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Medicinal and Phytopharmacological Properties of Bael Aegle marmelos correa Family Rutaceae

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Abstract

Natural products have played a pivotal role in the treatment of various ailments since time immemorial and also in the synthesis of various drugs. The present review has been written consulting various publications, Google Scholar, Pubmed, ScienceDirect, and Google search. Bael (Aegle marmelos correa) is considered a sacred tree by Hindus and is offered to lord Shiva while worshipping. It is found in the Indian subcontinent and Southeast Asia and is called by various names in different regions. Bael has been used as a traditional medicine in India and other Southeast Asian countries to treat different human disorders including diarrhea, chronic dysentery, constipation, gonorrhea, catarrh, diabetes, deafness, inflammations, ulcerated intestinal mucosa, intermittent fever, melancholia, and heart palpitation. It has been used to control fertility in humans. Phytochemical analysis has shown that Bael contains alkaloids, cardiac glycosides, anthocyanins, flavonoids, steroids, saponins, terpenoids, tannins, lignins, quinones, coumarins, proteins, carbohydrates, amino acids, reducing sugars, fat, and oils. The scientific evaluation has demonstrated that various parts of Bael inhibit the growth of bacteria, viruses, and fungi. It acts as an anti-inflammatory, antiallergic, antioxidant, and antidiarrheal agent. Various activities of Bael may be attributed to its ability to passivate different free radicals, and suppress nuclear factor-κB, tumor necrosis factor alpha, cyclooxygenase I and II, interleukins, AKT, and vascular endothelial growth factor. The scientific evaluation validates its traditional use and its potential as a future non-toxic medicine.

Keywords: *Aegle marmelos; Phytochemical; Antidiabetic; Antioxidants; NF-κB; COX-2*

Abbreviations

ABTS+·: 2,2'-Azino-Bis (3-Ethylbenzothiazoline-6-Sulfonic Acid Radical; AKT: Serine/Threonine Kinase; CNL: Cerebellar-Nodular-Lesion; COX: Cyclooxygenase; DPPH: 1,1-Diphenyl-2-Picrylhydrazyl; ERK: Extracellular Signal-Regulated Kinase; 5HT: 5-Hydroxytryptamine; IC: Inhibitory Concentration; IFN: Interferon; IL: Interleukin; NOS: Nitric Oxide Synthase; LD: Lethal Dose; LDH: Lactate Dehydrogenase; LDL-C: Low Density Lipoprotein Cholesterol; LOO: Lipid Peroxidation; LOX: Lipoxygenase; LPS: Lipopolysaccharide; MIP: Macrophage Inflammatory Protein; CMYB: V-Myb Myeloblastosis Viral Oncogene Homolog; NPs: Nano Particles; NF-kb: Nuclear Factor Kappa B; NO: Nitric Oxide; $O2^{-}$·: Superoxide Radical; ODC: Ornithine Decarboxylase; ·OH: Hydroxyl Radical; ROS: Reactive Oxygen Species; SOD: Superoxide Dismutase; STAT-3: Signal Transducer And Activator of Transcription-3; TNF-α: Tumor Necrosis Factor-Alpha; VEGF: Vascular Endothelial Growth Factor.

Introduction

The majority of plants on earth belong to angiosperms which constitute 80% of plants inhabiting the globe. It is estimated that 300,000-400,000 species of angiosperms grow on the earth and 21,000 angiosperms are of great medicinal value as they can produce numerous bioactive phytochemicals. These secondary metabolites provide various medicines for human healthcare [1,2]. Bael (*Aegle marmelos corrêa*) belongs to the Family Rutaceae which has 2085 species of woody trees and shrubs belonging to 162 genera [3].

The fruit of Bael is aromatic, and sweet, with a hard shell that does not break even in ripe fruits. The hard shell of the fruit is removed before its consumption. The characteristic aroma of Bael fruits is retained even after processing. The ripened Bael fruit is used to prepare Jams, nectars, sherbets, toffees, and ready-to-serve wine. The powder and slab are prepared from the Bael fruit. The Bael is grown throughout India for its fruit and medicinal properties [4]. Bael fruit and its slices are eaten as such or in the form of syrup to make ingredients for cakes in Thailand and Malaysia [5].

Scientific Position

Taxonomically Bael (*Aegle marmelos corrêa*) is classified as Kingdom: Plantae, Subkingdom: Tracheobionta, Super division: Spermatophyta, Division: Magnoliophyta: Class: Magnoliopsida, Subclass: Rosidae, Order: Sapindales, Family: Rutaceae, Genus Aegle Corr., Species *marmelos* (L.) Correa. Bael is scientifically known as *Aegle marmelos* and is also known as *Belou marmelos* (L.) Lyons, *Bilacus marmelos* (L.) Kuntze, *Crateva marmelos* L., *Crateva religiosa* Ainslie, and *Feronia pellucida* Roth.

Distribution

Bael (*Aegle marmelos correa*) is a subtropical plant native to the Indian subcontinent and Southeast Asia including Bangladesh, Myanmar, Pakistan, Thailand, Nepal, China, Cambodia, Fiji, Laos, Indonesia, Malaysia, Philippines, Tibet, Java, Vietnam, and Sri Lanka [6-8]. Bael originated in the Eastern Ghats and central India. It abundantly grows in plains, dry forests, and hilly areas of outer Himalayas, Shivalik hills, and South India up to 250-1200 m above sea level. Bael has an unusual tendency to acclimatize to a wide range of habitats therefore it is grown throughout the world. In India Bael grows in all states from north to south and east to west. It is grown in Assam, Bihar, Gujarat, Haryana, Himachal Pradesh, Jammu and Kashmir, Punjab, Uttarakhand, Uttar Pradesh, Rajasthan, Madhya Pradesh, Maharashtra, Chhattisgarh, Jharkhand, West Bengal, Andhra Pradesh, Karnataka, Kerala, Tamil Nadu, and Andaman Islands. It has great religious and mythological significance in India therefore Bael is usually planted near temples. Bael is a holy tree for Hindus and its trifoliate leaves are believed to be highly sacred and offered to Lord Shiva during his worship [9,10].

Botanical profile

Bael is a spiny tree growing sluggishly with a height of 12–15 m and 90–120 cm in diameter (Figure 1). The trunk of the Bael is short with soft, flaking, and thick bark (Figure 2). Leaves of Bael are 4-10 cm long, 2-5 cm wide, alternate, deciduous, pointed, pinnate, or ternate with a long petiole. The leaflets are broad, oblong, lanceolate, and crenulated. The leaves are thick, smooth, shining, green, or dark green colored with an aromatic smell. New developing leaves are pinkish maroon and glossy (Figure 3). Bael inflorescence is formed of tiny 4-7 fragrant flowers appear along the young branchlets having 4 recurved fleshy petals which are yellowish inside and greenish outside. The flowers are stalked, erect, 2 cm wide, and lax, having a sweet aroma that appears axillary or as terminal cymes. The flowers have shallow five short calyces with broad teeth and are pubescent. The ovary is ovoid to oblong tapering into a thick short style and the stigma is capitate and stamens are 50 or more in number (Figure 4) [8,11,12]. Bael fruits are 5-20 cm in diameter of varying sizes and round, ovoid, oblong, or pyriform in shape. The rind of Bael fruit is almost smooth, light yellow, brown, or cherry red, very hard, and turns stony when dry (hence the name wood apple). The Bael fruit pulp is firm brownish-red colored with 12 stony carpels containing one or more hairy seeds. The cavity between the carpel and surrounding seed contains a reddish-brown colored, transparent gluten-like or gummy resinous mass that becomes hard after drying (Figure 5). The fruit pulp is sweet or astringent having an agreeable aromatic odor. The seeds are flattened-oblong shaped, 1 cm long, 10-50 in number, and are encased in a gummy or transparent mucilaginous substance (Figure 5) that becomes solid after drying [12].

Figure 1: Bael (*Aegle marmelos*) tree in its natural habitat.

Figure 2: Bael (*Aegle marmelos*) stem and its bark.

Figure 3: Bael (*Aegle marmelos*) leaves. a: mature leaves and b: new leaves.

Figure 4: Bael (*Aegle marmelos*) flower. A: in native form and b: flower closeup.

Figure 5: Bael (*Aegle marmelos*) fruit. A: fruits in native form, B: fruits, C: opened fruit with seeds exposed and d: extracted seeds.

Colloquial Names

Various names of *Aegle marmelos* in different languages of the world are listed in Table 1. Commonly *Aegle marmelos* is known as Bael fruit, Bael fruit tree, Bael tree, Ball tree, Bel fruit, Bela tree, Bengal quince, Elephant apple, Golden apple, Holy fruit, Indian Bael, Indian quince, Maredoo, Quince-apple of India, Stone apple, and Wood apple in English. *Aegle marmelos* is known as Bel, Bela, Bel Patra, Villi, Shivadume, Shriphal in Hindi; Bilva, Bilvam, Bilva-phalam, Durāruha, Mahura, Nilamallika, Shivaphala, Shivadruma,

Sriphal, Pootivat, Pattraśreṣṭha; Satyaphala, Shaelpatra, Lakshmiputra, Shivestha in Sanskrit; Malura in Pali; Bel, Bael in Urdu; Bel in Assamese; Bel, Bilivaohal, and Billi in Gujarati; Bael, Bela, and Shriphal in Bengali; Bilpatra, Malura, and Kumbala in Kannada; Gorakamli in Konkani; Bela, Maredu, and Kaveeth in Marathi; Baela koovalam, Kuvalam, Maaredy, and Vilvam in Malayalam; Belo, Baela in Oriya; Beel, and Bil in Panjabi; Katori in Sindhi; Bilva, Bilvamu, Bilva-pandu, Maradu-pandu, Malu-remu-chettu, Sandiliyamu in Telugu, Bilva, Bilubam, Kuuviram, Villuvam, Vilvam, Vilvama, Vilva-maram, and Vilva-pazham in Tamil [8,13-18].

S.No.	Language	Names
1	Hindi	Bel, Bela, Bel patra, Villi, Shivadume, Shriphal
2	Sanskrit	Bilva, Bilvam, Bilva-phalam, Mahura, Shivaphala, Shivadruma, Sriphal, Pootivat, Shaelpatra, Lakshmiputra, Shivestha
3	Urdu	Bel, Bael
4	Assamese	Bel
5	Gujarati	Bel, Bilivaohal, Billi
6	Bengali,	Bael, Bela, Shriphal
7	Kannada	Bilpatra, Malura, Kumbala
8	Konkani	Gorakamli
9	Marathi	Bela, Kaveeth
10	Malayalam	Baela koovalam, Kuvalam, Maaredy, Vilvam
11	Oriya	Belo, Baela
12	Panjabi	Beel, Bil
13	Sindhi	Katori
14	Telegu	Bilva, Bilvamu, Bilva-pandu, Maradu-pandu, Malu-remu-chettu
15	Tamil	Bilva, Bilubam, Kuuviram, Villuvam, Vilvam, Vilvama, Vilva-maram, Vilva-pazham
16	Scientific	*Aegle marmelos* (L.) *Correa*, *Belou marmelos* (L.) Lyons, *Bilacus marmelos* (L.) Kuntze, *Crateva marmelos* L. *Crateva religiosa*, Ainslie and *Feronia pellucida* Roth
17	English	Bael fruit tree, bael tree, ball tree, bela tree, Bengal quince, elephant apple, golden apple, holy fruit, Indian bael, Indian quince, maredoo, quince-apple of India, stone apple, wood apple
18	Arabic	Safarjale-hindi, Shul
19	Burmese	Ohshit, Opesheet
20	Chinese	Mu ju, Yin du gou qi, Ying pi ju
21	Dutch	Slijmappelboom
22	French	Bel indien, Cognassier du Bengal, Coing de l'Inde, Oranger de Malabar
23	German	Belbaum, Bengalische quitte, Indische quitte, Schleimapfelbaum
24	Indonesian	Maja batuh, maja
25	Italian	Cotogno del Bengala, Cotogno d'India
26	Japanese	Berunoki, Igure marumerozu
27	Javanese	Modjo
28	Khmer	Phneou, pnoi
29	Laotian (Sino Tibetan)	Toum
30	Malay	Bel, Bila, Bilak, Maja, Maja batuh, Maja pahit
31	Nepali	Belapatra, Belpatra

32	Persian	Bah hindi, Safarjal-e-hindi, Shull
33	Portuguese	Marmeleiro-da-índia
34	Sinhalese	Beli
35	Spanish	Bela, Milva
36	Tagalog	Bael
37	Thai	Mapin, Matum
38	Turkish	Hind ayva agh
39	Vietnamese	Bau nau, Tráimam

Table 1: Colloquial names of Bael (*Aegle marmelos*) in various languages [3, 8-15].

Aegle marmelos is called as Safarjale-hindi, and Shul in Arabic; Ohshit, and Opesheet in Burmese, Mu ju, Yin du gou qi, and Ying pi ju in Chinese; Slijmappelboom in Dutch; Bel indien, Cognassier du Bengal, Coing de l'Inde, Oranger de Malabar, and Oranger du Malaba in French; Belbaum, Bengalische quitte, Indische quitte, and Schleimapfelbaum in German; Maja batuh, and Maja in Indonesian; Modjo in Javanese; Cotogno del Bengala, and Cotogno d'India in Italian; Berunoki, and Igure marumerozu in Japanese; Phneou, and Pnoi in Khmer; Toum in Laotian (Sino Tibetan); Bel, Bila, Bilak, Maja, Maja batuh, and Maja pahit in Malay; Belapatra, and Belpatra in Nepali; Bah hindi, Safarjal-e-hindi, and Shull in Persian; Marmeleiro-da-Índia in Portuguese; Beli in Sinhalese; Bela, and Milva in Spanish; Bael in Tagalog; Mapin, and Matum in Thai; Hind ayva agh in Turkish; Bau nau, and Tráimam in Vietnamese [8,16,17,19,20].

Bael in Traditional Medicine

The Bael has been used as medicine since ancient times in Ayurveda in India and other Southeast Asian countries. The Bael has been used as a medicine for 5000 years and it has been cited in Ramayan, Charak Samhita, Upvana Vinod, and Yajur Veda [9,21,22]. According to Charaka (1500 BC), the medicinal values of Bael have been appreciated by Indians for a very long time. Traditionally Bael has been used to control fertility, treatment of intestinal disorders, and intermittent fever, and is given after childbirth. It is also used as a fish poison [23]. The vomiting in pregnant women can be stopped by giving unripe fruit pulp of Bael in boiled rice water twice daily. The urinogenital disorders can be cured by giving unripe Bael fruit mixed with milk and sugar. The half-roasted unripe Bael fruit pulp mixed with sugar cures abscesses and dysentery in humans [16].

