IJPSR (2023), Volume 14, Issue 5 (Review Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 24 July 2022; received in revised form, 04 October 2022; accepted 04 November 2022; published 01 May 2023

A CRITICAL REVIEW ON THE MEDICINAL HERB *AEGLE MARMELOS* (LINN.) CORREA

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Keywords:

Aegle marmelos, Phytochemical constituent, Ethnobotanical uses, Pharmacological properties

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ABSTRACT: Plants are essential to the survival of every species on Earth. Animal and plant life have a history of mutual consumption since antiquity. Earth's sole producers are plant is a fact. As researchers learn more about plants, this assumption is being challenged. The Rutaceae family's citrus species *Aegle marmelos* (Bael), a well-known medicinal herb, has a lengthy study history. In addition to its useful nutrients, *A. marmelos* produces a wide range of secondary metabolites, or phytochemicals, during its whole life cycle. Roots, bark, stems, leaves, fruit, and flowers are all used by humans in some way or another obtained from the *A. marmelos* plant. Various phytochemical substances include various alkaloids, flavonoids, phenols, tannins, coumarins, saponins, carbohydrates, carotenoids, terpenoids, vitamins, and tannins generated by *A. marmelos* plants. The main phytochemical compounds isolated from *A. marmelos* plant are aegelenine, fragrine, halfordinol, marmelide, marmelosin, marmesin, marmin, psoralen, umbelliferone, limonene, rutin, skimmianine, lupeol, quercetin, esculetin, scopoletin, auraptene, seselin, *etc*. These phytochemical compounds obtained from the *A. marmelos* plant parts are being used since ancient times to cure various human ailments. The main focus of this review provides a critical analysis of these compounds and the ways in which these phytochemicals have the potential to treat a number of human health problems such as diarrhea, obesity, cancer, ulcer healing, chemoprotection, radioprotection, antiulcer, antimicrobial and antiviral activity, *etc.*

INTRODUCTION: The Indian super restorative herb bael (*Aegle marmelos*) has been well known since the time of Charak (1500 B.C.) [1]. Commonly known as Bael, *Aegle marmelos* (L.) Correa is belonging to the Rutaceae family and has been thoroughly used as conventional Indian medicine for various purposes. The cultivar varieties Kagzi Gonda, Gonda no 1, Gnda no 2, Kagzi Etawah, Mirzapuri, and Baghel are all part of the extensive range of options available. Information regarding the potential effects of bael can be obtained from various medicinal systems such as the Siddha, Unani, and Ayurvedic systems.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.14(5).2087-03

This article can be accessed online on www.ijpsr.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.14(5).2087-03

The word "bael" has many different meanings and names in different nations. "bilva," "Shivaphala," "Belo," "bel," "vilvamarum," "golden apple," "a wooden apple," "Bengal Quince," and "Indian Quince" are a few examples [2]. Legendarily, it also has great religious importance in Hindu rituals. This sacred tree's tripatra, or "holy leaf," has made significant contributions to Lord Mahadev [3]. *A. marmelos*, contains a variety of phytochemical substances including alkaloids, flavonoids, saponins, marmelin, limolin, tannins, phenolics, coumarin, *etc*.

Compounds taken from *A. marmelos* have many different uses, such as treating diarrhea, fighting cancer, preventing diabetes, healing ulcers, preventing obesity, *etc*. It has been discovered that virtually all parts of the plant participate in the production of various pharmacological actions. The traditional medical practice that is prevalent across the Asian continent uses the plant to both avoid and

cure a wide variety of ailments. Additionally, the plant exhibits anti-diarrheal, anti-inflammatory, anti-cancerous, anti-microbial, anti-viral, anti-diabetic, radioprotective, and antioxidant properties.

A. marmelos organic products are often used to tidy and tighten up the digestive tract. Consumption of this natural product for a few months releases old accumulated feces from the insides. It is by and large taken as 'sherbet', made by a mash of fruit. *A. marmelos* stem bark ethanolic separate were accounted for to deliver antiproliferative movement against different human growth cell lines [4].

