavan-3-ol, leucoanthocyanins, phlobotannins, rutin, marmesinin, β -sitosterol and skimmianine. The antifungal activity might also be due to secondary metabolites (Balakumar et al., 2011).

AM leaf extracts also show antifilarial activity and can be used for treating filarial infections (Sahare et al., 2008). Bael powder is helpful in treating intestinal parasitic infections such as those by *Entamoeba histolytica* and *Ascaris lumbricoides* (Walker, 1995 in Sarkar et al., 2020). Methanol leaf extract shows toxic effect with 100 % mortality in adult cattle tick and larvae of *Rhipicephalus microplus* at a concentration of 0.3 %, and 100 % mortality for larvae of *Paramphistomum cervi* at 0.2 % concentration (Elango & Rahuman, 2011). The hexane and chloroform extracts of AM leaves are good ovicidal, oviposition deterrents and potential repellents of Japanese Encephalitis vector *Culex tritaeniorhynchus* (Elango et al., 2010).

There has been extensive study on the antimicrobial properties of different AM extracts, and the extracts have been found to have potent antimicrobial activities against plethora of microbes. This makes the plant extremely useful for developing preparations and/or drugs on a large scale, and at a cheaper price to address shortage of antimicrobial formulations/drugs in developing and poor countries.

6.2. Anticancer activity

A. marmelos leaf extract has shown anticancer activity in several *in vitro* studies. For example, it is effective in inhibiting growth of human tumor cell lines such as erythroleukemic HEL, T-lymphoid jurkat, melanoma Colo38, leukemic K562, breast cancer cell lines (MDA-MB 231 and MCF-7) and B-lymphoid Raji (Lampronti et al., 2003; Lambertini et al., 2004). The leaf extract inhibits cell proliferation, inhibits or prevents spread of neoplasms in Ehrlich ascites carcinoma in mice (Jageti et al., 2005), and is cytotoxic towards SKBR3 human breast adenocarcinoma cell lines (Moongkarndi et al., 2004). Some of the phytochemicals isolated from AM such as cineole, butyl p-tolyl sulfide, eugenol, marmelin, 6-methyl-4-chromanone, butylated hydroxyanisole, citral, D-limonene, and lupeol, have antineoplastic activity (Baliga et al., 2013). Phytochemicals citral, rutin, lupeol, eugenol and anthocyanins

showed chemopreventive activity when tested with cancer inducing drugs such as DMBA (7, 12-dimethylbenz (a) anthracene) and diethylnitrosamine (Husain Khan & Sultana, 2011; Gupta et al., 2012; Baliga et al., 2013). The hydroalcoholic extract of AM leaf (HEAM) exhibits anticancer and immunomodulatory activities (Verma et al., 2013). It increased the neutrophil and monocyte counts and decreased inflammatory cytokines (IL-1 β and IL-6) in N-methyl N-nitrosourea (MNU)-induced hepatocarcinogenesis in Balb/c mice. It also reduces the expression of tumor gene *p53* and anti-apoptotic gene *Bcl2*. George et al. (2014) tested the anticancer activity of petroleum ether extract of AM against Dalton's lymphoma ascites, ascites tumors and Ehrlich's carcinoma in mice. The treatment restored total white blood cell count, macrophage phagocytosis, lymphocyte proliferation, hematopoiesis, and activated CD4⁺ and CD8⁺ cells. It also increased median survival time and life span of mice. These effects of extract were due to two major phytochemicals - xanthorrhizol and marmelosin. Based on the results, George et al. (2014) strongly recommended the use of these two phytochemicals for immunocompromised cancer patients, instead of chemotherapy.

AM extract hampers cancerous growth by targeting cell division. In sea urchin eggs, AM extract inhibited progression to first cleavage division (Costa-Lotufo et al., 2005) indicating that the extract could potentially impact cell division irrespective of the cell type. AM extracts inhibited/hampered cell division in human breast cancer cell lines MCF-7 and MDA-MB-231, by increasing ER α expression due to the phytochemical lupeol (Lambertini et al., 2004). Lupeol arrests the cell cycle at G1-S phase by decreasing the expression of cyclin D1, cyclin D2, and *cdk2* (Prasad et al., 2008). A novel compound isolated from AM extract, 1-hydroxy-5,7-dimethoxy-2-naphthalene-carboxaldehyde (marmelin), induced apoptosis of HCT-116 colon cancer cells and HEP-2 alveolar epithelial cancer cells by activating tumor necrosis factor- α (TNF- α), TNF receptor-associated death domain and caspase-3. The cell cycle was arrested at G1 phase (Subramaniam et al., 2008). Another novel compound, xylohamnoarabinogalactan I pectic polysaccharide - BAPP1, can be used to treat skin cancer as it inhibits activity of galectin-3, cytokines IL10/IL17, and tyrosinases, all of which are the key targets for treatment of skin cancer. The protective effects of AM extract were observed in *in vitro* studies as well as in skin cancer models. BAPP1 also improved gut microbiota, and may be developed as a potential drug against metastasis (Pynam & Dharmesh, 2019).