The unripe fruits of Bael act as astringent digestive, demulcent, and stomachic, and help to relieve piles. A mixture of one part of dried fruit powder and 2 parts of mustard oil is applied to treat burn wounds in Southern Chhattisgarh by traditional healers. Chronic dysentery, diarrhea, constipation, gonorrhea, and ulcerated intestinal mucosa are treated with ripe fruits which are also used as a tonic for the heart and brain. Ripe fruits act as laxative, and antiviral, and are used to treat epilepsy and parasitic infections. The melancholia, intermittent fever, and heart palpitation are treated by giving root decoction. Bael roots are one of the essential ingredients of dashmool' an Ayurvedic medicine. The Bael leaves are bitter, astringent, expectorant, febrifuge, and laxative and are topically applied on the inflamed parts. The ulcers and ophthalmic disorders are treated by applying a 'poultice' prepared from Bael leaves. Fresh leaves help to mitigate the weakness of the heart, beriberi, and dropsy and their juice is laxative and treats asthmatic complaints, eye affections, and ophthalmia. The leaves are used in the treatment of catarrh, diabetes, deafness, and inflammations. Eating young leaves of Bael causes sterility in males and abortions in females. The regular application of oil prepared by heating one teaspoon of Bael leaf juice, an equal quantity of sesame oil, a few black pepper seeds, and half a teaspoon of kalonji (*Nigella sativa*) on the scalp increases the resistance against cough and cold. This filtered oil can be stored for later use. The medicated Bael leaf oil relieves recurrent colds and arrests respiratory infections. Bael flower distillate acts as an antidysenteric, and expectorant. It is used as a tonic for the intestine and stomach, as a local anesthetic, and in the treatment of epilepsy [19,22].

Various experimental studies have confirmed numerous medicinal properties of Bael which are listed below.

Phytochemical Analysis

Table 2 summarizes the various phytochemicals detected in Bael.

Plant part	Extract type	Phytochemicals	References
Fruit	Aqueous, Ethanol, Hexane, Petroleum ether, Methanol, Acetone	Alkaloids, Anthocyanins, cardiac glycosides, flavonoids, glycosides, steroids, terpenoids, tannins, lignins, carotenoids, ascorbic acid, phenols, polyphenols, phlobatannins, saponins, sterols, inulin, proteins, carbohydrates, amino acids, reducing sugars, nonreducing sugars, gallotannic acid, oxalates, fat, and oils	[24-35]
Root	Ethanol and Aqueous	Phenols, flavonoids, alkaloids, flavonoids, proteins, phenols, quinones, reducing sugars, saponins, sugars, tannins, triterpenoids and coumarins	[36-39]
Stem	Aqueous, Ethanol, Ethyl acetate	Alkaloids, flavonoids, glycosides, phenols, tannins, sterols, terpenoids, carbohydrates, proteins, and amino acids	[39-42]
Leaf	Aqueous, Chloroform, Ethanol, Hexane, Petroleum ether Methanol, Acetone, Ethyl acetate, Phosphate buffer	Alkaloids, flavonoids, anthraquinone glycosides, cardiac glycosides, catechins, coumarins, diterpenes, emodins, fixed oils, fats, furanoids, leucoanthocyanins, steroids, sterols, triterpenoids, pseudotannins, proteins, phenolics, carbohydrates, fatty acids, phlobatannins, quinones, tannins, terpenoids, reducing sugars, sugars and saponins	[28,39,40,43-52]
Seed	Aqueous and methanol	Alkaloids, flavonoids, glycosides, phenolics, steroids, tannins, carbohydrates, proteins, amino acids, volatile oils, and fats	[53]

Table 2: Various phytochemicals analyzed from Bael (*Aegle marmelos*).

Flavonoids, phenols, total carotenoids, and ascorbic acid were detected in Bael fresh fruit pulp [24]. The alcoholic extract of fruit pulp of Bael contains alkaloids, flavonoids, steroids, terpenoids, tannins, lignins, inulin, proteins, carbohydrates, amino acids, reducing sugars, fat, and oils, whereas saponins and cardiac glycosides were also detected in aqueous extract in addition to all these phytoconstituents except alkaloids [25]. The alkaloids, glycosides, phenols, saponins, tannins, terpenoids, proteins, and carbohydrates were found in the ethanol fruit pulp extract whereas the aqueous extract was devoid of saponins, and tannins but contained sterols [26]. The fruit pulp extracted in petroleum ether showed flavonoids, saponins, sterols, and tannins, whereas, in addition, the benzene extract contained saponins, alkaloids, and proteins but not the sterols [27]. Fruit extract of Bael in ethanol, methanol, hexane, phosphate buffer, and water contained flavonoids and phenols and the maximum quantity was found in the hexane extract and least in the aqueous extract [28]. Fruit pulp showed the presence of reducing and nonreducing sugars, gallotannic acid, and oxalates [29]. Alkaloids, flavonoids, glycosides, saponins, tannins, phenols, and carbohydrates were detected in the ethanol extract of Bael fruit, whereas the aqueous extract showed the presence of flavonoids, glycosides, saponins, and polyphenols [30].

Aqueous fruit extract showed the presence of alkaloids, flavonoids, glycosides, sterols, terpenoids, phenolic compounds, saponins, proteins, carbohydrates, and amino acids [31]. Extraction of unripe Bael fruit in chloroform, ethyl acetate, methanol, and water led to the detection of alkaloids, flavonoids, glycosides, terpenoids, saponins, proteins, carbohydrates, and amino acids in all extracts except saponins in aqueous extract. The triterpenoids were also detected in the methanol extract, whereas petroleum ether contained steroids as well as triterpenoids [32]. The aqueous and methanol ripe Bael fruit pulp extracts showed the presence of alkaloids, coumarins, flavonoids, glycosides, phenolics, saponins, tannins, and proteins [33]. Hydroethanolic extract of Bael fruit and peel showed the presence of alkaloids, coumarin, glycoside phenol, tannins, terpenoids, resins, carbohydrates, and proteins [34]. Alkaloids, flavonoids, glycosides, terpenoids, phlobatannins, and reducing sugars were detected in the aqueous extract of Bael fruit [35].

Total phenol and flavonoid contents were least in the Bael root (1.7281 ± 0.049 and 1.087 ± 0.002 mg/g), more in the stem (7.4693 ± 0.047 and 1.400 ± 0.029 mg/g), and maximum (9.8367 ± 0.0235 and 8.248 ± 0.029) in the leaf all extracted in methanol [36]. The Bael leaves extracted in n-hexane showed the presence of cardiac glycosides, steroids, triterpenoids, and pseudotannins, whereas the aqueous extract possessed alkaloids, anthraquinone glycosides, catechins, fixed oils, fats, furanoids, proteins, phenolics and saponins [37]. Phytochemical analysis of chloroform Bael leaf extract led to the detection of alkaloids, amino acids, anthocyanins, cardio glycosides, coumarins, diterpenes, emodins, fatty acids, flavonoids, phlobatannins,

glycosides, phenols, saponins, tannin, carbohydrates and proteins [43]. The alkaloids, flavonoids, saponins, tannins, terpenoids, carotenoids, cardiac glycosides, and reducing sugars were identified in the aqueous and methanol Bael leaf extracts [44]. Bael leaf extracted in ethanol, methanol, ethyl acetate, phosphate buffer, and water showed the presence of flavonoids and phenols, and the maximum quantity was found in the methanol extract followed by the ethanol extract and least in the aqueous extract [28]. Cardiac glycosides, saponins, and tannins were detected in ethanol, chloroform, and water extracts of Bael leaf, whereas flavonoids were detected in both chloroform and water extracts, and steroids were found only in ethanol extract [45]. Phytochemical analysis of methanol, chloroform, petroleum ether, and aqueous extracts showed the presence of alkaloids in all fractions of Bael leaf and seed extracts but not in aqueous and chloroform extracts, whereas tannins were absent in all leaf extracts except chloroform and petroleum ether seed extracts of the Bael [46]. Flavonoids, phenol, tannins, and carbohydrates were detected in the ethanol extract of Bael leaf [47].

Quantitative estimation of aqueous Bael leaf extract showed the presence of alkaloids (15.58 ±0.05 mg/g), flavonoids (64.0±0.05 mg/g), and phenolics (30.34±0.01 mg/g) [48]. The alkaloids, phenolic compounds, sterols, and tannins were detected in the aqueous and methanol leaf extracts of Bael [49]. The alkaloids, flavonoids, phenols, saponins, steroids, tannins, and carbohydrates were identified in the aqueous Bael leaf extract whereas saponins were absent in the acetone and ethanol extracts. The ethanol extract was devoid of tannins [50]. Alkaloids, terpenoids, tannins, saponins, steroids, coumarins, leucoanthocyanins, and carbohydrates were present in the aqueous and ethanol extracts of the leaves and stem bark of Bael. Proteins and reducing sugars were detected in the stem extract in addition to these phytochemicals, however, coumarins were absent [40]. Bael leaf methanol extract contains alkaloids, flavonoids, saponins, tannins, steroids, glycosides, phlobatannins, quinones, coumarins, and proteins, whereas ethanol extract showed the presence of all phytochemicals except flavonoids and sugars. The acetone extract showed terpenoids in addition to all the phytochemicals detected for methanol extract but not the steroids. The terpenoids, flavonoids, saponins, tannins, steroids, glycosides, phlobatannins, quinones coumarins, sugars, and proteins were detected in the chloroform extract [51]. The ethyl acetate extract of the Bael stem showed the presence of alkaloids [41].

The aqueous leaf extract of Bael contained alkaloids, flavonoids, phenolic compounds, and saponins [52]. The aqueous extract of Bael leaf consisted of 16.36 mg rutin equivalent total flavonoids and 31.38 gallic acid equivalent total phenolics [54]. The ethanol and aqueous extracts of Bael root have been reported to contain alkaloids, flavonoids, saponins proteins, and tannins [38]. The aqueous and methanol seed extracts of Bael possessed alkaloids, flavonoids, glycosides, phenolics, steroids, tannins, carbohydrates, proteins, amino acids, volatile oils, and fats [53]. Alkaloids, flavonoids, glycosides, phenols, tannins, sterols, terpenoids, carbohydrates, proteins, and amino acids were present in the ethanol, ethyl acetate, and aqueous extracts of stem bark of Bael [42]. The Bael root and small twigs extracted in ethanol and water showed the presence of phenols, quinones, reducing sugars, saponins, sugars, tannins, and triterpenoids (except aqueous extracts). The aqueous extracts also contained alkaloids and the ethanol extracts showed the presence of coumarins additionally [55]. Anthocyanins, alkaloids, cardiac glycosides, flavonoids, saponins, tannins, and terpenoids have been reported from the 60% ethanol extract of Bael leaf [39]. The methanol extract of Bael leaf showed the presence of alkaloids, flavonoids, glycosides, phenols, and carbohydrates however phytosterols could not be detected in it [56].

Active Phytochemicals

Numerous active chemical components separated from the various parts of Bael (*Aegle marmelos*) are presented in Table 3.

S. No.	Part	Extract type	Phytochemicals	References
1	Leaf	Methanol Ethanol n-hexane Chloroform Ethyl acetate Petroleum ether Aqueous	O-(3,3-dimethylallyl-halfurdinol, N-2-ethoxy-2-(4-methoxy- phcnyl) ethyl-cinnamamide; N-2-mcthoxy-2-[4-(3',3'-bimethylallyloxy) phenyl]ethylcinnamtimide; N-2-methoxy-2-(4-methoxyphenyl) ethyl cinnamamide; N-2-(4-(3', 3'-dimethylallyloxy) phenyl] ethyl cinnamide; N-2-hydroxy-2-(4-(3', 3'-dimethylallyloxy) phenyl] ethyl cinnamide; N-4-methoxystyryl cinnamide; N-2-hydroxy-2-(4-hydroxyphenyl) ethyl cinnamide; marmenol or 7-geranyloxycoumarin [7-(2,6-dihydroxy-7-methoxy-7-methyl-3-octaenyloxy) coumarin], betulinic acid; praealtin D; 4-methoxy benzoic acid; trans-cinnamic acid; valencic acid; N-ρ-cis- and trans-coumaroyltyramine; montanine; rutaretin; anhydromarmeline; aegelinosides A and B; tembamide; dehydromarmeline, aegeline; O-methylether aegeline; shahidine; (2(trans-styryl)-5-(4-methoxyphenyl)-Δ2-oxazoline;cinnamamide; aegeline methyl ether; aegeline ethyl ether; N-(4-(3-methylbut-2-enyloxy) phenethyl) cinnamamide;.4H-pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-,1-butanol 3-methyl-; 1-butanol, 3-methyl-,acetate; 2,3 dioxabicyclo[2.2.2]oct-5-ene; 1-methyl-4-(1-methyl-ethyl)-(limonene dioxide 1); bicyclo[3.1.1] heptane-2,3-diol; 2,6,6-trimethyl (2,3-pinanediol); 2-cyclohexen-1-one, 4-hydroxy-3-methyl-6-(1-methyl ethyl)-; 1-dodecanol, 2,6-bis(1,1-dimethyl ethyl)-4-methyl (BHT); benzoic acid, 4-ethoxy-, ethyl ester; 2-propanol, 1,1'-[(1-methyl-1,2-ethanediyl) bis(oxy)]bis-(tripro-pylene glycol); 1-tetradecanol, acrylate; 1,3,4,5-tetra-hydroxy-cyclo hexanecarboxylic acid (quinic acid); tetradecanoic acid (myristic acid); 2(4H)-benzofuranone 5,6,7,7a-tetra- hydro-6-hydroxy-4,4,7a-trimethyl; 1-heptadecanol (1-Eicosanol); 1,3-cyclohexadiene, 2-methyl-5-(1-methyl ethyl)-(1-phellandrene); β-myrcene (1,6-octadiene, 7-methyl-3-methylene); 2-propenoic acid, 3-(4-hydroxy-3-methoxyphenyl)-, methyl ester; (cinnamic acid, 4-hydroxy-3-methoxy-, methyl ester); pentadecanoic acid; 3,7,11,15-tetramethyl-2-hexadecen-1-ol (phytol); hexadecenoic acid, methyl ester (palmitic acid methyl ester); 9-octadecenoic acid; heptadecanoic acid; 9,12,15-octadecatrienoic acid, methyl ester (linolenic acid, methyl ester); 2-hexadecen-1-ol, 3,7,11,15-tetramethyl (phytol isomer); cis-9-hexadecenal; octadecanoic acid (stearic acid); benzene, 1,2-dimethoxy-4-[[(4methylphenyl)-sulfonyl]methyl; cholest-5-en-3-ol (3.β)-; ergost-5-en-3-ol, (3.β)-; stigmasta-5,22-dien-3-ol; stigmast-5-en-3-ol, (3.β.)-; vitamin E; α-tocopherol; α-caryophyllene; β-caryophyllene; caryophyllene oxide; cis-Z-α-bisabolene epoxide; cis-α- santalol; 1-methylene-2b-hydroxymethyl-3,3-dimethyl-4B-(3-methyl-but-2-enyl)-cyclohexane; (2S,4R)-P-mentha-[1(7),8]-diene 2-2-hydroxide;	[44,51,54,56-70]