A. marmelos leaves were viewed as effective against collagen-promoting joint pain in Wistar pale-skinned person rats. Unripe Bael fruit extract aids in the hemorrhoids and piles treatment [5]. Ear infections, persistent inflammation, and pus discharge can all be treated with roots soaked in neem oil [5]. Sesilin isolated from the leave of *A. marmelos* has therapeutic potential for COVID-19 [6].

India is often called the "greenhouse of the world" due to its prominence as a global leader in producing phytomedicines [7]. Ten to fifteen percent of the about 300,000 species of higher plants are known to have been used in conventional medicine at some point. Concerning the number and value of its medicinal plant exports, India is second only to China [8].

Medicinal plants provide a sustainable resource for developing novel pharmaceuticals by providing a natural supply of beneficial phytochemicals [9]. Many distinct names for herbal medicine are being used in various countries of the entire world, including Ayurveda in India and Unani medicine in the Middle East and Korea [10]. The significant benefits guaranteed for medicinal purposes of medicinal plants in different afflictions are their well-being other than being conservative, cost-effective, natural, viable, and simple availability [12].

WHO says that 80% of the people in non-industrialized countries get their essential medical care from conventional drugs, the most common plant parts. They are a valuable source of pharmaceuticals and therapeutic products due to their secondary metabolism capacity to produce compounds with the potential for antimicrobial, anti-inflammatory, anticancerous, ulcer healing, wound healing, antiobesity, radioprotective, chemopreventive, and antidiabetic properties [13].

Plant Botanical Description: This tree has a short length and trifoliate leaves (as shown in **Fig. 1** and **2**. Centimeters in length, a small inflorescence, and a round natural woody product, as shown in **Fig. 3** [14]. There are spicules on the bael tree [2]. The leaflets on the trifoliate leaves range from three to five. Young leaves have a pale green tint, and as they mature, they become a faded green.

The outer surface of the tree trunk is bulky and fragile. The wounded bark produces an adhesive fluid that dries and becomes thick when exposed to the atmosphere [2]. The bloom of the bael tree has a bluish-green color. In addition to its pleasant aroma, its ebracteate, hypogynous, actinomorphic stalk is shown as being sexually accessible and attractive to both sexes [15]. The base color of Bael organic products is a light yellowish green [16]. The organic product's mash comes in a sticky yellow variation. Hard seeds are present within, and their outside surfaces are covered with tiny hairs.

TABLE 1: BOTANICAL DESCRIPTION OF DIFFERENT PARTS OF *A. MARMELOS* TREE [2, 8, 17, 18, 19]

S. no.	Plant Part	Botanical Description
1	Bark	The brownish or greyish bark has sharp, pointed spikes. It includes gums that form on injured twigs. These gums are gummy sap. First delicious, then throat-irritating
2	Leaves	Its trifoliate, round-based leaves are pointy. New leaves are pale green, but older ones have a darker hue
3	Flower	The blooms are bisexual and greenish or yellowish in appearance. Typically, leaves are fresh.
4	Fruit	The size of the bael fruit is between five and twelve centimeters, and its covering is quite tough. It starts off green but ripens to a golden-brown color. Internally, it can hold the pulp of up to 20 oranges
5	seeds	The seeds are firm, flattened-oblong, hairy, and wrapped in a sticky sac

FIG. 1: TRIFOLIATE LEAVE OF *A. MARMELOS*

FIG. 2: DISSECTION OF *A. MARAMELOS* FRUIT

FIG. 3: *A. MARMELOS* FRUIT

FIG. 4: *A. MARMELOS* PLANT-BEARING FRUITS

Vegetation and Diversity [7, 8, 15]: *Aegle marmelos* is a plant that is native to tropics regions and does best at an elevation that is around 1,400 meters above mean sea level. The majority of it may be found in dry woods and mountainous regions. The tree's origins may be found in the eastern ghat and central India. The bael tree is native to India, and you can often find it growing anywhere from the Himalayas to West Bengal, spanning central and south Asia. It is mainly found in the foothills of Uttar Pradesh, Bihar, Madhya Pradesh, Uttaranchal, Jharkhand, Chhattisgarh, Myanmar, East Coast, the Deccan Plateau, and Sri Lanka.