The hydromethanolic bark extract of AM showed antitumor and antioxidant activity against DMBA (7,12-dimethyl benzantracene) and croton oil induced papilloma in Swiss albino mice as it reduced tumor incidences, tumor burden and cumulative number of papilloma (Gupta et al., 2016). AM leaf extract inhibited proliferation of HEP G2 cell lines of hepatocellular carcinoma by preventing action of matrix metalloproteinases (MMPs) (MMP-2 and -9) (Sushmitha et al., 2021). These studies suggest AM extracts have potential to be used for anticancer treatments, as complementary and alternative medicine, as many of its bioactive compounds arrest cell cycle via different signaling pathways, selectively acting on dividing cells (cancer cells).

6.3. Antidiabetic activity

The AM leaf extracts have potential to be used in management of diabetes in the long-term. Aqueous extract of AM leaves causes hypoglycemia, enhances antioxidation *viz.* increases erythrocyte glutathione (GSH) levels, and decreases malondialdehyde (MDA) and glutathione transferase (GST) levels (Upadhyaya et al., 2004). Treatment of streptozotocin induced diabetic Wistar rats with aqueous leaf extract showed hypoglycemic effects *viz.* it reduced blood glucose levels, plasma thiobarbituric acid reactive substances (TBARS), ceruloplasmin, hydroperoxides and α -tocopherol while increased GSH and Vitamin C levels. Similarly, the methanolic leaf extract also shows hypoglycemic effects as observed in alloxan induced diabetic rats (Sabu & Kuttan, 2004).

The antidiabetic effect of AM fruit extract was more effective than

the antidiabetic drug glibenclamide (Kamalakkannan & Prince, 2003), the effect being due to its antioxidant activity (Abdallah et al., 2017). The reported studies for antidiabetic role of AM extracts are limited, hence, further studies are necessary to understand their mechanisms of action, which might open new windows to manage this global disease.

6.4. Antidiarrheal activity

The *A. marmelos* fruit, due to its astringent properties, has been frequently and traditionally used for the treatment of chronic diarrhea and dysentery, most effective being when used as dried fruit powder. Consumption of fruit powder is beneficial in diarrhea as it gradually makes the stool solid, and blood and mucus also disappear over time (Kumar et al., 2012). The pulp of unripe fruit has been potentially effective against production of enterotoxins by pathogenic bacteria and inhibits bacterial gut colonization (Brijesh et al., 2009; Rahman & Parvin, 2014; Sarkar et al., 2020). Bael decoction inhibits colonization of *E. coli* E134 and *Shigella flexneri*, the causative organisms of diarrhea (Rakulini & Sounthararajan 2019). Traditionally, bael juice, leaf, dried fruit pulp, aqueous extract of unripe fruit have been known to have anti-diarrhoeal properties (Joshi et al., 2009; Sekar et al., 2011; Rakulini & Sounthararajan, 2019). The unripe fruit extract reduces inflammation in case of inflammatory bowel disease (IBD). The inflammation is reduced due to inhibition of immunomodulatory cytokines (IL1, IL6, IL8) and TNF- α (Jagtap et al., 2004).

In addition to *E. coli* and *Shigella* spp., the antidiarrheal activities of AM have been confirmed against *Vibrio cholerae*, and *Entamoeba histolytica* (Mazumder et al., 2006; Brijesh et al., 2009; Joshi et al., 2009; Das et al., 2022). More specifically, AM extract shows strong inhibitory activity against *Shigella sonnei*, *S. boydii* and *S. flexneri* while it moderately inhibits *S. dysenteriae* (Mazumder et al., 2006). Chloroform extract of AM root is equally effective as ciprofloxacin, a drug used to treat bacterial infections (Rahman & Parvin, 2014). Tannin found in unripe fruit extracts has astringent properties and is a good remedy for diarrhea (Shoba & Thomas, 2001). Thus, the antidiarrheal activity of AM extract is actually due to its inhibitory action on pathogens *i.e.*, antimicrobial activity.