			7,8-dihydroxy-4-hydrofuroquinoline (aegelbine-A);4-hydro-7-hydroxy-8-prenyloxyfuroquino- line (aegelbine-B); ρ-hydroxy benzoic acid; L (-) – glyceraldehyde; tomatine; taurocholic acid sodium salt; chitin; octyl-β-d-glucopyranoside; heptyl-β-D-glucopyranoside; 2-(methylthio)-ethylamine; digitonin; ethylene glycol; dodecyl-β-D-glucopyranoside; α-curcumene;α-zingiberene; myrcene; α-sesquiphellandren; ethenone; 1,2-dicyclopropyl-; 1,7-nonadiene, 4,8-dimethyl-1-nitro-, (e)-; citronellyl propionate; nonanoic acid, methyl ester; 4,8-dimethyl-3(e),7- nonadienylthioacetate; marmin; 7-hydroxycoumarin; 2 triterpenoids epi-lupeol; stigmasterol; oleic acid; piperidine 3,3-dimethyl-; benzene, (1-methylene butyl); longifolene-12; flavone; 2,3,6,7-tetra methyl-; heptadecanoic acid 16 methyl, methyl ester; 11-eicosenoic acid, methyl ester; 2H-naphtalen-1-one,3,4-dihydro-6-methoxy-2-(4-methoxy benzylideno); estra-1,3,5(10)-trien-17a-ol,3-methoxy-17-(2-methylallyl)-; 1H-pyrrolo [2.3-b] quinoxalin-2- imine, 2,3,3a,4,9,9a-hexahydro-1, N-diphenyl; pcymene; pmentha1 (7),3diene; αamirenone; tetradeca-methylcycloheptasiloxane; methyl hexadecanoate; isophytol; ethyl hexadecanoate; 9,12octadecadienoic acid, methyl ester; 9,12,15octadecatrienoic acid, methyl ester; octadecanoic acid, methyl ester; 9,12octadecadienoic acid, ethyl ester; 9,12,15octadecatrienoic acid, ethyl ester; octadecanoic acid, ethyl ester; 5hydroxy7, 8, 2', 6'tetramethoxyflavone; 6hydroxy3,5 cyclolactone; 2,3bis (3,7,11,15tetramethyl hexadecoxy) propan1ol; 3methyl4,5dihydrobenz (h) imidazo [1,2c] quinazolinium1olate; 5,6dimethoxy1methylphen anthrene; noctadecane; retinoic acid; ganodermenonol; 3,4bis (4hydroxyphenyl) 3,4hexanediol; benchequiol; 24 (R)ergost5en3βol; 3,4dimethoxyacetophenone; stigmasta 5,22dien3ol; benzoic acid 4-[1-oxo-2-(1-pyrrolidinyl) ethyl]amino-, methyl ester, 2;,2'-dipiperidine; diphenylmethane; oleic acid, trimethylsilyl ester; 10-bromodecanoic acid, ethyl ester; docosa-8,14-diyn-cis-1,22-diol, bis (trimethylsilyl) ether; benzene, 1,1',1''-(1-ethanyl-2-ylidene)tris-; acetamide, n-[4-(chlorodifluoromethoxy)phenyl]-2-pyrrolidin-1-ylo; 2-hexanone; pentan-2-one; methyl-2-pentanone; 1-penten-3-ol; cyclopent-anol; ρ-mentha-1 (7),3-diene; 8-hexadecenal; (E)-1-(methoxy-methoxy)-1-tetradecee-3-ol; 1-dodecanol; heneicosane; cyclo-octasiloxane; dotriacontane; cyclononasiloxane; phthalic acid; hexadecanoic acid; cyclodecasiloxane; methyl linolelaidate; hentriacontane; 9,17-octadecadienal, α-neodene, tetracosamethyl	

			-cyclododecasilaxane; oleyl alcohol; cis-13-eicosenoic acid; nonahexacontanoic acid; nonacosane; benzoic acid; γ-tocopheryl; 1-heptadec-1-ynyl-cyclopentanol 7-pentadecyne; 13-docosenoic acid; docosanoic acid; Z,Z-10,12-hexadecadien-1-ol acetate; n-triacontane; tetracosamethyl-cyclododecasiloxane; (+)-(9.β.H)-labda-8(17), 13(E)-diene-5-ol; 15-tetracosenoic acid; cyclo-decasiloxane; farnesyl acetone; myo-inositol; (2,4-di-tert-butyl phenol and 3,5-di-tert-butyl-4-hydroxy propanoic acid); D-limonene; azulene; trans-farnesol deriv, β-cubenene, β-copaene; α- and β-amyrin; octacosane; tetra-tetracontane; pentatriacontane; palmitic acid; margaric acid; monopalmitin; octacosanol; cholesterol; campesterol; β-sitosterol; scopoletin; gallic acid; quercetin 3- arabinoside; quercetin; 5,7- dimethoxyflavanone; 6,2'- dihydroxyflavone; caffeic acid; kaempferol- 3- rhamnoside-4″-rhamnoside- 7- rhamnoside; ferulic acid; epigallocatechin; dihydroquercetin; formononetin-7- o- glucoside; phellamurin; quercetin 3- (6″- acetylglucoside); 7- hydroxy- 3- methylflavone; phloretin 2′-o-glucoside; rutin; apigenin-7-rutinoside-4′- glucoside; kaempferol; hexadecenoic acid; oleic acid; 9- Cis-1,3-eicosenoic acid; dasycarpidan-1-methanol, acetate (ester); digitoxin, z-(13,14-epoxy)tetradeg-11-en-ol acetate; 2,3-dimethyl-5-trifluoromethyl-1-phen-1,4-diol; ethyl isoallocholate.	

2	Leaf	Essential oil	α-pinene; β-pinene; sabinene; myrcene; limonene; (Z)-β-ocimene; γ-terpinene; ρ-menth-l,3,8-triene; linalool; piperitone; myrtenol; terpinen-4-ol; piperitol; trans-carveol; ρ-menth-4(8)-en-l-ol; cis-carveol; sabinol; myrtenyl acetate; ρ-menth-1 -en-BP,5P-diol; ρ-caryophyllene; α-humulene; α-elemene; ar-curcumene; caryophyllene oxide; α-thujene; camphene; α-phellandrene; α-terpinene; ρ-cymene; β-phellandrene; cis-sabinene hydrate; terpinolene; α-copaene; β-bourbonene; β-elemene; β-caryophyllene; β-gurjunene; γ-gurjunene; aristolene; germacrene D; valencene; α-selinene; bicyclogermacren; (Z)-α-bisabolene; cubebol; δ-cadinene; elemol; (E)-nerolidol; humulene epoxide; 3,7,11,15-tetramethyl-2-hexadecen-l-ol; limonene oxide, 2,6-dimethyl-1,3,5,7 octatetraene; eugenol; β -caryophyllene; β -selinene; 3-methyl-2-butenal, α-zingiberene; (3Z)-hexenol; benzaldehyde; α-farnesene; (E)-β-farnesene; (E,E)-α-farnesene; trans-cadina 1(6),4-diene; γ-curcumene; trans-muurola-4(14),5-diene; (E)-β-ocimene; epi-cubebol; cis-linalool oxide; germacrene A; trans-linalool oxide; α-cedrene; cis-p-menth-2,8-dien-1-ol; alloocimene; cis-limonene oxide; italicene ether; trans-limonene oxide; cis-sesquisabinene hydrate; (3Z)-hexenyl butanoate; α-terpineol; germacrene B; cis-piperitol; γ-isogeraniol; germacrene D-4-ol; nerol; p-anisaldehyde; eremoligenol; geraniol; caryophylla-4(12),8(13)-dien-5-ol; geranial; τ-muurolol; δ-elemene; α-muurolol; α-cubebene; β-eudesmol; α-cadinol; (3Z)-hexenyl hexanoate; epi-β-bisabolol; 7-epi-sesquithujene; epi-α-bisabolol; germacra-4(15),5,10(14)-trien-1α-ol; methyl perillate; shyobunol; (Z)-jasmone; (2Z,6Z)-farnesol; methyl n-methylanthranilate; (2Z,6E)farnesol; (E)-caryophyllene; (2E,6E)-farnesal; γ-elemene; (e)-phytol; verbenene; δ-3-carene; p-cymene; 1,8-cineole; γ -terpinene; 6-camphenone; cis-ρ-menth-2-en-1-ol; allo-ocimene; neo-allo-ocimene; citronellal; isoborneol; borneol; cryptone; carvone; iso-3-thujanyl acetate; α-duprezianene; γ -elemene; allo-aromadendrene; α-muurolene; γ -cuprenene; (Z)-sesquilavandulol; β-atlantol; (2Z,6E)-farnesol; (Z)-lanceol;.β-myrcene; isosylvestrene; δ-carene; β-ocimene; trans-2-hydroxycinnamic acid; 3-isothujanol; 4-terpineol; thuj-3-en-10-al; α-terpinyl isobutyrate; γ-muurolene; β-selinene; β-bisabolene; γ-cadinene; β-bisabolol; trans-ρ-mentha-1(7),8-dien-2-ol; 5-isopropyl-6-methyl-hepta-3,5-dien-2-ol; phenol, 2-methyl-5-(1-methylethyl); bicyclo(3.1.1) heptane-2,3-diol; 2,6,6-trimethyl-; 2-methoxy-4-vinylphenol; 1-benzoxirene-2,5-dione, 4-(3-oxobutyl) hexahydro-3,3,4-trimethyl; cyclohexanecarboxylic acid 3-fluorophenyl ester; menthol, 1'-(butyn-3-one-1-yl)-, (1R,2S,5R); ledene oxide-(II); spathulenol; cis-±-copaene-8-ol; himachalol; isoaromadendrene epoxide; tricyclo[5.2.2.0(1,6)] undecan-3-ol,2-methylene-6,8,8-trimethyl-; trans-longipinocarveol; naphthalene; 2,6dimethyl 3,5,7octatriene2ol; transcarveol;	[68,71-83]

			2cyclohexen1one; limonene epoxide; ρvinylguaiacol; αAcubebene; caryophyllene; bicyclo(3.1.1)hept 2 ene; βsesquiphellandrene; αhumulene; β-farnesene; αcedrene; 2epiαcedrene; δcadinene; 2,6bis (1,1dimethyl-ethyl)4methyl; nerolidol; cisZalphabisabolene epoxide; 3bromohomoadamantane; 3,5 cyclooctadien1one; αchamigrene; βmaaliene; bergamotene; α-hciseudesma6ene12al; geranylgeraniol; (S)(+)xanthorrhizol; myristinic acid; fumaric acid; hexahydrofarnesyl acetone; 4,7 dimethylpentacyclododecane4,7diol; 7,9ditertbutyl 1oxaspirodeca 6,9diene2,8dione; transZα bisabo lene epoxide; hexadecenoic acid; (E, E)farnesol; corymbolone; 2 methylz, z3,13octadecadienol; 5,9diamino2,4dimethyl pyrazolo naphtharidine; nheneicosane; trans αhimachalene; 2hexadecen1ol; linoleic acid; stearic acid; ndocosane; cis12octadecadienoic acid; 11,13dimethyl 12tetradecen1ol acetate; αterthienyl; majorenolide; phytan; thianthrene; ntetracosane; 13tetradece11yn1ol; 6methylindole; n pentacosane; 1,2benzenedicarboxylic acid; neicosane; 3methyl1,3 thiazole2thione; heptacosane a-bulnesene; 2-methyl-2- pentanol; ethyl isovalerate; β-cis-ocimene; ρ-mentha-1,4(8)-diene; ρ-allyl toluene; 3,9-epoxy-p-menta-1,8(10)-diene; pinocarvone; p-cymen-α-ol; (Z)-cinerone; 2-methyl-oct-2-enedial; guaia-1(10),11-diene; limonen-6-ol; carotol; ρ-cymen-8-ol; α-acorenol; trans-longipinocarveol; eudesm-7(11)-en-4-4-ol; calcitriol;D-limonene; αcaryophyllene;β-caryo-phyllene, transcyclopropane; γ-elemene; trans-β-caryophyllene; β -bisabolene; globulol; ledene alcohol; caryophyllene oxide; humulene-1,2-epoxide; rosifoliol; geranyl-α-terpinene; 3-methyl-2-(2-methyl-2-butenyl)-furan; trimethyl[2-(phenylthio)ethoxy]-silane; 6-allyl-2-cresol, pentanoic acid; 2-methyl-, anhydride; (+)-3-carene2-(acetylmethyl)- ; (2e)-7-ethoxy-3,7-dimethyl-2-octen-1-ol; beta-ionone epoxide; 10,12-hexadecadien-1-ol; 9,12,15-octadecatrienoic acid, ethyl ester, (z,z,z)-; 9,12-octadeca-diynoic acid, trimethylsilyl ester; 13-hexyloxacyclotridec-10-en-2-one; and cholesta-3,5-diene.	
3	Stem	Ether, n-Hexane, Methanol, Ethyl acetate Petroleum ether, Chloroform, Ethanol, Water	Umbelliferone; skimmianine; marmesin; marmin; γ-sitosterol; (-)-lyoniresinol 2α-O-β-glucopyranoside (3); and (-)-4-epi-lyoniresinol 3α-O-β-D-glucopyranoside; (+)-lyoniresinol 3α-O-β-D-gluco-pyranoside; (-)- lyoniresinol 3α-O-β-D-glucopyranoside; 7-(7-chloro-6R-hydroxy-3,7-dimethyl-2-octenyloxy)coumarin; 7-[6R-(β-D-glucopyranosyloxy)-4R,7-dihydroxy-3,7-dimethyl-2-octenyloxy] coumarin; aegline; chloromarmin; skimmiarepin A and skimmiarepin C; β-D-galactopyranoside; psoralene, imperatorin; 70-O-ethylmarmin; 2-O-ethyltembamide; epoxyaurapten; scopoletin; 3,5 di-tert-butyl -4-hydroxy propanoic acid; β-fargarine; trisorralen; oxosoralen; 7,8,9-trimethoxy-4,5-dihydro-1 H-benzo indazole; α-amyrin.	[68,84-91]
4	Root	Petroleum ether, Chloroform, Ethyl acetate, Methanol, Ethanol, Dichloro-methane, Water	Decursinol; marmesin; marmin; haplopine; skimmianine (4,7,8-trimethoxyfuro[2,3-b]quinoline); γ-fagarine; xanthotoxin; umbelliferone; lupeol; aegeline (N-2-hydroxy-2(4-methoxy-phenyl) ethylcinnamamide); aeglemarmelosine; psoralene, imperatorin.	[23,90,92-94]