Systematic Categorization: In **Table 2**, the A. marmelos plant is categorized systematically.

TABLE 2: SYSTEMATIC CATEGORIZATION OF *A. MARMELOS* PLANT [8, 20]

S. no.	Kingdom	Plantae
1	Subkingdom	Tracheobionta
2	Super Divison	Spermatophyta
3.	Divison	Magnoliophyta
4.	Class	Magnoliopsida
5.	Subclass	Rosidae
6.	Order	Sapindales
7	Family	Rutaceae
8.	Genus	Aegle
9.	Species	Marmelos

***Aegle marmelos'* Vernacular Names [2, 8, 20]:** The Indian super restorative herb bael (*Aegle marmelos*) has been well known since the time of Charak (1500 B.C.)[1]. Its common name is Bael.

TABLE 3: VERNACULAR NAMES OF *A. MARMELOS* [8, 22, 23]

S. no.	Languages	Vernacular Names
1.	Bengali	Bel, Shreefal
2.	Burmese	Ohshit, Opesheet
3.	English	Wood/stone apple, Bengal Quince, Indian Quince
4.	French	Oranger du malabar
5.	Hindi	Bel, Belgiri,Beli
5.	Indonesian	Mojo tree
6.	Javanese	Modjo
7.	Khmer	Banu
8.	Lao (Sino-Tibetan)	Toum
9.	Latin	Aegle marmelos
10.	Malay	Pokok Maja Batu
11.	Marathi	Kaveeth
12.	Nepali	Bel, Gudu
13.	Old Hindi	Sir phal
14.	Sanskrit	Shreephal, Bilva, Bilwa, Vilwa, Shivadrum
15.	Tamil	VilvaMaram, VilvaPazham
16.	Telugu	Maredu
17.	Thai	Mapin, Matum, Tum
18.	Urdu	Bel
19.	Vietnames	*Mbau Nau, Trai Mam*

Aegle marmelos (L.) correa belongs to the Rutaceae family and used in traditional Indian drugs for diverse purposes. The word "bael" has many different meanings and names in different nations. "bilva," "Shivaphala," "Belo," "bel," "vilvamarum," "golden apple," "a wooden apple," "Bengal Quince," and "Indian Quince" are a few examples as shown in **Table 3** below [21].

Ethnobotanical uses: One of the really important Indian herbal remedies, *A. marmelos* has a numerous applications. Many different medications may be made from different plant sections. Eating fruit may treat most ailments, making it an essential element of a healthy diet. Ophthalmia, ulcers, and gastrointestinal disorders may all be cured with a two-times dose of bael leaf extract. Bael leaf ointment is used to cure eye problems. Taken two times a day, a combination of boiling rice water and immature fruit peel prevents morning sickness in pregnant women. Fruit is a good choice for those recovering from diarrhea. In **Table 4** ethnobotanical uses of different parts of the *A. marmelos* plant are described below in detail.

TABLE 4: ETHNOBOTANICAL USES OF *A. MARMELOS* PLANT PARTS [2, 8, 24]