6.5. Anti-Inflammatory activity

Inflammation is the manifestation of an underlying infection/medical condition. Histamine release is one of the characteristics of inflammation, and the alcoholic extracts of AM have been shown to inhibit the histamine induced contractions (Surekha et al., 2021). Lupeol, skimmianine, and citral are anti-inflammatory compounds present in AM extracts that mediate histamine-mediated signaling (Geetha & Varalakshmi, 2001). The root bark extracts show anti-inflammatory activity due to skimmianine and lupeol (Benni et al., 2011). Two other compounds in AM extract, β -caryophyllene and caryophyllene oxide, also show anti-inflammatory effects against lymphoma and neuroblastoma cells, by upregulating pro-apoptotic genes, and downregulating anti-apoptotic genes (Sain et al., 2014). The dried flower extract of AM was found to show optimum anti-inflammatory effects in Wistar rats (Kumari et al., 2014). Treatment with unripe fruit extract showed a dose-dependent reduction in intestinal inflammation in rats with inflammatory bowel disease, with reduced MDA levels and increased SOD activity (Behera et al., 2012). An extensive study was done by Rajaram et al. (2018) to study anti-inflammatory activity of extracts of young roots and mature parts of AM plants collected from different regions of India. They tested a total of 191 extracts, out of which 44 extracts inhibited cyclooxygenase-2 (COX-2), and 38 inhibited COX-1. The young root extracts from plants collected from Gujarat and Odisha showed most potent anti-inflammatory effects. Their results suggested that the age of plants and the region in which they are grown play an important role in deciding their anti-inflammatory activities.

6.6. Antioxidant activity

The antioxidant activity of *A. marmelos* is due to the presence of phytochemicals - anthocyanin, coumarin lignans, steroids, flavones, isoflavones, flavonoids, tannins, catechins and isocatechins (Mujeeb et al., 2014; Kumar et al., 2016; Veer & Singh, 2019). Compared to ripe fruit, unripe fruit exhibits higher percentage of free radical inhibition i.e., has more antioxidant property (Rajan et al., 2011; Gupta et al., 2018; Rasool & Dehghan, 2022), so unripe fruit can be used as a natural treatment for free radical induced damage and also as an adjuvant with other drugs to increase effectiveness of the treatment (Gupta et al., 2018).

Powdered fruit pulp is a good source of antioxidants and acts by inhibiting lipid peroxidation (Rahman et al., 2024). Bael fruit powder is a good alternative to reduce free cholesterol and ester cholesterol levels (Jagetia et al., 2003). Leaves are also a rich source of antioxidants such as ascorbic acid, polyphenols and β -carotene (Kumar et al., 2016; Perumal et al., 2018). In fact, leaves have higher antioxidant and total phenolic content than fruits (Wali et al., 2016). 50 % ethanolic extract of leaves reduces the lipid peroxidation and increases the levels of hepatic antioxidants such as SOD, CAT and glutathione (Chockalingam et al., 2012).

The methanolic extract of AM leaves reduces the oxidative stress as observed in alloxan induced diabetic rats. Lipid peroxidation, conjugated diene and hydroperoxide levels were reduced in serum and liver; activity of CAT and GPx was increased from Day 9 onwards, while SOD and glutathione levels increased on Day 12 in diabetic rats (Sabu & Kuttan, 2004). Likewise, the aqueous fruit extract of AM increased the levels of GPx, SOD, CAT, and glutathione content in streptozotocin diabetic rats. The fruit extract was more effective in reversing the drug induced diabetic effects than the drug glibenclamide (Kamalakkannan & Prince, 2003). Thus, AM extracts are rich source of antioxidants and have potential to be developed as natural and conjugate treatment alternative for diseased conditions primarily facilitated by reactive oxygen species (ROS).

6.7. Anti-ulcer activity

AM extracts have been used to treat ulcers in traditional medicinal practices. Experimental studies in the past few decades have provided evidences for it. For example, the methanolic and aqueous seed extracts showed anti-ulcer effects in pylorus ligation induced ulcers. This effect might be due to flavonoids in AM seeds (Sharma et al., 2011). AM fruit pulp extracts also showed anti-ulcer effects on aspirin-induced gastroduodenal ulcers in rats, as fruit extract is a rich source of antioxidants which reversed the damage caused by aspirin (Das & Roy, 2012). Similarly, the anti-ulcer activity of aqueous leaf extract is also due to its ability to upregulate the antioxidant mechanism (Madhu et al., 2012).

The 50 % ethanolic extract of dried fruit pulp treatment showed curative effects due to its antibacterial activity against intestinal pathogens in 2,4,6-trinitrobenzene sulfonic acid (TNBS)-induced colitis in rats, and promoted colonic antioxidant mechanism and reduced colon damage due to free radicals and myeloperoxidase (MPO) (Ghatule et al., 2014). The traditional use of bael extracts for treating ulcers can be developed further as many of its constituents having anti-ulcer activity have been identified. It has huge potential to be developed as an alternative medicine for ulcer treatment.