5	Fruit	Acetone, n-hexane, Ethyl acetate Ethanol Methanol, Benzene, Petroleum ether, Chloroform	Alloimperatorin; imperatorin; β-sitosterol; marmelin; ageline; O-methylhalfordinol; O-isopentennylhalf-ordinol; xanthotoxin; marmamide-A and marmamide -B; N-benzoyltyramine methyl ether; marmesiline; 6-(4-acetoxy-3-methyl-2- butenyl)-7-hydroxycoumarin; 6-(2-hydroxy-3-hydroxymethyl-3-butenyl)-7- hydroxycoumarin; marmelonine; 8- hydroxy-smyrindiol; marmelosin; scopoletin; umbelliferone; Psoralen; 3'-prenyloxypsoralen; marmin; xanthotoxol; afzelin; 1-decanylgodoleate (capryl 9Z-eicosenoiate); behenyl oleate (1-docosanyl cis-9-octadecenoate); 2;6;10;14-tetramethyl dec-15-en-14-olyl salicylate (isophytylsalicylate); lacceroic acid; γ-elemene; tetracontane; tetracosane; nanocosane; hexacosane; cyclohexane; caryophyllene; azulene; β-sesquiphellandren; 1;3 cyclohexane; quinoline; pranqenin; germacrene; 1-methyl-4-(5-methyl methylene-4-hexenyl); 3-(1;5-dimethyl 4hexenyl)-6-methylene- hexadecane; n-hexadecanoic acid; octadecane; docosane; heneicosane; 4-hydroxy-7h- furo(3-2-g)chromen-7-one; squalene; gallic acid; 2;3 -dihydroxy benzoic acid; chlorogenic acid; ρ -coumaric acid; vanillic acid; rutin; oxalic acid; tartaric acid; malic acid; lactic acid; acetic acid; citric acid; succinic acid; fumaric acid; propionic acid; ascorbic acid; thiamine; riboflavin; niacin; pantothenic acid; pyridoxine; biotin; cobalamins; α-carotene acid; β-carotene; γ-carotene; δ-carotene; α-tocopherol; β-tocopherol; γ-tocopherol; δ-tocopherol; O-(3;3-dimethylallyl) halfordinol; valencic acid; heraclenin; auraptene; 2-methoxy-4-vinylphenol; 1-(3,5-dimethoxyphenyl)ethan-1-one; (E)-4-(3-hydroxyprop-1-en-1-yl)-2-methoxyphenol; 3-deoxyestradiol; methyl 7,10,13-hexadecatrienoate; oleic acid; ethyl iso-allocholate; γ-sitosterol; sitostenone; cholest-1-eno[2,1-α] naphthalene 3',4'-dihydro; tetra-decanoic acid; methyl palmitate; palmitic acid; octadecanal; methyl octadeca-9,12-dienoate; methyl 16-methylhepta decanoate; octadeca-9,12-dienoic acid; vaccenic acid; octadec-13-enoic acid; stearic acid;, icosanoic acid; 2-hydroxycyclopenta decan-1-one; 3-pentadecylphenol; heptacosane, marmelosin, marmesin, aegeline, psoralen, scopoletin, and umbelliferon.	[95-110]
6	Seed	Petroleum ether, n-Hexane	Galactose; glucose; arabinose; rhamnose; 2-isopropenyl-4-methyl-1-oxa-cyclopenta[b]anthracene-5,10-dione; (+)-4-(20-hydroxy-30-methylbut-30-enyloxy)-8H-[1,3]dioxolo [4,5-h]chromen-8-one; imperatorin; β-sitosterol; plumbagin; 1-methyl-2-(30-methyl-but-20-enyloxy)-anthraquinone; β-sitosterol glucoside; stigmasterol; vanillin; salicin; methyl ester of lauric acid, myristic acid, palmitic acid, palmitoleic acid, stearic acid; oleic acid; linoleic acid; arachidic acid; behenic acid; methyl esters of dodecanoic acid; methyl tetradecanoate; pentadecanoic acid; 9-hexadecanoic acid; hexadecanoic acid; 14-methyl-, 9,12-hexadecadienoic acid; heptadecanoic acid; 9-octadecenoic acid (z)-, 9,12- octadecadienoic acid, eicosanoic acid, 11-eicosenoic acid, docosanoic acid. octanoic acid ester, ethyl ester 9,12,15-octadecatrienoic acid; 7-(3'-methylbut-2-enyloxy)-2H-chromen-2-one; umbelliferone; skimmianine; 3,5,7-trihydroxy-2-(4'-hydroxy-3'-isopentyloxy-phenyl-4H-chromen-4-one.	[111-114]

Table 3: Different active chemicals isolated from various parts of Bael (*Aegle marmelos*).

Leaves: Four alkaloids O-(3,3-dimethylallyl-halfurdinol, N-2-ethoxy-2-(4-methoxyphenyl) ethyl cinnamamide, N-2-methoxy-2-[4-(3',3'-bimethylallyloxy) phenyl] ethylcinnamtimide and N-2-methoxy-2-(4-methoxyphenyl) ethylcinnamamide have been isolated from the methanol and ethanol extracts of Bael leaves [56]. The alkaloids, N-2-(4-(3',3'-dimethylallyloxy) phenyl] ethylcinnamide, N-2-hydroxy-2-(4-(3',3'-dimethyl-allyloxy) phenyl] ethylcinnamide, N-4-methoxystyrylcinnamide and N-2-hydroxy-2-(4-hydroxy-phenyl)ethylcinnamide were separated from the n-hexane extract of Bael leaves [57]. The marmenol or 7-geranyloxycoumarin [7-(2,6-dihydroxy-7-methoxy-7-methyl-3-octaenyloxy) coumarin], betulinic acid, praealtin D, 4-methoxy benzoic acid, trans-cinnamic acid, valencic acid, N-ρ-cis- and trans-coumaroyltyramine, montanine, and rutaretin have been separated from the methanol extract of Bael leaves [58]. Anhydromarmeline (14 mg), aegelinosides A and B (50 mg), tembamide (8 mg), dehydromarmeline (11 mg), aegeline (65 mg), and O-methylether aegeline (20 mg) have been isolated from the chloroform leaf extract of Bael [59]. Petroleum ether extract of fresh Bael leaves showed the presence of shahidine i.e. 2(trans-styryl)-5-(4-methoxyphenyl)-Δ2-oxazoline [60].

The methanol extract of Bael leaves showed the presence of cinnamamide, aegeline, aegeline methyl ether, aegeline ethyl ether, and N-(4-(3-methylbut-2-enyloxy) phenethyl)-cinnamamide [61]. Various phytochemicals detected from the methanol extract of Bael leaf include 4H-pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-,1-butanol,3-methyl-, acetate, 2,3dioxabicyclo[2.2.2]- oct-5-ene, 1-methyl-4-(1-methyl- ethyl)-(limonene dioxide 1), bicyclo-[3.1.1]-heptane- 2,3-diol, 2,6,6-trimethyl(2,3-pinanediol), 2-cyclohexen-1-one, 4-hydroxy-3-methyl-6-(1-methylethyl)-,1-dodecanol, 2,6-bis(1,1-dimethylethyl)-4-methyl (BHT), benzoic acid, 4-ethoxy-,ethyl ester, 2-propanol, 1,1'-[(1-methyl-1,2-ethanediyl) bis(oxy)] bis-(tri-propylene glycol), 1-tetradecanol, acrylate, 1,3,4,5-tetrahydroxycyclo- hexanecarboxylic acid (quinic acid), tetra-decanoic acid (myristic acid), 2(4H)-benzofuranone 5,6,7,7a-tetrahydro-6-hydroxy-4,4,7a-trimethyl, 1-heptadecanol (1-eicosanol), 1,3-cyclo-hexadiene, 2-methyl-5-(1-methylethyl)-(1-phellandrene), 1,6-octadiene, 7-methyl- 3-methylene (β-myrcene), 2-propenoic acid, 3-(4-hydroxy-3-methoxyphenyl)-, methyl ester (cinnamic acid, 4-hydroxy-3-methoxy-, methyl ester), pentadecanoic acid, 3,7,11,15-tetramethyl-2-hexadecen-1-ol (phytol), hexadecenoic acid, methyl ester (palmitic acid methyl ester), 9-octadecenoic acid, heptadecanoic acid, 9,12,15-octadecatrienoic acid, methyl ester (linolenic acid, methyl ester), 2-hexadecen-1-ol, 3,7,11,15-tetramethyl (phytol isomer), cis-9-hexadecenal, octadecanoic acid (stearic acid), benzene, 1,2-dimethoxy-4-[[(4methylphenyl) sulfonyl]methyl, cholest-5-en-3-ol (3.β)-, ergost-5- en-3-ol, (3.β)-, stigmasta-5,22-dien-3-ol, stigmast-5-en-3-ol, (3.β.)-, vitamin E and α-tocopherol [39].

The α-caryophyllene and β-caryophyllene, caryophyllene oxide, cis-Z-α-bisabolene epoxide, santalol, cis-α,1-ethylene-2b-hydroxymethyl-3,3-dimethyl-4B-(3-methyl-but-2-enyl)-cyclohexane, and (2S,4R)-P-mentha-[1(7),8]-diene 2-2-hydroxide were separated from the petroleum ether extract of Bael leaf [63]. The chloroform and petroleum ether extracts of Bael leaf led to the isolation of two new furoquinoline alkaloids- 7,8-dihydroxy-4-hydro-furoquinoline (aegelbine-A), and 4-hydro-7-hydroxy-8-prenyl- oxyfuroquinoline (aegelbine-B), respectively together with a known alkaloid aegeline, in addition, the petroleum ether extract also contained ρ-hydroxybenzoic acid (phenolic acid) [64]. FTIR analysis of methanol Bael leaf extract resulted in the isolation of L (-)-glyceraldehyde unnatural form, tomatine, taurocholic acid sodium salt, chitin, octyl-β-d-glucopyranoside, heptyl-β-D-glucopyranoside, 2-(methylthio)-ethylamine, digitonin, ethylene glycol polymer-bound, and dodecyl-β-D-glucopyranoside whereas gas chromatography (GC) and mass spectroscopy (MS) analysis led to the separation of α-curcumene, α-zingiberene, mycrene, α-sesqui-phellandrene, ethanone, 1,2-dicyclo-propyl-,1,7-nonadiene, 4,8-dimethyl-1-nitro-,(e)-, citronellyl propionate, nonanoic acid, methyl ester, phytol and 4,8-dimethyl-3(e),7- nonadienyl thioacetate [65].

The hexane, chloroform and ethyl acetate extracts of Bael leaf and stem bark yielded an alkaloid aegeline (10.0 mg), two coumarins- marmin (39.9 mg), 7-hydroxycoumarin (24.2 mg), and 2 triterpenoids epi-lupeol (6.5 mg) and stigmasterol (5.0 mg) [65]. Oleic acid, piperidine,3,3-dimethyl-, benzene, (1-methylene butyl), longifolene-12, flavone, tetra decanoic acid, anthraquinone, 2,3,6,7-tetra methyl-, heptadecanoic acid, 16 methyl, methyl ester, 11-eicosenoic acid, methyl ester, phytol, 2H-naphtalen-1-one, 3,4-dihydro- 6-methoxy-2-(4-methoxybenzylideno), estra-1,3,5(10)-trien-17a-ol,3-methoxy-17- (2-methyl -allyl)- and 1H-pyrrolo [2.3-b] quinoxalin-2-imine, 2,3,3a,4,9,9a-hexahydro-1, N-diphenyl have been detected in the ethanol leaf extract of Bael [66]. Mostly steroidal compounds including p-cymen, p-mentha-1(7),3-diene, α-amirenone, tetra-decamethylcyclohepta- siloxane, methyl hexadecanoate, isophytol, ethyl hexadecanoate, methyl ester of 9,12-octadecadienoic acid, methyl ester of 9,12,15-octa-decatrienoic acid, methyl ester of octadecanoic acid, ethyl ester of 9,12-octadecadienoic acid, ethyl ester of 9,12,15-octadecatrienoic acid, ethyl ester of octadecanoic acid, 5-hydroxy-7,8,2',6'-tetramethoxyflavone, 6-hydroxy-3,5 cyclolactone, 2,3-bis(3,7,11,15-tetramethyl- hexadecoxy) propan-1-ol, 3-methyl-4,5-dihydrobenz(h)-imidazo[1,2-c]quinazolinium-1-olate, 5,6-dimethoxy-1-methylphenanthrene,

n-octadecane, retinoic acid, ganodermenonol, 3,4-bis (4-hydroxyphenyl)3,4-hexa-nediol, benchequiol, 24 (R)-ergost-5-en-3β-ol, 3,4-dimethoxyaceto-phenone, and stigmasta-5,22-dien-3-ol have been isolated from the petroleum ether fraction of aqueous Bael leaf extract [67].

Mostly steroidal compounds including p-cymen, p-mentha-1(7),3-diene, α-amirenone, tetra-decamethylcyclohepta- siloxane, methyl hexadecanoate, isophytol, ethyl hexadecanoate, methyl ester of 9,12-octadecadienoic acid, methyl ester of 9,12,15-octa-decatrienoic acid, methyl ester of octadecanoic acid, ethyl ester of 9,12-octadecadienoic acid, ethyl ester of 9,12,15-octadecatrienoic acid, ethyl ester of octadecanoic acid, 5-hydroxy-7,8,2',6'-tetramethoxyflavone, 6-hydroxy-3,5 cyclolactone, 2,3-bis(3,7,11,15-tetramethyl- hexadecoxy) propan-1-ol, 3-methyl-4,5-dihydrobenz(h)-imidazo[1,2-c]quinazolinium-1-olate, 5,6-dimethoxy-1-methylphenanthrene, n-octadecane, retinoic acid, ganodermenonol, 3,4-bis (4-hydroxyphenyl)3,4-hexa-nediol, benchequiol, 24 (R)-ergost-5-en-3β-ol, 3,4-dimethoxyaceto-phenone, and stigmasta-5,22-dien-3-ol have been isolated from the petroleum ether fraction of aqueous Bael leaf extract [68].

GC-MS analysis of acetone and methanol extracts of Bael leaf resulted in the identification of benzoic acid, 4-[1-oxo-2-(1-pyrrolidinyl)ethyl]amino-, methyl ester, 2,2'-dipiperidine, diphenylmethane, nonanoic acid, oleic acid, trimethylsilyl ester, 10-bromo- decanoic acid, ethyl ester, phytol, docosa-8,14-diyn-cis-1,22-diol, bis (trimethylsilyl) ether, benzene, 1,1',1''-(1-ethanyl-2-ylidene)tris- and acetamide, n-[4-(chlorodifluoromethoxy)- phenyl]-2-pyrrolidin-1-ylo [47]. GC-MS analysis of ethanol extract of Bael leaf led to the isolation of 2-hexanone, pentan-2-one, methyl-2-pentanone, 1-penten-3-ol, cyclopentanol, ρ-mentha-1(7),3-diene, ρ-cymene, 8-hexa-decenal, (E)-1-(methoxymethoxy)-1-tetra decee-3-ol, 1-dodecanol, heneicosane, cycloocta-siloxane, tetra-decamethylcyclo- heptasiloxane, dotriacontane, cyclononasiloxane, phthalic acid, hexadecanoic acid, cyclodecasiloxane, tetra-decanoic acid (myristic acid), methyl linolelaidate, oleic acid, octadecanoic acid, hentriacontane, 9,12,15-octadecatrienoic acid, methyl ester (linolenic acid, methyl ester), 9,17-octadecadienal, octadecanoic acid (stearic acid), α-neodene, sulfurous acid, phenol, tetracosamethylcyclododecasilaxane, oleyl alcohol, 2-propenoic acid 3-(4-hydroxy-3-methoxyphenyl)- methyl ester (cinnamic acid, 4-hydroxy-3-methoxy-, methyl ester), cis-13-eicosenoic acid, nonahexacontanoic acid, nonacosane, benzoic acid, vitamin-E, γ-tocopheryl, 1-heptadec-1-ynyl-cyclopentanol, 7-pentadecyne, 13-docosenoic acid, docosanoic acid, Z,Z-10,12-hexadecadien-1-ol acetate, n-triacontane, tetracosamethyl- cyclododecasiloxane, (+)-(9.β.H)-labda-8(17), 13(E)-diene-5-ol, 15-tetracosenoic acid, benchequiol, retinoic acid, cyclodeca-siloxane, farnesyl acetone [50].

The ethanol Bael leaf extract contains polyols, quinic acid, and myo-inositol. The Bael leaf, twigs, unripe fruit stem bark, and essential oil possess alkylated phenols (2,4-di-tert-butylphenol and 3,5-di-tert-butyl-4-hydroxypropanoic acid), terpenes (D-limonene, α- and β-caryophyllene, azulene, trans-farnesol derivative, β-cubenene, β-copaene, α-amyrin, and β-amyrin), alkanes and alkenes (nonacosane, octacosane, tetratetracontane, pentatriacontane, etc.), fatty acids and fatty alcohols (palmitic acid, stearic acid, margaric acid, oleic acid, monopalmitin, octacosanol), sterols (cholesterol, campesterol, β-sitosterol), coumarins (scopoletin, umbelliferone, oxsoralen, trisorralen, and β-fargarine), and indazole derivative (7,8,9-trimethoxy-4,5-dihydro-1-H-benzo-[g]indazole) [69]. Gallic acid, quercetin 3- arabinoside, quercetin, 5,7- dimethoxy-flavanone, 6,2'-dihydroxyflavone, caffeic acid, kaempferol-3-rhamnoside-4″-rhamnoside-7-rhamnoside, ferulic acid, epigallocatechin, dihydroquercetin, formononetin-7-o-glucoside, phellamurin, quercetin 3-(6″-acetyl glucoside), 7- hydroxy-3-methyl flavone, phloretin 2′-o-glucoside, rutin, apigenin-7-rutinoside-4′-glucoside, and kaempferol have been detected from the alkaloid free extract of Bael leaf [70]. Hexadecenoic acid, oleic acid, 9- Cis-1,3-eicosenoic acid, dasycarpidan-1-methanol, acetate (ester), digitoxin, z-(13,14-epoxy)tetradeg-11-en-ol acetate, 2,3-dimethyl-5-trifluoromethyl-1-phen-1,4-diol, and ethyl isoallocholate have been reported from the ethyl acetate extract of Bael leaf [71].