S. no.	Plant Part	Ethnobotanical use
1.	Leaves	Abscess, pain, vision problems, stomach disturbances, vomiting, cuts, ulcers, dropsy, thiamine deficiency, heart failure, cholera, diarrhea, cardiotonic, blood glucose, animal injury, neurological diseases, hair medication, respiratory tonic, child delivery. Animal wound healing, worm control, feed for sheep, goats, augmentation of breathing, and Sedated cats' contraction of the denervated nictitating membrane
2.	Fruit	Some of the diseases this herb treats include diarrhoea, stomach or digestion-related problems neurological and cardiac tonic, ulcer, antiviral, intestinal parasites, gonorrhoea, and epilepsy
3	Root	Dog bites, gastrointestinal issues, cardiac conditions, periodic fevers, antiamoebic, hypoglycemia, rheumatoid arthritis
4.	Bark	Gastrointestinal problem, periodic fevers, cardiac disorder
5.	Seed	Febrifuge
6.	Flower	Cough syrup, epilepsy
7.	Whole plant	Back pain, dog and snake bite, pain in breast, cholera, loose motions, diabetes, diarrhoea, dysentery, pyrexia, eye problems, gastrointestinal and stomachabnormalities, jaundice, laxative, nausea, nocturnal fever, cardiac problems, stomach disorder, vomiting, tonic, cuts and wounds
8.	Root, Bark	Fish venom
9.	Seed Mucilage	Walls construction
10.	Seed oil	Laxative effect, Used in aromatherapy, skincare, and Compressor
11.	Wood	Beads worn by members of the lowest caste and specific couches for rheumatic sufferers.
12.	Gum around seed	It enhances the stickiness of aqueous-based paints.
13.	Unripe fruit rind, Bark	Yellow colour dye
14.	Stem	Oil and sugar mills pestles

Nutritional Value of *Aegle marmelos* (% or per 100 gram): Experiments of the physical and mechanical characteristics of bael fruit have shown that it contains a lot of minerals and vitamins. **Table 5** shows the most important parts from a health perspective.

TABLE 5: NUTRITIONAL VALUE OF *A. MARMELOS* PLANT [8, 24, 25]

S. no.	Components	Value Percentage
1.	Water	64.2
2.	Protein	1.8
3.	Fat	0.2
4.	Minerals	1.5
5.	Fiber	2.2
6.	Carbohydrate	30.6
7.	Calcium	0.09
8.	Phosphorus	0.05
9.	Potassium	0.6
10.	Iron	0.3
11.	Vitamin A	186
12.	Vitamin B1	0.01
13.	Nicotinic Acid	0.9

14.	Riboflavin	1.2
15.	Vitamin C	0.01
16.	Calorific value	129

Phytochemical Constituent: Diverse groups of biochemical compounds, including fatty acids, Coumarins, Terpenoids, alkaloids, and amino acids, have been extracted from the diverse regions of *A. marmelos*, which have been the subject of extensive inquiry. Chemical components extracted from *Aegle marmelos* are described in depth in **Table 6.**

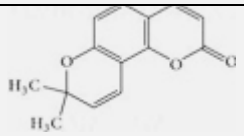
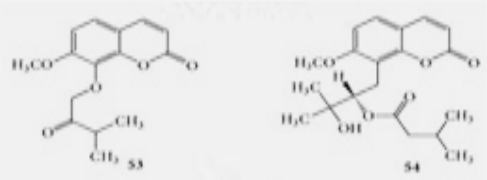
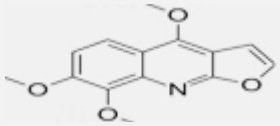
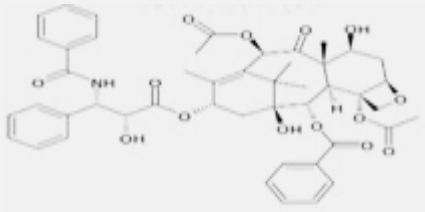
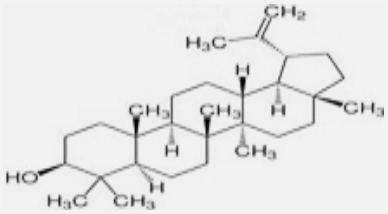
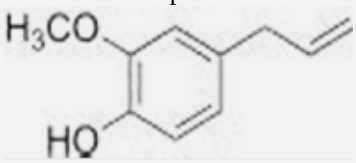
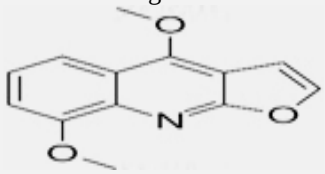
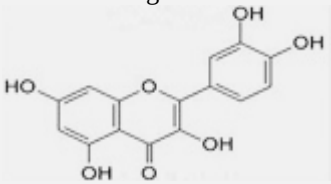
TABLE 6: PHYTOCHEMICAL CONSTITUENT PRESENT IN *A. MARMELOS* PLANT