6.8. Diuretic activity

Diuretics are used in medical conditions such as hypertension and edematous disorders, to increase excretion of sodium and water in urine. The organic extract of ripe fruit increases urine output and sodium excretion in urine. The plant can be explored for developing treatments for hypertension, heart failure, liver failure or any other edematous condition (Singh et al., 2013). Tapping of this property of *A. marmelos*

would be useful in addressing several diseases.

6.9. Hepato-, renal- and cardio-protective activity

Traditional uses of AM extracts have shown that the plant has protective functions for liver, heart and kidney. Experimental evidences have confirmed these practices to some extent, however, a lot still needs to be discovered. For example, pre-treatment with whole plant methanolic extract protected rats from CCl₄-induced liver toxicity by reducing lipid peroxidation, and activity of xanthine oxidase, and serum toxicity markers such as serum glutamic-oxaloacetic transaminase (SGOT), serum glutamate pyruvic transaminase (SGPT) and lactate dehydrogenase (LDH). Antioxidant parameters i.e., glutathione reductase (GR), GSH, GPx, CAT and quinone reductase (QR), were improved by extract treatment (Khan & Sultana, 2009). Similarly, AM leaf extract is effective in treating doxorubicin (DOX)-induced hepatotoxicity (Panda & Kar, 2009). The leaf extract treatment reduced TBARS levels, GPx levels, but it improved glutathione levels, SOD activity, CAT activity, and Vitamin E and C levels in alcohol induced liver injury in albino rats (Singanan et al., 2007). Some other studies have also reported hepato-protective effects of bael extracts (Singh et al., 2000; Singh & Rao, 2008; Khan & Sultana, 2009; Rathee et al., 2018).

Diabetic nephropathy (DN) is a complex and severe complication of diabetes and its prognosis is mostly fatal. AM leaf extracts protected rats from alloxan induced DN, by reducing fasting blood sugar, blood urea, total cholesterol, creatinine and renal TBARS. It increased the levels of GSH and CAT, strengthening the antioxidant status. Overall, it decreased tubular dilation, glomerular expansion, and inflammatory cells (Bhatti et al., 2013). The nephroprotective activity of bael extract is actually by reducing oxidative stress (Ahmad et al., 2016).

AM extracts also show protective effects for heart. For example, leaf extract decreased the levels of LDH and creatine kinase (CK) in the heart in isoprenaline induced myocardial infarction (MI) in rats. Pretreatment with leaf extract increased Na⁺-K⁺ ATPase activity and decreased Ca²⁺ ATPase in heart and aorta, respectively. It decreased cholesterol and triglyceride levels while increased phospholipids in heart and aorta. Thus, all the parameters disturbed by isoprenaline treatment were restored with leaf extract pretreatment (Prince & Rajadurai, 2005). A drug, isoproterenol (ISO) induces myocardial infarction. Treatment with ISO (85 mg/kg body weight) increased the levels of plasma nitric oxide, C-reactive protein, cardiac tissue lipid peroxidation, homocysteine, apolipoprotein B, and liver 3-hydroxy-3-methyl glutaryl CoA reductase activity, while decreased activity of lipase, paraoxonase-1 and cardiac tissue taurine levels. Pretreatment of ISO treated rats with AM fruit extract for 45 days restored the levels of the above parameters to near normal, and thus, showed strong cardioprotective activity (Krishna et al., 2017). DOX is a drug used in chemotherapy, but it shows adverse effects including cardiotoxicity. Treatment of rats with DOX increased the activity of serum creatine kinase-MB (CK-MB), SGPT and tissue lipid peroxidation (LPO), while it decreased activities of SOD, CAT and GSH. The serum lipids were increased and high-density lipoprotein (HDL) levels were decreased. Panda and Kar (2009) tested whether cardiotoxicity and hepatotoxicity induced by DOX can be countered by the use of a cardenolide - periplogenin, isolated from AM leaves. They observed that cotherapy (DOX and AM leaf extract therapy) reversed the adverse effects of DOX in 4 weeks. The therapeutic efficacy of periplogenin was found to be better than vitamin E (α -tocopherol) (Panda & Kar, 2009). The malfunctioning of liver, kidney and heart are quite common these days due to changes in the food habits and lifestyle. AM extracts have potential to be developed into formulations that could be used as an alternative form of treatment for the medical conditions arising due to their malfunctioning. Looking at the cost of manufacturing and other expenses, these formulations would certainly be cheaper alternatives than the regular drugs.