Leaf oil: Hydro distillation of Bael leaves led to the extraction of leaf oil that contained α-pinene, β-pinene, sabinene, myrcene, limonene, (Z)-β-ocimene, γ-terpinene, ρ-menth-l,3,8-triene, linalool, piperitone, myrtenol, terpinen-4-ol, piperitol, trans-carveol, ρ-menth-4(8)-en-l-ol, cis-carveol, sabinol, myrtenyl acetate, ρ-menth-1-en-BP, 5P-diol, ρ-caryophyllene, α-humulene, α-elemene, ar-curcumene and caryophyllene oxide [72]. α-thujene, α-pinene, camphene, sabinene, β-pinene, myrcene, α-phellandrene, α-terpinene, ρ-cymene, limonene, β-phellandrene, (Z)-β-ocimene, cis-sabinene hydrate, terpinolene, linalool, α-copaene, β-bourbonene, β-elemene, β-caryophyllene, β-gurjunene, α-humulene, γ-gurjunene, aristolene, germacrene D,

valencene, α-selinene, bicyclogermacren, (Z)-α-bisabolene, cubebol, δ-cadinene, elemol, (E)-nerolidol, caryophyllene oxide, humulene epoxide, 3,7,11,15-tetramethyl-2-hexadecen-l-ol are separated from the Bael leaf hydro distillate [73]. The hydro distillation of twigs and leaves of Bael resulted in the isolation of α-pinene, camphene, sabinene, myrcene, ρ-cymene, limonene, (Z)-β-ocimene, linalool, limonene oxide, 2,6-dimethyl-1,3,5,7 octatetraene, eugenol, β-elemene, β-caryophyllene, germacrene D, β-selinene and caryophyllene oxide, α-humulene and terpinen-4-ol. However, leaves were devoid of camphene, germacrene D, and caryophyllene oxide [74].

3-methyl-2-butenal, α-zingiberene, (3Z)-hexenol, α-pinene, α-humulene, benzaldehyde, α-farnesene, (E)-β-farnesene, (E,E)-α-farnesene, sabinene, trans-cadina-1(6), 4-diene, myrcene, γ-curcumene, limonene, ar-curcumene, (Z)-β-ocimene, trans-muurola-4(14),5-diene, (E)-β-ocimene, epi-cubebol, γ-terpinene, cis-linalool oxide (furanoid), germacrene A, α-terpinolene, trans-linalool oxide (furanoid), linalool, α-cedrene, cis-p-menth-2,8-dien-1-ol, cubebol, alloocimene, δ-cadinene, cis-limonene oxide, trans-cadina-1,4-diene, italicene ether, trans-limonene oxide, cis-sesquisabinene hydrate, (3Z)-hexenyl butanoate, elemol, α-terpineol, germacrene B, cis-piperitol, (E)-nerolidol, trans-carveol, (3Z)-hexenyl benzoate, γ-isogeraniol, germacrene D-4-ol, nerol, 1-epi-cubenol, p-anisaldehyde, eremoligenol, geraniol, caryophylla-4(12),8(13)-dien-5-ol, geranial, τ-muurolol, δ-elemene, α-muurolol (=torreyol), α-cubebene, β-eudesmol, α-copaene, α-cadinol, (3Z)-hexenyl hexanoate, epi-β-bisabolol, 7-epi-sesquithujene, epi-α-bisabolol, β-elemene, germacra-4(15),5,10(14)-trien-1α-ol, methyl perillate, shyobunol, (Z)-jasmone, (2Z,6Z)-farnesol, methyl n-methylanthranilate, (2Z,6E)farnesol, (E)-caryophyllene, (2E,6E)-farnesal, γ-elemene and (e)-phytol have been detected by GC-MS analysis of Bael leaf essential oil [75]. α-Thujene, α-pinene, camphene, verbenene, sabinene, β-pinene, myrcene, α-phellandrene, δ-3-carene, α-terpinene, p-cymene, limonene, β-phellandrene, 1,8-cineole, (z)-β-ocimene, (e)-β-ocimene, γ-terpinene, terpinolene, 6-camphenone, linalool, cis-ρ-menth-2-en-1-ol, alloocimene, cis-ρ-mentha-2,8-dien-1-ol, neo-alloocimene, citronellal, isoborneol, borneol, cryptone, α-terpineol, myrtenol, trans-carveol, cis-carveol, carvone, iso-3-thujanyl acetate, δ-elemene, α-cubebene, (3z)-hexenylhexanoate, α-duprezianene, β-elemene, (E)-caryophyllene, γ-elemene, α-humulene, (E)-β-farnesene, alloaromadendrene, trans-cadina-1(6),4-diene, ar-curcumene, germacrene D, α-muurolene, γ-cuprenene, trans-cadina-1,4-diene, cis-sesquisabinene hydrate, germacrene B, (E)-nerolidol, caryophyllene oxide, (z)-sesquilavandulol, β-atlantol, (2Z,6E)-farnesol, (Z)-lanceol, and (E)-phytol have been separated from the essential leaf oil of Bael [76].

The essential oil of Bael leaves yielded α-pinene, β-myrcene, α-phellandrene, isosylvestrene, δ-carene, β-ocimene, trans-2-hydroxycinnamic acid, γ-terpinene, terpenolene, linalool, 3-isothujanol, 4-terpineol, thuj-3-en-10-al, α-terpineol, δ-elemene, α-cubebene, γ-elemene, α-humulene, α-terpinyl isobutyrate, γ-muurolene, γ-curcumene, valencene, β-selinene, α-muurolene, β-bisabolene, γ-cadinene, and β-bisabolol [77]. Trans-carveol, trans-ρ-mentha-1(7),8-dien-2-ol, 5-isopropyl-6-methyl-hepta-3,5-dien-2-ol, phenol, 2-methyl-5-(1-methyl-ethyl), bicyclo(3.1.1)heptane-2,3-diol, 2,6,6-trimethyl-,2-methoxy- 4-vinylphenol, 1-benzoxirene-2,5-dione, 4-(3-oxobutyl) hexahydro-3,3,4-trimethyl, cyclo-hexanecarboxylic acid, 3-fluorophenyl ester, menthol, 1'-(butyn-3-one-1-yl)-,(1R,2S,5R), ledene oxide-(II), elemol, spathulenol, caryophyllene oxide, cis-α-copaene-8-ol, himachalol, isoaromadendrene epoxide, tricycle (5.2.2.0(1,6)) undecan-3-ol, 2-methylene-6,8,8-trimethyl- and trans-longipinocarveol have been reported from the leaf oil of Bael [78].

The essential oil of Bael leaf contained naphthalene, 2,6-dimethyl- 3,5,7-octatriene-2-ol, trans-carveol, 2-cyclohexen-1-one, limonene epoxide, ρ-vinylguaiacol, α-A-cubebene, copaene, β-elemene, caryophyllene, bicyclo(3.1.1)hept-2-ene, β-sesqui-phellandrene, α-humulene, β-farnesene, α-cedrene, 2-epi-α-cedrene, δ-cadinene, 2,6-bis(1,1-dimethylethyl)-4-methyl, β-bisabolene, nerolidol, cis-Z-alpha-bisabolene epoxide, 3-bromohomoadamantane, 3,5 cyclo-octadien-1-one, α-chamigrene, β-maaliene, bergamotene, α-h-cis-eudesma-6-ene-12-al, geranyl-geraniol, (S)-(+)-xanthorrhizol, myristinic acid, fumaric acid, hexahydrofarnesyl acetone, 4,7 dimethyl-pentacyclododecane-4,7-diol, 7,9-di-tert-butyl-1-oxaspirodeca-6,9-diene-2,8-dione, (E,E)- farnesol, trans-Z-α-bisabolene epoxide, hexadecenoic acid, corymbolone, 2 methyl-z, z-3,13-octadecadienol, 5,9-diamino-2,4-dimethyl-7h-pyrazolonaphthyridine, n-heneicosane, trans-α-himachalene, 2-hexadecen-1-ol, linoleic acid, stearic acid, n-docosane, cis-12-octadecadienoic acid, 11,13-dimethyl-12-tetradecen-1-ol acetate, alpha-terthienyl, thianthrene, phytan, majorenolide, n-tetracosane, 13-tetradece-11-yn-1-ol, 6-methylindole, n-penta cosane, 1,2-benzenedicarboxylic acid, n-eicosane, 3-methyl-1,3 thiazole-2-thione, and heptacosane [79]. β-caryophyllene (29.6%), α-humulene (13.3%), γ-muurolene (9.8%), ar-curcumene (7.5%), β-elemene (7.5%), δ-cadinene (5.2%) and α-bulnesene (2.9%) were detected in the essential leaf oil of Bael [80] .

The essential oil of Bael leaf exhibited the presence of α-pinene, 2-methyl-2-pentanol, myrcene, α-phellandrene,

β-phellandrene, limonene, (Z)-β-ocimene, (E)-β-ocimene, ρ-cymene, β-elemene, β-caryophyllene, α-humulene, cryptone, δ-cadinene, ar-curcumene, trans-carveol, caryophyllene oxide, and n-hexadecanoic acid [81]. GC-MS analysis of volatile leaf oil led to the isolation of L-β-pinene, ethylisovalerate, limonene, β-phellandrene, β-cis-ocimene, ρ-mentha-1,4(8)-diene, β-linalool, ρ-allyl toluene, 3,9-epoxy- p-menta-1,8(10)-diene, pinocarvone, terpinen-4-ol, γ-gurjunene, ρ-cymen-α-ol, α-terpineol, (Z)-cinerone, β-elemene, 2-methyl-oct-2-enedial, guaia-1(10),11-diene, ρ-caryophyllene, caryophyllene oxide, limonen-6-ol, carotol, ρ-cymen-8-ol, spathulenol, isoaromadendrene epoxide, α-acorenol, trans-longi pinocarveol, eudesm-7(11)-en-4-4-ol, phytol, calcitriol and fenretinide [82]. D-limonene, α-phellandrene, α-pinene, (E)-β-ocimene, ρ-cymene, and sabinene were isolated from the essential Bael leaf oil [83]. Bael leaf essential oil contained α and β-caryophyllene, limonene, β and γ-elemene, and transcyclopropane [69]. γ-Elemene, trans-β-caryophyllene, β -bisabolene, globulol, ledene alcohol, caryophyllene oxide, humulene-1,2-epoxide, rosifoliol, geranyl-α-terpinene, 3-methyl-2-(2-methyl-2-butenyl)- furan, trimethyl[2-(phenylthio) ethoxy]silane, 6-allyl-2-cresol, pentanoic acid, 2-methyl-, anhydride, (+)-3-carene, 2-(acetylmethyl)-, (2e)-7-ethoxy-3,7-dimethyl-2-octen-1-ol, β-ionone epoxide, 10,12-hexadecadien-1-ol, 9,12,15-octadecatrienoic acid, ethyl ester, (z,z,z)-, 9,12-octadeca-diynoic acid, trimethylsilyl ester, 13-hexyloxacyclotridec-10-en-2-one and cholesta-3,5-diene have been reported from the bael leaf essential oil after gc-ms analysis [84].

Stem: Stem bark extracted in ether yielded umbelliferone, skimmianine, marmesin, a new coumarin marmin, and γ-sitosterol [85,86]. The methanol extract of Bael stem bark contains four lignan-glucosides, (-)-lyoniresinol2α-O-β-glucopyranoside, (-)-4-epi-lyoniresinol- 3α-O-β-D-glucopyranoside, (+)-lyoniresinol α-O-β-D-glucopyranoside and (-)- lyoniresinol 3α-O-β-D-glucopyranoside, two coumarins 7-(7-chloro-6R-hydroxy-3,7-dimethyl-2-octenyloxy) coumarin, 7-[6R-(β-D-gluco-pyranosyloxy)-4R, 7-dihydroxy-3,7-dimethyl- 2-oct-enyloxy]-coumarin, aegline, and chloromarmin [87,88]. The ethyl acetate stem bark extract of Bael has been reported to contain skimmiarepin A and skimmiarepin C [89]. Umbelliferone β-D-galactopyranoside has been extracted from the methanol extract of Bael stem [90]. Umbelliferone, psoralene, marmin, imperatorin, and skimmianine have been isolated from the stem bark of Bael extracted in petroleum ether, chloroform, ethyl acetate, methanol, ethanol, and water. The amount of these phytochemicals was least in the petroleum ether extract whereas their quantity was highest in methanol, ethanol, chloroform, ethyl acetate, and water extracts in this order [91]. 70-O-ethylmarmin, 2-O-ethyltembamide, marmin, epoxyaurapten and skimmianine have been separated from the ethanol extract of the stem bark of Bael [92]. Hexane extract of stem bark has been reported to consist of umbelliferone, scopoletin, 3,5 di-tert-butyl-4-hydroxy propanoic acid, β-fargarine, trisorralen, oxosoralen, 7,8,9-trimethoxy-4,5-dihydro-1 H-benzoindazole, and α-amyrin [69].

Root: Root bark contains the coumarin decursinol, marmesin, marmin, and an alkaloid, haplopine, skimmianine, γ-fagarine, xanthotoxin, umbelliferone and lupeol [23]. The roots of Bael extracted in petroleum ether showed the presence of N-2-hydroxy-2(4-methoxyphenyl) ethyl cinnamamide (aegeline) and 4,7,8-trimethoxy- furo[2,3-b] quinoline or skimmianine [93]. Aegle-marmelosine has been isolated from the dichloromethane extract of roots and twigs of Bael [94]. Umbelliferone, psoralene, marmin, imperatorin, and skimmianine were detected in the methanol extract of Bael root bark [95]. The later study on the petroleum, ether, chloroform, ethyl acetate, methanol, ethanol, and water extracts of Bael root bark also showed the presence of the above phytochemicals and their quantity was least in the petroleum ether extract which was maximum in methanol, ethanol, chloroform, ethyl acetate, and water extracts in this order [91].