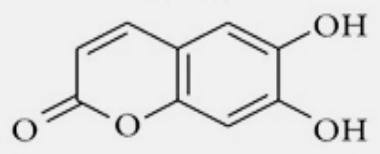
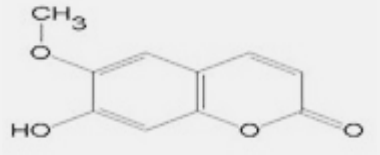
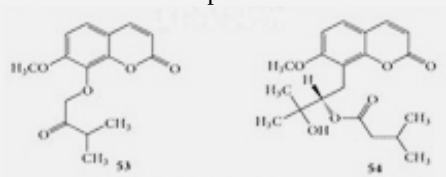
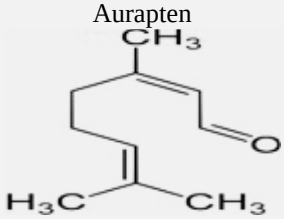
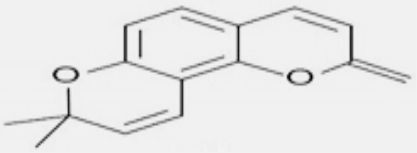
S. no.	Chemical Compounds	Names of Chemical Compounds	Parts of the plant	Biological Activity
1	Alkaloids [8,24,25]	Aegelenine, Aegeline, Aegelinosides A Aegelinosides B Dictamine, Ethyl cinnamamide Ethyl cinnamate Fragrine Halfordinol	Fruits and Leaves	Antidiabetic, antibacterial, anti-inflammatory, alpha glucosidase inhibitor, anti-cancerous
2	Coumarins[2,8,24,25]	Alloimperatorin Imperatorin Isoimperatorin Marmelide, Marmelosin, Marmesin, Marmin, Psoralen, Umbelliferone, Methyl ether, Xanthotoxol, Zanthotoxol	all parts	Antidiabetic, antioxidant, anti-inflammatory, and Anti analgesic
3	Carotenoids	Alpha- Carotenoid, Beta Carotenoid, Delta- carotenoid, Gamma - carotenoid	Fresh Fruit	Healthy Pigment
4	Terpenoids [8,24,25,26]	Caryophyllene, Cineol, Cubedol, Elemol, Epi-cubebal Hexanyl hexanoate, Humulene Isosylvestrene Limonene, Linalool, Myrcene, P-cymene, Terpinolene, Valencene Caryophyllene, Cineol Linalool, Methyl perilate, Myrcene, P-cymene, Terpinolene, Valencene	Fruit, leaves and bark	
5	Vitamins [8, 27]	Thiamin, Riboflavin, Niacin, Ascorbic Acid, Pyridoxin, Pantothenic acid, Biotin, Cobalamines, Riboflavin	Fruits and Leaves	
6	Tannins [2,8]	4,7,8-trimethoxyfuroquinoline	Fruits and Leaves	Antimicrobial and helpful in reducing blood pressure, Yellow dye for calico and silk fabrics
7	Carbohydrates [2,8]	Xylose, Threose, Glucose, Galactose, Fructose, Arabinose, Sucrose, Galactouronic acid	Fruits	Anti-inflammatory, Wound healing
8	Flavonoids [8]	Rutin, Flavone, Flavone-3-ols, Flavones, glycosides		Antidepressent, Anticonvulsant, Antidiabetic
9	Fatty Acids [8,28]	Ricinoleic, linolenic, oleic, linoleic, palmitic, myristic	Seeds	Antimicrobial Activity
10	Essential oils [2,8,29]	Alpha-Pinene, Beta-Myrcene, Alpha-Phellandrene, Isosylvestrone, Delta-Carene, Beta-Ocimene, Linalool, Terpenolene, Alpha-Cubebene, Alpha-Terpineol, Delta-Elemene, Gama-Elemene	Leaves	Antifungal, antimicrobial, and insecticidal activity