6.10. Wound healing effect

Healing of wound occurs in four stages - coagulation, inflammation and debridement of wound, cellular proliferation and repair, and tissue remodelling and collagen deposition. The methanolic leaf extract of AM accelerates wound repair in *excision* and *incision* wounds (Jaswanth et al., 2001; Toppo & Pawar, 2016). The phytochemicals such as flavonoids, alkaloids, sterols, and EO found in *A. marmelos* are immensely efficient for wound treatment as they enhance the antioxidant activity. These components additionally enhance the rate of epithelization, wound contraction, tensile strength, and the hydroxyproline content which increases the efficacy of wound healing (Sarkar et al., 2020). The methanolic seed extract effectively healed the wound in Wistar albino rats. Granulation tissue showed increased levels of antioxidants (glutathione, SOD and CAT) and collagen determinants, while levels of myeloperoxidase and oxidative stress markers were decreased. The fruit extract also showed enhanced wound healing by a similar mechanism (Gautam et al., 2014). The AM extract is as effective in wound healing as the drug nitrofurazone (Veerappan et al., 2007). Thus, it offers a natural treatment option for wound healing.

6.11. Antipyretic activity

AM extracts have been found to be effective in their antipyretic actions. Ethanolic and aqueous leaf extracts showed significant antipyretic effects in Brewer's yeast induced pyrexia, in dose dependent manner, as they significantly reduced the body temperature. In fact, the antipyretic effects were comparable to that of paracetamol (Jyothi et al., 2024). The methanolic extract of dried ripe fruit showed central and peripheral analgesic effect *in vivo*. Hence, it can be used to prepare herbal preparations to treat pain disorders safely and effectively (Yaqeen et al., 2015). Methanolic leaf extract showed similar analgesic effects in rats (Shankarananth et al., 2007). Thus, AM leaf extracts could be developed as a cheaper alternative for the regular antipyretic drugs.

6.12. Antihyperlipidemic activity

AM unripe fruit pulp has been reported to decrease the lipid levels in Type 2 diabetic patients (Aziz et al., 2024). Administration of aqueous leaf extract to streptozotocin induced diabetic rats reduced lipid profile *i.e.*, lowered total cholesterol, triglycerides, high density lipoproteins (HDL), low density lipoproteins (LDL) and very low-density lipoproteins (VLDL) in diabetic rats as compared to control diabetic rats (Devi et al., 2010). Triglyceride dissolution decreased blood cholesterol levels, potentially due to fat transport from adherent adipose tissue. 50 % ethanolic leaf extract significantly reduced the serum cholesterol and triglyceride levels in hyperlipidaemic rat models (Triton WR 1339 treated and diet-induced) (Vijaya et al., 2009). AM extracts can potentially improve lipid profile, however, more research is needed to identify the phytochemicals responsible for it and their mechanism of action.

6.13. Antifertility activity

The leaf, fruit and seed of *A. marmelos* affect the male fertility. Agrawal et al. (2012) tested the effect of methanolic bark extract on male fertility in rats, and observed dose and duration dependent reduction in testosterone levels and reduced weight of testes and seminal vesicles. These characteristics indicated reduced male fertility. Semen quality parameters such as sperm density, motility, viability and acrosomal integrity were also reduced. During histopathological study, they observed exfoliation of elongated spermatids, nuclear chromatin condensation and degeneration, and prominent spaces within germinal epithelium indicating testicular toxicity. However, after the extract treatment was withdrawn, the rats showed restoration of fertility (morphological and physiological) over a period of time. This study, and another study by Chauhan and Agarwal (2008) with 200 and 300 mg/kg

doses of leaf extract, confirmed antifertility effects of AM. They associated antifertility effects of AM extracts to two phytochemicals - marmarin and fagarine. Another, important observation was that the fertility could be completely restored after withdrawal of AM extract treatment, hence, effects of *A. marmelos* on fertility are reversible (Agrawal et al., 2012). AM leaf extract shows dose dependent drop in sperm motility *i.e.*, from progressive to non-progressive movement, and finally becoming immotile at 100 µg/ml (Gunasekaran et al., 2023). Due to the antifertility effects of AM extracts, and the fact that the effects are reversible, AM extracts may be considered as an alternative to produce effective male contraceptives, an area where efforts have largely failed.

6.14. Antigenotoxic activity

Since AM extracts show antioxidant, anti-cancer and anti-inflammatory effects, in addition to other effects, it is but natural to think that they might also be toxic to the genetic material. In this line, Kaur et al. (2009) tried to find if AM extracts did have any genotoxic effects or not. They checked the effects of methanol, acetone and aqueous extracts of *A. marmelos* in human lymphocytes and *E. coli*. They found that all the extract preparations were non-genotoxic as they had IF (induction factor) values <1.5. In fact, they could effectively reduce the IF induced by mutagens - H₂O₂ and S9 dependent Aflatoxin B1. The antigenotoxic activity of *A. marmelos* might be attributed to polyphenols present in its extracts. Pre-treatment of mice, which were exposed to DOX (a chemotherapeutic anticancer drug), with AM extracts, reduced the DOX-induced genotoxicity in its bone marrow, which was evident from the reduced frequency of micronucleated polychromatic erythrocytes (MPCE) and micronucleated normochromatic erythrocytes (MNCE) (Venkatesh et al., 2007). The protective effect of extract might be due to inhibition of free radicals and improved antioxidant status.