Fruit: The furanocoumarin, alloimperatorin, imperatorin, and β-sitosterol were isolated from Bael fruit [96]. The acetone extract of unripe fruit of Bael showed marmelin, aegeline, O-methylhalfordinol, O-iso-pentennylhalfordinol, alloimperatorin, imperatorin, and xanthotoxin [97]. Two pyridylamides- marmamide-A and -B and N-benzoyltyramine methyl ether were isolated from the ethanol extract of unripe Bael fruit [98]. Acetone extract of green Bael fruit showed the presence of alkaloid marmesiline, 6-(4-acetoxy-3-methyl-2-butenyl)-7-hydroxycoumarin, 6-(2-hydroxy-3-hydroxymethyl- 3-butenyl)-hydroxycoumarin, 8-hydroxysmyrindiol and marmelonine [99]. Marmelosin, scopoletin, and umbelliferone have been isolated from the methanol extract of Bael fruit [100]. Two coumarins marmelosin and psoralen were isolated from Bael pulp [101]. The raw fruits of Bael showed the presence of furanocoumarins 3'-prenyloxypsoralen, imperatorin, xanthotoxin [102]. Acetone extract of Bael fruit led to the isolation of a flavonoid afzelin, and three coumarins-marmelosin, marmin, and xanthotoxol [103]. The Bael fruit pulp chloroform extract has been reported to contain heraclenin (fluorocoumarin) and auraptene (coumarin) [104]. 2-Methoxy-4-vinylphenol, 1-(3,5-dimethoxyphenyl) ethan-1-one, (E)-4-(3-hydroxyprop-1-en-1-yl)-2-meth-oxyphenol, 3-deoxyestradiol, methyl 7,10,13-hexadeca-trienoate, oleic acid, ethyl iso-allocholate, γ-sitosterol, sitostenone, cholest-1-eno[2,1-α] naphthalene, 3',4'-dihydro have been detected from the methanol (70%) fruit extract of Bael. The hexane extract of Bael fruit contained tetradecanoic

acid, methylpalmitate, palmitic acid, octadecanal, methyl octadeca-9,12-dienoate, methyl 16-methylheptadecanoate, octadeca-9,12-dienoic acid, vaccenic acid, octadec-13-enoic acid, stearic acid, icosanoic acid, 2-hydroxycyclopentadecan-1-one, 3-pentadecylphenol, tetracosane and heptacosane [105].

The methanol extract of Bael fruit led to the isolation of 1-decanylgodoleate (capryl 9Z-eicosenoiate), behenyl oleate (1-docosanyl cis-9-octadecenoate), 2,6,10,14-tetramethyl dec-15-en-14-olyl salicylate (isophytylsalicylate), and lacceroic acid [106]. GC-MS analysis of petroleum ether, methanol, and ethanol extracts of Bael fruit pulp led to the detection of γ-elemene, tetracontane, tetracosane, nanocosane, and hexacosane in all extracts whereas cyclohexane, caryophyllene, and azulene were detected in all but not in the ethanol extract. β-sesquiphellandrene, 1,3 cyclohexane, quinoline, pranqenin were isolated from the methanol extract. Germacrene, 1,3 cyclohexadiene, 1-methyl-4-(5-methyl1methylene-4-hexenyl), 3-(1,5-dimethyl4hexenyl)-6-methylenehexadecane, n-hexadecanoic acid, octadecane, docosane, heneicosane, and 4-hydroxy-7h-furo(3-2-g)chromen-7-one were separated from the petroleum ether Bael fruit extract, whereas squalene was detected in both the petroleum ether and ethanol fruit extracts [107]. Gallic acid, 2,3 -dihydroxy benzoic acid, chlorogenic acid, ρ-coumaric acid, vanillic acid, rutin, oxalic acid, tartaric acid, malic acid, lactic, acetic acid, citric acid, succinic acid, fumaric acid, propionic acid, ascorbic acid, thiamine, riboflavin, niacin, pantothenic acid, pyridoxine, biotin, cobalamins, α-carotene acid, β-carotene, γ-carotene, δ-carotene, α-tocopherol, β-tocopherol, γ-tocopherol and δ-tocopherol have been isolated from the hydroethanol extract of Bael fruit [108]. The methanol extract of hard shell of bael fruit contains 4-hydroxybenzeneacetic acid; 5-oxo-pyrrolidine-2-carboxylic acid methyl ester; 1-[3-methyl-3-butenyl] pyrrolidine; trans-sinapyl alcohol; 5-[hydroxymethyl]-2-furaldehyde and 2,4- dihydroxy-2,5-dimethyl-3[2H]-furan-3-one [109]. The acetone extract of Bael fruit showed the presence of O-(3,3-dimethylallyl) halfordinol, aegeline, marmeline, imperatorin, xanthotoxol, valencic acid, vanillic acid, and rutin [110]. Marmelosin, marmesin, aegeline, psoralen, scopoletin, and umbelliferon have been isolated from the methanol fruit pulp extract of Bael [111].

Seed: The ethanol Bael seed extract showed the presence of galactose, glucose, arabinose, and rhamnose [112]. 2-isopropenyl-4-methyl-1-oxa-cyclopenta[b]anthracene-5,10-dione and (+)-4-(20-hydroxy-30-methyl-but-30-enyloxy)-8H-[1,3]dioxolo[4,5-h]chromen-8-one, 1-methyl-2-(30-methyl-but-20-enyloxy)-anthraquinone, imperatorin, β-sitosterol, plumbagin, β-sitosterol glucoside, stigmasterol, vanillin, and salicin have been isolated from the Bael seeds [113]. GS MS analysis of Bael seed oil resulted in the separation of methyl esters of lauric acid, myristic acid, palmitic acid, palmitoleic acid, stearic acid, oleic acid, linoleic acid, linolenic acid, arachidic acid, and behenic acid. The seed oil also contains methyl esters of dodecanoic acid, methyl tetradecanoate, pentadecanoic acid, 9-hexadecanoic acid, hexadecanoic acid, 14-methyl-,9,12-hexadecadienoic acid, heptadecanoic acid, 9-hexa-decenoic acid, 9-octadecenoic acid (z)-, 9,12-octadecadienoic acid, eicosanoic acid, 11-eicosenoic acid, docosanoic acid. octanoic acid, and ethyl ester of 9,12,15-octadecatrienoic acid [114]. The imperatorin, 7-(3'-methylbut-2-enyloxy)-2H-chromen-2-one, umbelliferone, skimmianine, and a new flavanone 3,5,7-trihydroxy-2-(4'-hydroxy-3'-isopentyl- oxyphenyl-4H-chromen-4-one have been isolated from the defatted seeds of Bael [115].

The molecular structures of some of the important active biomolecules isolated from different parts of Bael are presented in Figure 6.

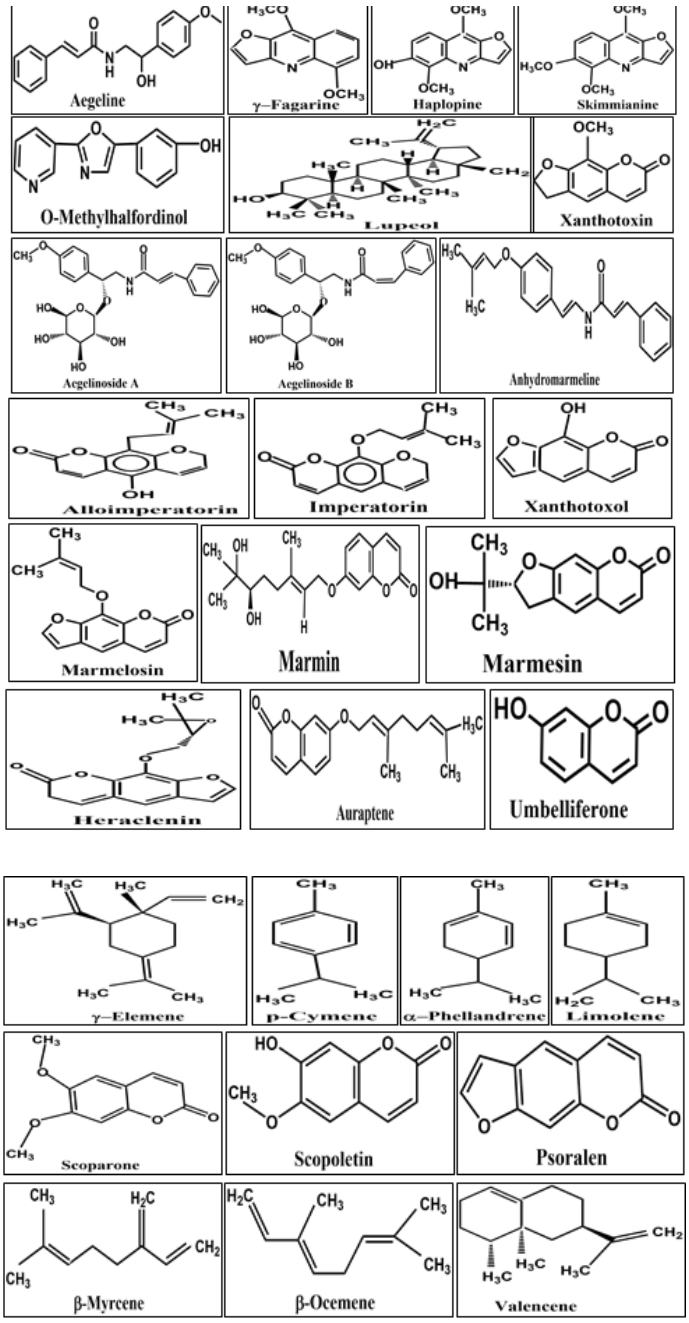

Figure 6: Molecular structure of various isolated compounds from Bael (Aegle maremlos).

Toxicity Evaluation

The safety evaluation of any pharmacophore is of utmost importance before its human application and Bael has been reported to be non-toxic at the doses for human use as indicated by numerous preclinical investigations. Swiss albino mice administered intraperitoneally with 1000, 1500, 1750, 2000, 2125, 2250, 2375, and 2500 mg/kg of 50% ethanol Bael leaf extract did not induce mortality up to 1750 mg/kg. A further increase in the leaf extract dose to 2000, 2125, 2250, and 2375 mg/kg led to an increase in mortality by 10, 20, 50, and 80%, respectively and all animals died at a dose of 2500 mg/kg in acute toxicity studies. The lethal dose (LD) 50 was found to be 2250 mg/kg body weight in mice [116]. The acute toxicity of hydroethanolic (50%) Bael fruit extract was tested in mice where the intraperitoneal administration of 1, 2, 3, 4, 5, and 6 g/kg body weight extract

did not induce mortality even at 6 g/kg and hence it was considered safe [117]. Acute toxicity studies of total ethanol, methanol, total aqueous, and whole aqueous extracts of Bael leaf administered (intraperitoneally) at a dose of 1000, 1500, 2000, and 2500 mg/kg body weight in Wistar rats led to LD50 of 1660, 1445, 1549, and 1318 mg/kg body weight for total alcohol, total aqueous, whole aqueous and methanol Bael leaf extracts, respectively. The acute toxicity studies did not show any adverse effect except the stoppage of the heart in a systolic stand-still. The daily intraperitoneal administration of 50, 70, 90, and 100 mg/kg body weight of each extract for 14 days in Wistar rats did not cause any toxicity in rats [118]. Intraperitoneal administration of 1, 1.2, 1.5, and 2 g/kg aqueous Bael fruit extract led to the LD50 of 1.6 g/kg in Swiss albino mice [119].

The oral administration of 2000 mg/kg body weight of aqueous Bael leaf extract did not produce any toxicity as there was no alteration in the food and water intake. The extract also did not induce mortality [120]. The methanol fruit extract of Bael was found to be nontoxic at a dose of 5000 mg/kg body weight in rats after oral administration. The hematological profile, liver, spleen, kidney, and body weight remained unaltered indicating the safety of Bael fruit extract [121]. The methanol extract of (70:30 methanol and water) extract of Bael fruit administered orally at graded doses of 500, 1000, 2500, 5000, and 7500 mg/kg body weight in Swiss albino mice did not produce any behavioral and physiological changes in the animals during the observation period of 24 h. All test animals survived even after a dose of 7500 mg/kg indicating the safety of fruit extract [122]. The oral administration of ethanol extract of Bael fruit produced mortality at a dose of 2 g/kg body weight in Swiss albino mice and LD50 was greater than 1250 mg/kg, which did not exert any toxicity [123]. Mice orally administered with 500, 1000, and 2000 mg/kg body weight of hydroalcoholic (60% ethanol and 40% water) extract of unripe fruits did not exhibit visible signs of toxicity and also did not produce mortality even at 2000 mg/kg [124]. In another study, oral administration of methanol Bael leaf extract did not produce toxicity up to 2000 mg/kg in albino rats [125]. Administration of 820, 880, 970, 1100, 1230, and 1450 mg/kg of Bael leaf oil in Swiss albino mice resulted in an LD50 of 1051.96 mg/kg [83].

Antimicrobial

The methanol, aqueous-methanol, and aqueous extracts of stem/stem bark, root/root bark, leaves, and fruits of Bael and marmelide inhibited the growth of human Coxsackie viruses (B1-B6) in a concentration dependent way and maximum inhibition was observed at 1000 µg/ml for all leaf and stem/stem bark extracts. The aqueous extract of root bark and marmelide inhibited the viral growth at 62.5µg/ml and this concentration for methanol root extract was 500µg/ml. Similarly, the aqueous fruit extract inhibited the growth of the virus at 250µg/mL whereas for methanol fruit extract it was 500µg/ml [126]. The methanol extract of the bark and fruit of Bael was active against *Bacillus subtilis*, *Staphylococcus aureus* (Gram Positive), *Klebsiella pneumoniae*, *Proteus mirabilis*, *Escherichia coli*, *Salmonella paratyphi* A and *Salmonella paratyphi* B (Gram Negative), whereas the chloroform extract was active against all bacteria except *Klebsiella pneumoniae* [127]. Petroleum ether, dichloromethane, chloroform, ethanol, and aqueous extracts of Bael leaves inhibited the growth of *Micrococcus glutamicus*, *Lactobacillus bulgaris*, *Streptococcus faecalis*, *Staphylococcus aureus*, *Bacillus stearothermophilus*, *Staphylococcus pyogenes*, *Micrococcus gluteus*, *Bacillus cereus* and two strains of Gram-negative bacteria- *Escherichia coli* and *Pseudomonas aeruginosa*. The chloroform and ethanol extract were active against these bacteria except *Lactobacillus bulgaris* and *Bacillus cereus*, whereas other extracts were ineffective against all the species [128]. The petroleum ether extract of the leaf callus of Bael showed antibacterial activity against *Salmonella typhi* (maximum), *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, and *Klebsiella pneumoniae* (minimum) in decreasing order [129].

Petroleum ether, acetone, methanol, and water extracts of leaves were tested against *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Serratia marcescens*. The petroleum ether extract arrested the growth of only *Pseudomonas aeruginosa*, whereas acetone extract inhibited the growth of *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The methanol extract was active against *Pseudomonas aeruginosa*, *Escherichia coli*, and *Serratia marcescens* whereas the aqueous extract was not effective as an antimicrobial agent [130]. The aqueous extract of Bael fruit attenuated the growth of *Escherichia coli* at a concentration of 500µg/mL due to its ability to decrease RNA transcripts of the outer membrane protein (omp) C and ompR genes. The extract also reduced activated caspase 3 and increased Hsp 70 levels in rat ileal loop infected with *Escherichia coli* [131]. The methanol extract of Bael leaves and flowers showed antibacterial activity against *Escherichia coli*, *Staphylococcus aureus*, *Salmonella typhi*, *Proteus mirabilis*, and *Pseudomonas aeruginosa* [132]. The essential oil of Bael inhibited the growth of the fungus *Aspergillus flavus* in a concentration dependent manner and complete growth inhibition was recorded at a concentration of 750µL/L [133]. The ethanol and aqueous extracts of Bael leaf inhibited the growth of *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Bacillus subtilis* in a concentration dependent manner (0.5 to 2.5 mg/mL) [134]. The essential oil of the Bael leaf inhibited the spore germination of italicize Fusarium udum in a concentration dependent way [135]. Hexane, benzene, chloroform, ethyl

acetate, methanol, and aqueous extracts of Bael leaves arrested the growth of *Trichophyton mentagrophytes*, *Trichophyton rubrum*, *Microsporum canis*, *Microsporum gypseum*, and *Epidermophyton floccosum* in a concentration dependent manner [136]. The Bael leaf extracted in ethanol exhibited antibacterial activity against *Escherichia coli*, *Salmonella typhi*, *Staphylococcus aureus*, and *Bacillus subtilis* [137]. The petroleum ether, chloroform, and methanol extracts of Bael leaf showed antibacterial activity against *Staphylococcus aureus*, β *Streptococcus haemolyticus* group A, *Proteus mirabilis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Salmonella typhi*, and fungi *Candida albicans*, *Candida tropicalis*, and *Aspergillus flavus* [138]. Silver nanoparticles (Nps) prepared from aqueous Bael leaf extract have been reported to inhibit the growth of *Staphylococcus aureus*, *Citrobacter koseri*, *Bacillus cereus*, *Pseudomonas aeruginosa*, and *Escherichia coli*, and fungus *Candida albicans*, where *Citrobacter koseri* was less sensitive (IC50 1.25 mg/mL) and *Pseudomona aeruginosa* was most sensitive (IC50 0.07825 mg/mL) [139].