S. no.	Part of the Plant used	Phytochemical Constituent
1.	Fruit	Caffeic cinnamamide acid, arbutin, chlorogenic acid, p-coumaric acid, p-coumaroyl, quinic acid, protocatechuic acid, carotenes
2.	Leaves	Rutin, Beta- sitosterol, glycosides, marmeline, aegelin, marmesinin, balfordiol, phenyl ethyl, lupeol
3.	Stem Bark	Skimmiarepin A, Skimmiarepin B, lignan glucoside compound

4.	Fruit Shell [33]	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

TABLE 7: CHEMICAL STRUCTURE OF SOME PHYTOCHEMICALS

S. no.	Chemical Structures	Biological Activity
1.	 Marmelosin	Anti-inflammatory, Anti-bacterial Analgesic effect [31]
2.	 Marmin	Infertility [32]
3.	 Skimmianine	Anti-inflammatory
4.	 Taxol	Anticancerous [33]
5.	 Lupeol	Anticancerousm Chemopreventive Anti-inflammatory [34,35]
6.	 Eugenol	Anticancerous Chemopreventive[34]
7.	 Fagarine	Infertility[32]
8.	 Quercetin	Antiulcer [9]

9.	 Esculetin	Antiobesity[36]
10.	 Scopoletin	Hypothyroidism [37]
11.	 Aurapten	Antidiabetic [38]
12.	 Citral	Anticancerous Chemopreventive[34]
13.	 Seselin	Effective against SARS-COVID [26]

Pharmacological Properties of *Aegle marmelos*:

Efficacy in Treating Diarrhea: Diarrhoeal illnesses are among the most prevalent infectious diseases globally, accounting for 3.2% of all mortality of around 1.8 million people annually (WHO report, 2014). The antidiarrheal efficacy of chloroform concentrate of the base of *A. marmelos* was relatable to ciprofloxacin and typically effective in counter to *Vibrio cholera*, *Escherichia coli* (*E. coli*), and *Shigella* species [39]. The unripe natural product mash of *A. marmelos* hindered bacterial development by destroying epithelial tissue and stimulating the synthesis of certain enterotoxins. This highlight the numerous probable routes of action of *A. marmelos* in different kinds of diarrhea, which validates its inclusion in classic Indian scriptures as well as its continuous utilization by local networks to cure the disorders [40]. To alleviate diarrhea, Palestinians drink fruit juice orally (five times a day). Beneficial in the ailment of diarrhea, looseness of the bowels due to amoebic infection, and various diseases of the Elementary canal [41]. The leaves and unripe fruit of the plant also can be used to demonstrate the antidiarrheal efficacy of *A. marmelos*. By using the minimum hindering concentration (MIC) method, the activity of this substance can be assessed. Tannin, found in A. marmelos, is known for its astringent properties, making it an excellent treatment for diarrhea. In a study using albino rats with inflammatory bowel disease (IBD), it was shown that using extract from immature fruit was particularly successful in reducing the inflammation in the intestinal lumen. The action inflammatory mediators present in unripe A. marmelos fruit extract are IL-1, IL- 6, IL- 8, and TNF (tumor necrosis factor), which reduce the intestinal inflammation of albino rats. These mediators include IL-1, IL-6, and IL-8. The immature fruit extract can also inhibit intestinal morbidity and secretion, which is a useful measure of the medication's ability to treat diarrhea.

Antibacterial Activity: The antimicrobial activity of *A. marmelos* ethanol concentrate of the leaves and fruit showed the most inhibitory action against

multi-drug-resistant *E. coli*, with the largest inhibitory zone when compared to standard anti-toxins. The movement of MDR E. coli is also restricted [42]. Togashi N and Shiraishi (2007) accounted for the most elevated antimicrobial activity against *S. aureus* [43]. Butylated hydroxytoluene (BHT), commonly abbreviated as phenol 2,6-bis (1,1-dimethyl ethyl-4-methyl), is a cell reinforcement shown to demonstrate considerable antibacterial activity, specifically inhibiting the growth of gram-positive bacteria over those of the gram-negative Enterobacteriaceae family. *A. marmelos* displayed antigiardial and antiretroviral activity, while it showed no antibacterial action [40].