6.15. Radioprotective activity

Treatment strategies of many diseases such as cancer make use of radiotherapy, which not only affect the target diseased cells but also harm the neighboring healthy cells. Hence, as a protective measure, radioprotective compounds can be used that protect the healthy cells. The harmful effects of radiation are generally mediated by generation of free radicals or ROS, hence using natural antioxidant compounds would be a good strategy (Baliga et al., 2010). Ionizing radiations not only damage DNA but they also cause widespread damage by generating ROS (Ren et al., 2023). Bael leaves and fruit have natural free radical scavenging activity (Pathirana et al., 2020), as injection of bael extract before irradiation reduces lipid peroxidation in cells (Jagetia et al., 2003).

Jagetia et al. (2004) studied the protective role of AM leaf extracts on radiation induced harm to mice. They pretreated mice before exposing them to various doses of radiation *i.e.*, 6–11 Gy ⁶⁰Co γ-radiations. Treatment with AM extracts reduced severity of radiation sickness and enhanced the dose dependent survival rate, with mice surviving radiations as high as 10 Gy. Radioprotective effects of AM extract treatment were due to free radical scavenging, arrest of lipid peroxidation and increase in glutathione levels (Jagetia & Venkatesh, 2005). AM leaf extract also reduces the DNA damage caused due to radiation in human peripheral blood lymphocytes and mouse bone marrow cells *in vitro* (Jagetia & Venkatesh, 2007). Bael leaf extracts show better results than bael fruit extracts in offering protection from radiations (Baliga et al., 2013). Thus, bael extracts have potential to be used as an alternative to alleviate the side effects of radiation therapy, especially in cancer treatment.

6.16. Anthelmintic activity

Development of resistance to commonly used anthelmintics has paved way to search for alternative methods. The aqueous and

methanolic extracts of AM show anthelmintic activity, as they inhibit hatching of eggs and larval development (Soni et al., 2023). EO extracted from leaves and rind of AM are also anthelmintic, as they penetrate the skin of worms and cause blood vessel constriction leading to killing of worms (Mehmood et al., 2024). The anthelmintic activity of AM was also observed in *Pheretima posthuma*. The ethanolic extracts were found to be more impactful than aqueous extracts, with flavonoids being primarily responsible for this function (Sridhar et al., 2014). The usage of natural anthelmintics holds potential as an alternative method to treat parasitic infections in humans, livestock and pet animals.

7. Nutritional value of *A. marmelos*

Underutilized fruits such as *A. marmelos* fruits are primary source of support for poor people. Various products of AM such as fruits, powders and nutraceuticals, not only help fight hidden hunger, but poverty and malnutrition as well (Rahman et al., 2024; Ritika et al., 2024). The fruit of *A. marmelos* is rich in various nutrients such as carbohydrates (sugar and glucose), vitamins, fatty acids, minerals and amino acids (Bhardwaj & Nandal, 2015). The food value of bael is 88 cal/100g which is much better than other common fruits such as guava (59 cal/100g), apple (64 cal/100g), and mango (36 cal/100g) (Sekar et al., 2011; Bhardwaj & Nandal, 2015). It also has good fibre content (hemicellulose, cellulose, lignin, pectin), and 61 % moisture content (Gupta et al., 2018). The fruit is rich in vitamins such as vitamin A, vitamin C and vitamin B group (B1, B2, B3) which makes it a good antioxidant and also prevents rancidity and loss of color (Bhardwaj & Nandal, 2015; Khanal et al., 2023). The edible part of fruit contains minerals such as iron, phosphorus, copper, zinc, potassium, calcium, magnesium and their salts (Sarkar et al., 2020; Khanal et al., 2023). The rich source of nutrients in bael makes it an excellent food source for recommended diets (Gurjar et al., 2019; Bhattacharjee et al., 2020; Rahman et al., 2024). Region wise differences in nutrients are also there. For example, fruit pulp from countries such as India, Pakistan and Bangladesh, contains different concentrations of carbohydrates (Sharma et al., 2022). In Karachi, Pakistan, the moisture content in leaves, fruit and seeds was found to be approximately 71 %, 63 % and 53 % respectively. Among the vitamins, vitamin C was present in highest proportion (73.2 mg%) in fruits. Seeds were rich in proteins with nine essential amino acids, and fruit pulp was rich in carbohydrates, vitamins C, B1, B2 and B3. The leaves had all nutrients that seed and fruit possessed, hence were consumed fresh also (Lakht-e-Zehra

et al., 2015).