The 50% methanol extract of ripe fruit of Bael inhibited the growth of *Staphylococcus aureus*, *Bacillus subtilis*, *Staphylococcus epidermidis* (gram-positive) *Escherichia coli*, *Shigella flexneri*, and *Pseudomonas aeruginosa* (gram negative) in a concentration dependent way [140]. The Bael leaves extracted in ethanol showed a concentration dependent decline in the growth of *Bacillus subtilis*, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Klebsiella pneumonia*. The *Bacillus subtilis* and *Escherichia coli* were more sensitive than the other bacteria and were also more sensitive to the treatment than *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Klebsiella pneumonia* [140]. Bael leaf essential oils prevented the proliferation of Staphylococcus aureus, *Bacillus cereus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and fungi *Candida albicans* and *Aspergillus niger* [75]. The hexane, ethanol, methanol, and water extracts of Bael leaves inhibited the growth of skin pathogens including *Staphylococcus epidermidis*, *Staphylococcus saprophyticus*, *Micrococcus luteus*, *Pseudomonas fluorescens*, *Pseudomonas putida*, *Bacillus licheniformis*, and *Bacillus subtilis*. The ethanol leaf extract attenuated the growth of all bacteria tested whereas the aqueous extract was ineffective against *Bacillus licheniformis*, and *Pseudomonas putida*. The hexane extract inhibited the growth of *Staphylococcus epidermidis* only. The methanol extract did inhibit the growth of *Staphylococcus epidermidis*, and *Bacillus licheniformis* [142]. AgNps prepared from Bael fruit prevented the growth of *Escherichia coli*, *Bacillus cereus*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* in a concentration dependent manner, and a maximum effect was detected at 60µg/ml [143].

Aqueous and ethanol extracts of Bael fruits were potent inhibitors of the growth of *Escherichia coli* [144]. The methanol extract of unripe and ripe Bael fruit had significant antibacterial activity against *Escherichia coli* and *Staphylococcus aureus* [145]. Petroleum ether, ethanol, and water extracts of Bael fruit pulp inhibited the growth of *Staphylococcus aureus* in a concentration dependent manner [146]. The petroleum ether, chloroform, and ethyl acetate extracts of Bael restrained the growth of *Lactobacillus*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Salmonella typhi*, *Escherichia coli* and *Pestolotia foedans*, *Paecilomyces variotii*, and *Fusarium oxysporum* in a concentration dependent manner [147]. The growth of *Bacillus subtilis*, *Enterococcus faecalis*, *Staphylococcus aureus*, *Escherichia coli*, *Vibrio cholerae*, and *Pseudomonas aeruginosa* was arrested by the aqueous Bael leaf extract [148]. AgNps of Bael have been reported to attenuate the growth of *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeuruginosa*, and *Candida albicans*, where *Candida albicans* was more sensitive than the other bacteria [149].

The ethyl acetate extract of Bael leaf effectively inhibited the growth of *Bacillus subtilis*, *Staphylococcus epidermidis* and *Enterococcus faecalis* (gram negative) and *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella typhi*, at 1000 µg/ml, whereas the isolated quinone was highly effective against all these bacteria and additionally to *Aspergillus clavatus*, *Aspergillus furnigates*, *Aspergillus flavus*, *Aspergillus niger*, *Aspergillus oryzae*, *Aspergillus pullulans*, *Botrytis cinerea*, *Botrytis elliptica*, *Candida albicans*, *Cotoneaster acumninatus*, *Cochliobolus lunata*, *Epidermophyton floccosum*, *Fusarium culmorum*, *Fusarium oxysporum*, *Fusarium solani*, *Gibberella moniliformis*, *Humicola grisea*, *Penicillium chrysogenum*, *Penicillium notatum*, *Penicillium roqueforti*, *Scytalidium lignicola*, *Scytalidium vaccinii*, *Scytalidium brevicaulis*, *Scytalidium fusca*, *Trichophyton mentagrophytes*, *Trichophyton roseum*, and *Trichophyton viridiae* fungi [150]. Marmelosin and marmin (coumarins) isolated from Bael fruit pulp inhibited the growth of *Mycobacterium tuberculosis* H37Ra and *Mycobacterium bovis* having an IC50 of 12.46µg/mL and 4.31µg/mL respectively. Marmelosin and marmin also arrested the growth of *Staphylococcus aureus*, *Bacillus subtilis*, and *Escherichia coli*, whereas marmelosin was ineffective against *Staphylococcus aureus* [103]. Acetone, ethanol, methanol, chloroform, and petroleum ether Bael fruit extracts inhibited the growth of *Escherichia coli*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Aspergillus brasiliensis* and *Candida albicans* [151]. The essential Bael leaf oil inhibited the growth of *Streptococcus faecalis*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Staphylococcus aureus*, *Sarcina lutea*, *Arthrobacter citreus* and *Escherichia coli* and fungi *Aspergillus niger* and *Candida albicans* [77]. The methanol extract of Bael stem bark arrested the growth of *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas auriginosa*, and *Enterococcus sp*. in a concentration dependent manner [152].

Ethyl acetate extract of Bael leaf showed antibacterial activity against *Escherichia coli*, *Salmonella sp*., and *Shigella sp*. [153]. The methanolic Bael leaf extract attenuated the growth of *Bacillus subtilis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, and *Escherichia coli* concentration dependently, whereas chloroform leaf extract was effective only at 100 mg/ml [154]. The aqueous and methanol fruit extract exhibited antibacterial activity against *Staphylococcus aureus*, *Bacillus sp*., *Escherichia coli* and *Pseudomonas aeruginosa*, and fungi *Aspergillus niger*, *Mucor sp., Penicillium sp*., *Rhizopus sp* [155].

Fruits of Bael extracted in acetone, ethanol, 80% methanol, chloroform, and petroleum ether arrested the growth of *Escherichia coli*, *Bacillus subtilis*, and *Staphylococcus aureus*, whereas *Pseudomonas aeruginosa* was sensitive to 80% ethanol and chloroform extracts and resistant to all other extracts. All these extracts inhibited the growth of *Candida albicans*, whereas acetone, 80% methanol, and chloroform extracts were also active against *Aspergillus brasiliens*is [156]. The ethanol leaf and fruit extract showed significant antibacterial activity against multidrug-resistant *Escherichia coli*, whereas hexane and chloroform extracts were moderately active [157]. The growth of *Bacillus cereus*, *Bacillus subtillis*, *Staphylococcus aureus*, *Escherichia coli*, *Shigella dysenteriae*, and *Shigella sonneri* was attenuated by aqueous, methanol, and ethanol extracts of Bael leaf and among them methanol extract was most effective against *Bacillus subtillis* [40].

The ethanol extract of Bael leaf effectively inhibited the growth of *Escherichia coli, Corynebacterium* spp., *Staphylococcus* spp., and *Bacillus* spp. isolated from endometriotic cows [158]. The dichloromethane, ethanol, ethyl acetate, methanol, n-hexane, and petroleum ether extracts and leaf oil of Bael arrested the growth of *Sarcina lutea*, *Bacillus subtilis*, *Paracoccus denitrificans*, *Escherichia coli*, *Klebsiella pneumoniae*, *Xanthomonas campestris*, and *Proteus vulgaris*. All extracts of Bael leaf significantly retarded the growth of *Paracoccus denitrificans*. Petroleum ether and n-hexane extracts impeded the growth of *Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Sarcina lutea*, *Pseudomonas vulgaris*, and *Xanthomonas campestris* and were most active. The growth of *Bacillus subtilis* was also attenuated by ethanol, methanol, and ethyl acetate extracts. A moderate growth arrest was seen for *Klebsiella pneumoniae* by ethyl acetate, dichloromethane, and methanol Bael leaf extracts [78]. The acetone, methanol, chloroform, and essential leaf oil of Bael showed antibacterial and antifungal activity against *Bacillus subtilis*, *Bacillus cereus*, *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus fecalis*, *Alcaligens denitrificans*, *Campylobacter coli*, *Pseudomonas alcaligens*, *Alcaligens denitrificans*, *Micrococcus luteus* and *Klebsiella pneumoniae* and fungi *Alternaria alternata*, *Curvularia lunata*, and *Bipolaris specifera* [159].

The aqueous fruit extract of Bael arrested the growth of *Escherichia coli*, *Klebsiella pneumoniae*, and *Shigella flexneri* gram negative as well as gram positive strains such as *Staphylococcus aureus*, *Bacillus subtilis* in a concentration dependent way [160]. The hexane, ethyl acetate, aqueous, methanol, and ethanol extracts of Bael leaf attenuated the growth of, *Staphylococcus aureus*, *Bacillus subtilis*, *Klebsiella pneumoniae*, *Pseudomonas vulgaris* and *Shigella flexneri* in a concentration dependent way [67]. Bael leaf ZnFe2O4 Nps inhibited the growth of *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Bacillus subtilis* [161]. The 70% methanol extract of Bael stem bark inhibited the growth of *Bacillus subtilis*, *Enterococcus faecalis*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Salmonella enterica* subsp. enterica serovar typhi with a minimum inhibitory concentration (MIC) of 25, 25, 12.5, 25, 25, and 50mg/ml, respectively. The hexane Bael stem bark extract was active only against *Bacillus subtilis*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* with a MIC of 25mg/ml. The hexane extract was also active against *Escherichia coli*, whereas the methanol extract was ineffective [105]. Bael leaf essential oils prevented the proliferation of *Staphylococcus aureus*, *Corynebacterium diphtheriae*, *Escherichia coli*, and *Proteus mirabilis* [81].

The copper-doped gold nanoparticles (Cu-AuNPs) of methanol extract of Bael leaf inhibited the growth of *Staphylococcus aureus*, *Salmonella typhi*, *Bacillus subtilis*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, and *Klebsiella oxytoca* in a concentration dependent manner and maximum inhibition was detected at a concentration of 400µL whereas no inhibition was detected for *Streptococcus mutans*, *Escherichia coli*, *Vibrio parahemolyticus* and *Micrococcus luteus* [162]. The AgNps of Bael fruit peel aqueous extract arrested the growth of *Escherichia coli* depending on the concentration with a maximum effect at 100µg/mL [163]. The AgNps prepared from Bael fruit pulp aqueous extract attenuated the growth of *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pyogen*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, and *Candida albicans* [164]. Solid nanoparticles prepared from the Bael leaf oil inhibited the growth of *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli, Pseudomonas aeruginosa* bacteria, and fungi *Candida albicans* and *Aspergillus fumigatus* [165]. The growth of *Staphylococcus aureus Enterococcus faecalis*, *Micrococcus luteus*, *Pseudomonas aeruginosa*, and *Escherichia coli* was arrested by the AgNPs (prepared from the aqueous Bael fruit) concentration dependently [166]. Aqueous Bael leaf extract and AgNps have been reported to inhibit the growth of *Streptococcus* sp., *Streptococcus aureus*, *Klebsiella* sp, and *Pseudomonas aeruginosa* fungi *Aspergillus niger*, *Aspergillus flavus*, *Candida* sp and *Penicillium* sp. concentration

dependently and AgNps were better than the aqueous extract [167].

Antioxidant

Bael leaf extracted in 50% ethanol inhibited the generation of DPPH, hydroxyl (•OH), superoxide (O_2-•), NO, and $ABTS^+$ free radicals in a concertation dependent manner [168]. The ethanol, ethyl acetate, and water extracts of Bael bark scavenged DPPH radicals, where ethyl acetate extract was most active. All extracts showed increasing antioxidant activity indicated by the reduction in the peroxides and formation of phosphomolybdate [53]. Aqueous extract of Bael fruit scavenged DPPH radical in a concentration dependent manner with an IC50 of 17.37 ± 2.71 mg/mL [169]. Unripe fruit extracted in water scavenged DPPH, •OH, O2•-, NO• and ABTS•+ radicals in a concentration dependent manner [170]. The methanol (50%) extracts of Bael fruit, leaf, and stem bark scavenge nitric oxide •OH radicals in a concentration dependent manner with IC50 of 550, 300, and 350 µg/mL for fruit, leaf, and stem bark extracts, respectively. The leaf extract was the most active among all the three extracts evaluated [171]. The pulp, rind, and seed of Bael extracted in hexane, chloroform, ethyl acetate, acetone, and methanol were tested for their ability to scavenge DPPH radicals. The hexane extract did not show any activity whereas the chloroform extract was the least active. These extracts were freeze-dried or oven-dried. The methanol extract was the most active followed by ethyl acetate and acetone. The freeze-dried pulp (IC50 83.82 µg/mL), rind (IC50 109.52 µg/mL), and seed (IC50 of 121.32 µg/mL) extracts showed marginally better activity than the oven-dried pulp IC50 of 84.87 µg/mL, rind IC50 of 111.37 µg/mL and seed IC50 of 123.51 µg/mL [172]. The Bael stem bark extracted in n-hexane methanol, and ethyl acetate scavenged DPPH and NO free radicals depending on their concentration, leading to an IC50 of 37.056 µg/mL, 43.379 µg/mL, and 66.180 µg/mL for methanol, ethyl acetate, and n-hexane extracts, respectively for DPPH radicals. The IC50 for NO was 28.377µg/mL, 45.853µg/mL, and 66.980µg/mL for ethyl acetate, methanol, and n-hexane extracts, respectively [173].

The methanol, ethanol, and aqueous extracts of Bael leaf dose dependently inhibited the formation of DPPH radicals. The ferric reducing power was maximum for ethanol extract, which also inhibited linseed oil-induced LOO in vitro to a maximum extent [174]. The hydroalcoholic fruit extract of Bael scavenged DPPH and ABTS free radicals with an IC50 of 351±37 and 228±25 µg/mL, respectively [175]. The ethyl acetate and methanol Bael leaf extracts showed scavenging of DPPH radicals and increased ferric reducing power depending on concentration with an IC50 of 191.4±1.5 µg/mL for ethyl acetate extract and IC50 of 249.3±9.4 µg/mL for the methanol extract [176]. The methanol extract of dehydrated Bael fruit inhibited the production of DPPH radicals in a concentration dependent manner [177]. Bael leaf ethanol (50%) extract inhibited the generation of DPPH, and ABTS free radicals with an IC50 of 160.47± 8.51 µg/mL and 282.46 ± 44.11 µg/mL, respectively. The leaf extract increased ferric reducing power in a concentration dependent manner with an IC50 of 147.33 ± 23.21 mM Fe2+/g DW [178]. Methanol (30% water), aqueous, ethyl acetate, chloroform, and butanol extracts of Bael ripe fruit increased ferric reducing power and inhibited the DPPH radical and activity of LOX in vitro. The ethyl acetate extract was more potent than the other extracts [179].