A. marmelos unripe product is used as an enemy of a diarrhoeal specialist in conventional medication. The outcomes reported in the review suggest that the decoction of *A. marmelos* has some control over a few types of irresistible diarrhoeal illnesses brought about by Enteropathogenic and Enteroinvasive Escherichia coli, heat-labile (LT) secreting Enterotoxin *E. coli, Vibrio cholera*, and *S. flexner*, and somewhat it can likewise control giardiasis and rotaviral diseases [40]. Nonetheless, it may not be successful against loose bowels brought about by heat-stable (ST) delivering ETEC [40]. Diluted ethanolic extracts of *Aegle marmelos* leaves, respectively, showed inhibition against E. *coli, S. aureus, Streptococcus,* and *Bacillus subtilis* in 2009. The ethanolic extract demonstrated a much higher activity level than the aqueous concentrate. *B. subtilis* had the strongest antibacterial activity, followed by *S. aureus, E. coli,* and *P. aeruginosa* [44].

The crude methanolic extract of *A. marmelos* fruit showed antibacterial action against bacterial pathogens, indicating its antimicrobial potential [45]. Different amounts of hydroalcoholic leaf extracts of *Aegle marmelos* were examined for *in-vitro* antioxidant and antibacterial activities. *In-vivo* pain reliever and grip strength actions (at 100 mg/ml and 200 mg/ml concentration) were also investigated. Leaf extract showed that marmelos contain antioxidant properties. *S. aureus, B. cereus, L. monocytogenes, E. coli, S. Typhimurium, Y. enterocolitis, V. cholera,* and *S. flexneri* are susceptible to the antibacterial effects of *A. marmelos* extract. The hydroalcoholic leaf extracts of *A. marmelos* exhibited no muscle relaxant or grip strength properties [46]. *Aegle marmelos* roots possess potent antimicrobial activity [47]. Marmelide, which also comes from *A. marmelos,* has indeed been discovered to be more useful and cost-effective than the antimicrobial drug ribavirin. Due to its virucidal effect, marmelide is able to block the first steps in the replication process, including adsorption and penetration. In their study of the Ranikhet disease virus, Dhar *et al.* reveal that the juice of the *A. marmelos* plant develops antiviral properties. Extracts of the juice, fruit, and leaves of *A. marmelos* also have antimicrobial properties.

Fruits and their powder may protect against enteric pathogens such as *Ascaris lumbricoides* and *E. histolytica*, making *A. marmelos* a valuable and cost-effective alternative to other plants [48] and showing significant efficacy against Filariae. The fruit extract of *A. marmelos* was used to create AgNPs. Biofilm-forming bacteria were detected on the hull of the ship. Analysis of 16S rDNA for the ability to cause microfouling. Biofilm formation by bacteria may be inhibited by using green nanoparticles [49].

Activity against SARS-COVID-2: Seselin, a chemical constituent obtained from the leaves of *A. marmelos* and tested against many SARS-CoV-2 targets, including the viral spike protein S2, the COVID-19 major protease, and the SARS-CoV-2 (2019-nCoV) free enzyme. Seselin bound to receptors with a binding energy of 6.3 kcal/mol, spike protein S2 with a binding energy of 6.9 kcal/mol, and COVID-19 major protease with a binding energy of 6.7 kcal/mol.

As shown by a docking study with three distinct receptors, intermolecular hydrogen bonds and stacking interactions are responsible for stabilizing the complexes with the lowest projected energy. Results from a molecular dynamics simulation and an MM/PBSA (Molecular mechanism/Poisson Boltzmann surface area) study confirmed that seselin binds to its target receptors and has therapeutic potential for COVID-19 [7]. Marmin, which was isolated from *A. marmelos*, was shown to be a possible inhibitor of RNA-dependent RNA polymerase and 3CLpro of SARS-COVID-2 by an *in-silico* investigation [50].