The phytochemical and nutritional components of bael (Fig. 3) are involved in a variety of biochemical processes inside our body which makes it a potential food ingredient. Fruit can be processed in multiple ways to produce various nutraceuticals. There are considerable changes in the nutritional composition at different stages of ripening and maturity of fruit. The unripe fruit is richer in nutrients than ripened fruit, hence the former is a better choice for processing for food and nutraceutical products (Bhattacharjee et al., 2020; Gurjar et al., 2019; Riaz et al., 2022). Plant nutraceuticals have both nutritional and pharmaceutical properties. They not only act as alternative and rich food sources, but also improve efficacy of the treatment when used alongside traditional medical procedures. They have been found useful as supplements for complex diseases such as cancer, obesity, celiac disease (Al-Odat et al., 2024; Guzmán-Carrasco et al., 2024; Jahdkaran et al., 2024) and also improve gut microbiota in humans (Kunnummal et al., 2024).

Fruit processing entails both fruit preservation and various food applications for consumption. Fruit quality is a crucial aspect impacting the quality of processed final products, and includes its nutritive value, phytochemical content, aesthetic appeal, flavor, and texture. The conditions and quality of the raw material influence the way of end product usage. The stability of the phytochemicals is impacted by processing, coupled with nutritional and antioxidant profile deficits. Processing method and process parameter optimization can reduce phytochemical loss and assist retain the pharmacological and nutraceutical benefits of processed foods (Venthodika et al., 2021). Processing of food includes microwave drying, sun drying, hot air drying, and freeze drying. The processing changes the nutritional composition of the product as compared to the raw fruit (Hazra et al., 2020). Some food items and/or nutraceuticals obtained by processing bael fruit and pulp, and prepared with proper optimization methods to maintain its nutritive values are presented in Table 3.

8. Conclusion

The limited presence of the plant in Southeast Asia, along with a lack of awareness among masses about its remarkable properties, warrants more research on its therapeutic and nutritional potential. While working on the review, we found a comparable number of review papers and original research papers. Most of the research on elucidating the

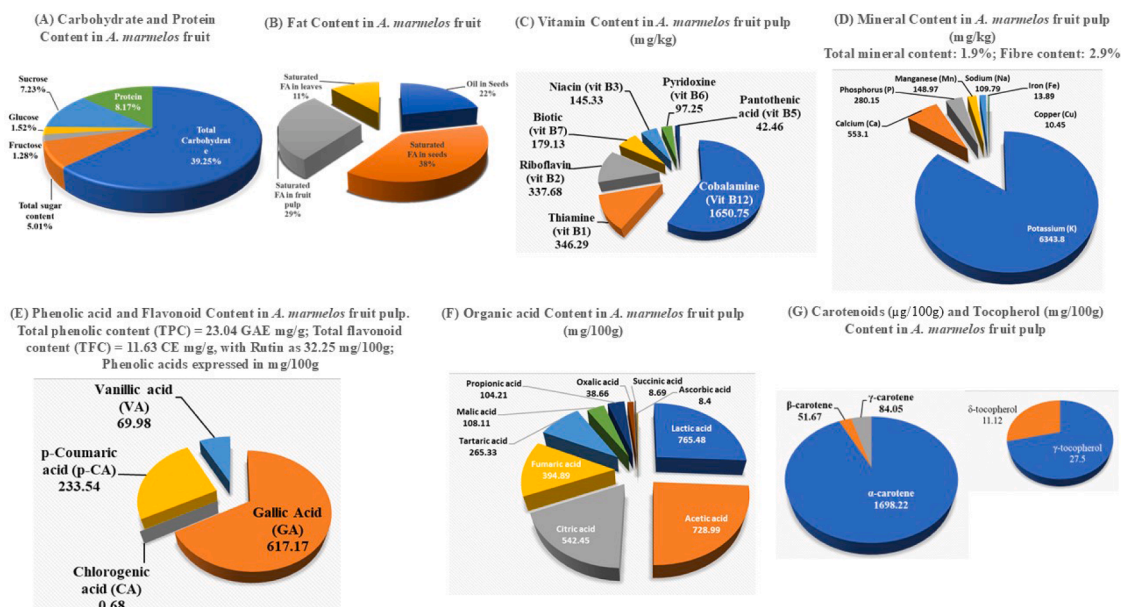


Fig. 3. A general quantitative profile of phytochemicals in fruit pulp of *A. marmelos*. Adapted from Hazra et al. (2020) and Sharma et al. (2022).

Table 3Different processed products obtained from *Aegles marmelos* fruit having nutritional value.