Methanol extracts of Bael leaf, ripe fruit, half-ripe fruit, and seed scavenged DPPH and NO radicals in a concentration dependent manner, and the maximum scavenging was observed for half-ripe fruit with an IC50 of 251.2µg/mL (DPPH) and 46.364µg/mL (NO). The methanol extract of all parts showed a dose dependent rise in cupric reducing antioxidant capacity, where a maximum antioxidant capacity was detected for the leaf extract [180]. Bael flower extracted in 50% ethanol and water scavenged DPPH, and •OH radicals. Both flower extracts inhibited LDL oxidation and DNA strand scission and increased ferrous chelating activity [181]. Marmelosin isolated from Bael fruit has been reported to scavenge DPPH free radicals with an IC50 of 15.4 ± 0.32 µM [182]. The aqueous fruit extract of Bael exerted antioxidant action by scavenging DPPH and ABTS+ free radicals and by elevating the phosphomolybdenum reduction activity and ferric reducing power concentration dependently [160]. The hexane, ethyl acetate, aqueous, methanol, and ethanol extracts of Bael leaf scavenged DPPH radicals and elevated the phosphomolybdenum reduction activity and ferric reducing power concentration dependently [67].

The 70% methanol and hexane extracts of stem bark inhibited the formation of DPPH radical depending on the concentration with an IC50 of 961.53 µg/mL for the methanol extract, whereas the hexane extract was not as effective as the methanol extract [105]. The water, acetone, and ethanol extracts of Bael leaf scavenged DPPH radical and increased antioxidant activity (cyclic voltammetry) the water extract was more effective than the acetone and ethanol extracts [45]. The ethanol extract of Bael leaf scavenged DPPH free radicals and increased ferric reducing power concentration dependently. It also inhibited 2,7-dichlorofluorescein diacetate (DCF-DA)-induced ROS formation in a similar manner in HepG2 cells [50]. The Bael seed extracted in petroleum ether, chloroform, ethyl acetate, methanol, and distilled water scavenged hydrogen peroxide, DPPH, and NO• radicals in a concertation dependent fashion, and ethyl acetate extract was more powerful than the other extracts [183]. Bael leaf essential oil concentration dependently

inhibited DPPH and ABTS+• radicals [84].

Anti-Inflammatory

Ethanol (50%) extract of Bael fruit has been reported to inhibit carrageenan-induced paw edema in Sprague Dawley rats significantly in a dose dependent manner and the effect of 200 mg/kg was almost similar to phenylbutazone [184]. The petroleum ether, chloroform, diethyl ether, ethanol, acetone, and methanol extracts of Bael leaves attenuated carrageenan-induced paw edema and cotton pallet-induced granuloma in the rats. All extracts reduced the rat paw edema and granuloma, and the methanol extract was most effective for the former whereas diethyl ether was highly effective in the latter indicating that Bael leaf extracts possess anti-inflammatory activity [185]. The petroleum ether, ethanol, and aqueous extracts of Bael leaves attenuated carrageenan-induced paw edema in Wistar rats in a time dependent manner. The ethanol leaf extract was most effective with maximum inhibition and the aqueous leaf extract was least effective with minimum inhibition of carrageenan-induced rat paw edema [186].

The anti-inflammatory activity of aqueous Bael root extract was tested in carrageenan-induced paw edema and cotton pallet-induced granuloma in albino rats, which was found to significantly attenuate both the carrageenan-induced paw edema and cotton pallet-induced granuloma in albino rats [187]. The aqueous, methanol, and ethyl acetate extracts and NiNps of Bael leaf inhibited membrane stabilizing efficacy and protease inhibitory efficacy in a dose dependent manner, where 100µg/mL was found to be most effective. The anti-inflammatory action was greatest for the NiNps followed by the methanol, ethyl acetate, and aqueous leaf extracts [188]. Aqueous and ethanol extracts of Bael flowers alleviated carrageenan-induced paw edema in Wistar rats in a dose dependent manner and maximum effect was observed at 2 h post-treatment. The ethanol extract showed antihistamine activity and protected heat-induced erythrocyte membrane lysis indicating that ethanol Bael flower extract acts as an anti-inflammatory agent [189]. Methanol leaf extract of Bael reduced the lipopolysaccharide (LPS)-induced formation of nitric oxide (NO) and tumor necrosis factor (TNF-α) and interleukin (IL-8) mRNA expression in a concentration dependent manner in A459 cells [190].

The ethanol extract of Bael leaf inhibited the carrageenan-induced rat paw edema dose dependently [191]. The anti-inflammatory activity of Bael root bark/stem bark/leaves collected from different Indian states and extracted in petroleum ether, ethanol, ethyl acetate, and water were studied in LPS-treated RAW 264.7 cells by analyzing the cyclooxygenase (COX) I and COX II and lipoxygenase (LOX) 5 and anti-inflammatory cytokines IL-2, and proinflammatory cytokines IL-1β, IL-6 and macrophage inflammatory protein-1alpha (MIP-1α) activation. Out of 191 extracts, 44 extracts inhibited COX-II whereas only 38 extracts inhibited COX-I and none inhibited the LOX-5. Out of 44 extracts that inhibited COX-II, 17 extracts did activate anti-inflammatory cytokines IL-2 and inhibited proinflammatory cytokines IL-1β, IL-6, and MIP-1α. Roots (2-3 years old) from Gujarat and 1 year old from Odisha exerted the most potent anti-inflammatory action. These three extracts also inhibited carrageenan-induced paw edema in Balb/c mice [192].

Marmelosin isolated from Bael fruit exerted anti-inflammatory activity by reducing NO formation, and proinflammatory cytokines including TNF-α, nuclear factor kappa B (NF-κB), tyrosinase, and galectin-3 in Raw 264.7 mouse leukemic macrophage cells [182]. The Bael fruit pulp gel has been reported to reduce carrageenan-induced rat paw edema dose dependently and 25% gel was most effective as an anti-inflammatory agent [193]. The ethanol extract of Bael leaves suppressed the expression of TNF-α and interferon-γ (IFN-γ) in LPS-challenged Balb/c mouse cultured splenocytes [68]. Hydroalcoholic extract (70:30) of Bael fruit reduced carrageenan-induced paw edema in Wistar albino rats significantly depending on the dose [194]. The alkaloid-free hydroalcoholic extract of Bael has been reported to attenuate the levels of TNF-α, IL-6, and IL-1β [70].

Antiallergic

Aegeline an alkaloid isolated from Bael leaf has been reported to prevent dinitrophenylated bovine serum albumin (DNP24-BSA), thapsigargin, and ionomycin-induced histamine release from rat basophilic leukemia (RBL-2H3) cells. This inhibition was stronger against Ca2+ stimulants thapsigargin and ionomycin [195]. Almost a similar effect has been observed in RBL-2H3 treated cells with marmin, a coumarin, present in the root bark of Bael. The marmin also inhibited the thapsigargin-induced histamine release from rat peritoneal mast cells (RPMC) [195]. Similarly, marmin also prevented DNP24-BSA and phorbol myristate acetate (PMA)-induced histamine synthesis in RBL-2H3 cells [196].

Antidiarrheal Activity

Diarrhea is characterized by loose, watery, and frequent bowel movements usually caused by malnutrition and is common in children and can last several days but less than 14 days. Approximately 1.7 billion cases of childhood diarrhea are reported each year and 525,000 children succumb to death every year. It is the third leading cause of death. The diarrhea is mainly caused by the infection from Rotavirus and *Escherichia coli*, however, *Cryptosporidium*, *Salmonella*, *Campylobacter*, *Vibrio cholerae*, and *shigella species* also cause diarrhea [197]. The Bael has been found to

arrest diarrhea experimentally. The aqueous and methanol extracts of Bael unripe fruit inhibited castor oil-induced diarrhea in a dose dependent manner in Swiss albino mice and the methanol extract was more potent in comparison to the aqueous extract [198]. The Bael fruit extract reduced castor oil-induced diarrhea in mice and also antagonized the contractile responses stimulated by acetylcholine (Ach), histamine, serotonin, and barium chloride in guinea pig ileum in vitro [199]. The Sprague Dawley rats administered with different doses of ethanol (50%) extract of Bael fruit showed a dose dependent reduction in the castor oil-induced diarrhea, intestinal propulsion, and fecal matter [200]. The Bael has been reported to be active against diarrhea due to its ability to kill viruses and bacteria. The Bael root chloroform extract has been reported to inhibit castor oil-induced diarrhea in a dose dependent manner in Wistar rats by preventing the growth of *Shigella* spp., *Escherichia coli*, and *Vibrio cholerae* in vitro [201].

The aqueous seed extract of Bael inhibited the growth of β-lactam–resistant *Shigella dysenteriae* and *Shigella flexneri* by altering porin channels owing to the downmodulation of RNA transcripts of ompC and ompR genes and could be effective in preventing diarrhea in vivo [202]. The ethanol Bael fruit pulp extract inhibited the growth of *Shigella flexneri*, *Shigella sonnei*, and *Shigella boydii* effectively except for *Shigella dysenteriae* where the response was least indicating that it effectively prevented diarrhea [123]. The crude aqueous extract of Bael unripe fruit inhibited the rotavirus dilution, *Escherichia coli* E134, and *Shigella flexneri* invasion of HEp2 cells in vitro. The extract also inhibited the formation of cholera toxin by *Vibro cholerae* [203]. The n-hexane extract of Bael leaf arrested castor oil-induced diarrhea in Wistar albino rats [37]. Aqueous leaf extract of Bael protected Wistar rats against castor oil-induced diarrhea and retarded gastrointestinal transit time in a dose dependent fashion [120]. Bael fruit aqueous extract inhibited castor oil-induced diarrhea in a dose dependent manner in Swiss albino mice [204].

Ethanol extract of Bael leaf prevented castor oil-induced diarrhea in a dose dependent manner in rats [191]. Methanol and water (70:30) extracts of Bael fruit inhibited the castor oil and tannic acid-induced diarrhea in Swiss albino mice in a dose dependent manner [122]. Methanol extract of fruit pulp of Bael protected Sprague Dawley rats from castor oil-induced diarrhea where treatment of 30 mg and 1600 mg/kg completely inhibited diarrhea [121]. The ethanol extract of the unripe fruit of Bael effectively reduced castor oil-induced diarrhea dose dependently in Swiss albino mice [124]. Water soluble fraction of Bael fruit inhibited the growth of *Vibrio cholerae* Inaba 569B and Escherichia coli 114 dose-dependently. The fraction also showed antidiarrheal activity against castor oil-induced diarrhea in mice [205].

Mechanism of Action

Bael contains several phytochemicals and the different actions of Bael are attributable to alteration in various cellular pathways depending on the effect produced by it (Figures 7 & 8).

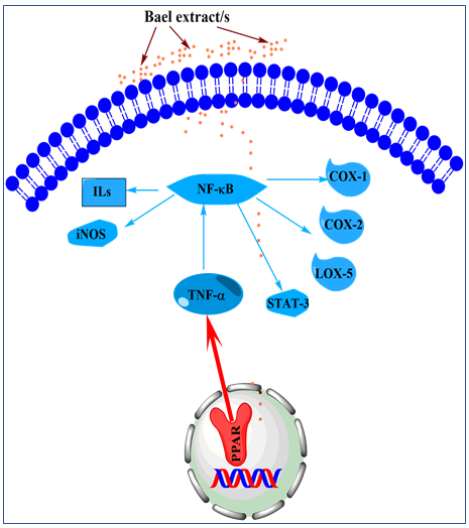

Figure 7: The activation of PPAR by Bael causes downmodulation of TNF-α, NF-κB, COX-I, COX-II, LOX-5, iNOS and various interleukins that leads to anti-inflammatory action.

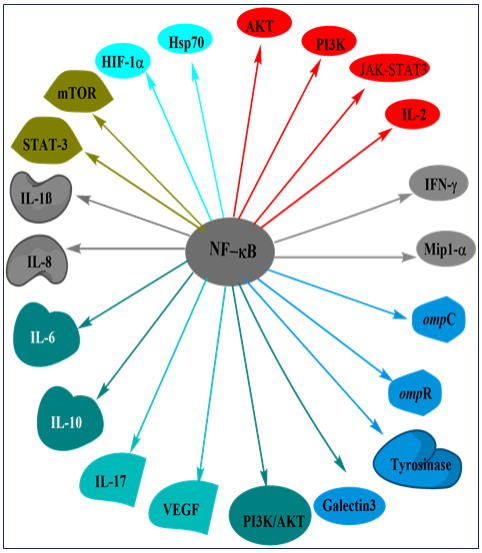

Figure 8: The attenuation of NF-κB by Bael leads to the suppression of IFN-γ, Mip1-α, HIF-α, Hsp70, PI3K/AKT, IFN-γ MIP-1α, ompC, ompR, IL-8, IL-1β, IL-6, IL-10, IL-17, MIP-1α, tyrosinase galectin-3, and activation of PI3K, AKT, IL-2, JAK-STAT3, leading to a decline in inflammatory responses.

The scavenging of various free radicals by Bael seems to be an important aspect of its conducive effects on various medicinal ailments listed in this review [39,44,47,100,112,113,115,116,120,124, 125,191,192].

The downmodulation of TNF-α, NF-κB, Hsp70, PI3K/AKT, mTOR, HIF-1α, IFN-γ, IL-8, IL-1β, IL-6, IL-10, IL-17, MIP-1α, COX-I, COX-II, LOX-5, ompC, ompR, VEGF, STAT-3, AKT, tyrosinase and galectin-3 accompanied by activation of IL-2 by Bael and its active components seem to arrest the inflammatory pathways [70,192,202,207,208].

Conclusions

Bael is native to the Indian subcontinent and Southeast Asia. Bael fruits are edible, eaten fresh, or in the form of sharbat, jellies, and Jams. Bael synthesizes alkaloids, anthocyanins, flavonoids, glycosides, phenols, tannins, sterols, terpenoids, carbohydrates, proteins, quinones, reducing sugars, saponins, and phenols and some of the important bioactive molecules are mamelosin, psoralene, marmin, imperatorin, auroptene, umbelliferone, skimmianine scopoletin, aegeline, etc. It is used to treat ulcerated intestinal mucosa and is given after childbirth. The scientific evaluation has demonstrated that Bael acts as an antimicrobial, anti-inflammatory, antidiabetic, antihyperlipidemic, antidiarrheal, and antioxidant agent. The protective effect of Bael seems to be due to its capacity to passivate ROS and suppress inflammatory pathways by downregulating TNF-α, NF-κB, Hsp 70, HIF-1α IFN-γ and IL-8, IL-1β, IL-6, IL-10, IL-17, MIP-1α, COX-I, COX-II, LOX-5, ompC, ompR, c-jun VEGF, and STAT-3, at molecular level. The pleiotropic activities of Bael indicate its prospects as a future medicine for clinical applications to treat various human diseases in traditional as well as modern medicine. To be acceptable as a modern drug for clinical use exhaustive systematic research is required in different preclinical and clinical models to unfurl the mechanism of action of its active biomolecules and firmly establish its medicinal utility in treating various human ailments.

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