Plant part used	Product	Mechanism of extraction	Features	Reference
Fruit pulp	Fruit juice	Juice extracted using enzymes pectinase and cellulose	Enzymatic extraction	Anurag et al. (2014)
	Fermented fruit juice	Extraction with water and preservation by pasteurization at 80 °C	Pasteurization	Sarkar et al. (2020)
	Fruit beverage	Fermentation	Higher H ₂ O ₂ , DPPH and ABTS activity	Asghar et al. (2016)
		Extracted juice is fortified with pectin, whey protein, and carboxymethyl cellulose	Enrichment with proteins	Singh et al. (2000)
		Beverage prepared with bael fruit juice and aloe vera juice	New product: shelf life 15 days	Sarkar et al. (2020)
		Beverage prepared with bael fruit juice and fortified with lime and jaggery	New product	Ullikashi et al. (2017)
	Ready to serve (RTS) beverage	Bael juice mixed with guava juice: beverage becomes brownish, sugar and acidity increases, while vitamin C and phenolic content decreases	New product	Rakesh et al. (2007)
		Bael juice mixed with Jalgerra and tamarind juice	New product; Preservation	Sarkar et al. (2020)
		Bael juice mixed with citrus fruit juices such as sweet orange, lime, pineapple	New product; Can be preserved for up to 2 months	Sarkar et al. (2020)
	Jam	Made from bael and apple pulp: Ascorbic acid and phenolic content decreases	Functional food	Asghar et al. (2016)
		Bael fruit pulp and sugar in 1:1 ratio	New product	Ullikashi et al. (2017)
		Bael fruit pulp and mango pulp in 1:1 ratio	New product	Bhardwaj and Nandal (2015)
		Bael fruit pulp and mango fruit pulp (1:1) mixed and preserved in sugar syrup	Preservation in sugar syrup	Sarkar et al. (2020)
		Bael fruit pulp preserved in sugar syrup: 75 % sugar and 0.3 % citric acid	New product;	Sarkar et al. (2020)
	Candy	Bael fruit pulp preserved with sugar syrup in 1:1 ratio	New product	Ullikashi et al. (2017)
		Bael fruit pulp preserved with sugar syrup; enriched with cardamom, cinnamon and citric acid	New product	Jagatia et al. (2005)
	Toffee	Bael fruit pulp mixed with butter, milk powder, and preserved in sugar syrup	Heated at 100–154 °C	Anurag et al. (2014)
	Bael powder	Dehydration followed by grinding	Preservation; moisture adsorption isotherm; freeze drying	Anurag et al. (2014); Hazra et al. (2017)
Unripe fruit	Panjiri	Mix dehydrated bael fruit pulp, butter oil and sugar in a ratio of 1:1:1.5 and roast	New product: dehydration and grinding	Anurag et al. (2014); Venthodika et al. (2021)
	Wine	Bael juice fermented with yeast (7.87 % ethanol)	Medicinal wine rich in antioxidants	Sarkar et al. (2020); Venthodika et al. (2021)
	Beer	Fermented bael juice	1.75 % protein	Singh and Nath (2004)
	Bael preserve	Unripe fruit pulp, sugar and citric acid prepared for 6 days	Ayurvedic product	Sarkar et al. (2020)
		Unripe fruit pulp, sugar and water in a ratio of 1:1.25:1; boiled	New product	Anurag et al. (2014)
	Dehydrated bael preserve	Unripe fruit pulp treated with sulphur dioxide and heated at 55–60 °C	New product	Anurag et al. (2014)
Bael fruit seed	Seed oil	Extracted with ultrasonic treatment or microwaves	Biofuel	Sarkar et al. (2020)
Bael peel and pomace	Used as a cattle feed	Peel is dried and grinded	Utilizing waste	Sarkar et al. (2020)

bioactive components and their mechanism of action has been reported from India, and a handful from other Southeast Asian countries. So, clearly there are gaps in research that need to be filled. The tree is robust and can be grown in all types of soils, and it has huge potential to be used in alternative and complementary medicine along with its usefulness as a complementary food. The IUCN status of the plant is 'near threatened', and considering its huge potential as a medicinal plant, there is an urgent need to conserve and propagate the plant, which is only possible by spreading awareness about it. Although, several reviews are available on the therapeutic and nutritional properties of *A. marmelos*, majority of these have not discussed its properties or mechanisms in length. We attempted to bring all aspects about the plant together, so that current and future researchers can get a comprehensive understanding of the remarkable potential the plant holds, and to engage in meaningful research in future.

9. Limitations

As our purpose was to comprehend all the aspects of *A. marmelos*, we had to discuss the traditional uses of the plant, characterization of phytochemicals, and even its nutritional potential, which made the article little lengthy. Since, the plant has many properties which are being used to treat a plethora of human diseases, a lot of research needs to go into unfolding the hidden potential of *A. marmelos* and to bring it at

forefront for alternative treatment strategies.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.focha.2025.100935](https://doi.org/10.1016/j.focha.2025.100935).

Data availability

No data was used for the research described in the article.

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