Insecticidal and Antifungal Activity: Effectiveness of isolating beta-sitosterol from Aegle marmelos Correa leaf extracts to treat larval stages. The overall comparison demonstrated that beta-sitosterol was more effective against *C. quinquefasciatus* (Southern house mosquito), which offers access to additional research and the prospect of using beta-sitosterol in the near future as a natural herbal repellent [11].

Rejuvenating ointment obtained from *A. marmelos* tree leaves exhibits antifungal activity against *Trichophyton mentagrophytes, Trichophyton rubrum, Microsporum gypseum, Microsporum audounii, Microsporum treat, Epidermophyton floccosum, Aspergillus niger, Aspergillus flavus,* and *Histoplasma capsulatum*, among other parasites observed on animals [9]. The restorative ointment from the *A. marmelos* leaves could block the Ca2+ dipicolinic corrosive digestion route and possibly impair spore germination. Ca2+ particle uptake and use by the spore is an important factor to consider regarding whether these will grow or remain dormant. Subsequently, *A. marmelos* may demonstrate antifungal activity by inhibiting the vegetative infectious body inside the host or in the strong media. This is a potential component of *A. marmelos* leaf oil's beneficial effect against parasite infection [51].

Antimalarial Activity: The antimalarial effects of the alcoholic extracts and leaves of the A. marmelos fruit have been tested inside the living body and outside the living body in the designed environment for the experiment. The seeds seem to have some inhibitory effect in both cases [52]. A Researcher showed that hexane, cold methanol, and hot methanol extracts stop the growth of *Klebsiella pneumonia, Micrococcus luteus, Enterococcus faecalis,* and *Streptococcus faecalis in-vitro*. Their study demonstrates that these three extracts do not have any effect on *E. coli* and *Proteus vulgaris* [53].

Anticancer Action: Cancer disease is a significant general medical condition, the second most noteworthy reason for death in all kinds of people in creating and emerging nations [54]. According to WHO 2020 report, the death rate primarily due to cancer is approximately 10 million, with a lopsided ascent in disease cases and passings in emerging nations with restricted assets to handle the issue [55].

In-vitro studies using leukemia cell lines (K562, T-lymphoid immortal, B-lymphoid first continuous human cell line, erythroleukemic HEL, malignant Colo38, and breast cancer cell lines Michigan Cancer Foundation (MCF7) and MDA-MB-231 (formed from pleural effusion of Caucasian female with malignant adenocarcinoma 1) showed that *A. marmelos* leaf extracts were highly effective [24].

In *A. marmelos*, the presence of marmelin inhibits the proliferation of epithelial malignant growth cells (HCT-116 colon and Human epithelial type 2, alveolar epithelial cancer cells), but not regular cells (mouse undeveloped organism fibroblasts) Marmelin induced apoptosis *via* activated caspase-3, which was blocked by pretreatment with caspase-3 inhibitors, as well as TNF-a (Tumour Necrosis factor-alpha), TNFR1 (Tumour Necrosis Factor Receptor 1), and TRADD mRNA and protein articulation, G1 cell cycle capture, and intervention. As with apoptosis-inducing ligands, Marmelin triggered the executioner proteins caspase-8 and Bid in response to the entry of cytochrome C, suggesting a link between the death receptor and mitochondrial pathways may be important in the development of cancer.

Marmelin inhibits extracellular kinase phosphorylation and AKT/PKB signaling in both cultured cells and xenografts. AKT (Serine Threonine Kinase) is frequently altered in several disorders, despite its crucial role in maintaining cell viability, promoting cell proliferation, and enhancing cell invasiveness. The Constant activity of AKT may be essential for the long-term survival of some growth cells. Marlin decreases cell survival by lowering AKT levels [34, 56]. Anti-cancer properties are exhibited by the important diterpenoid molecule known as taxol.

There is evidence that the endophytic parasite Bartaliniarobillardoides which was extracted from the medicinal plant *Aegle marmelos* is responsible for the synthesis of taxol. Through HPLC (high-performance liquid chromatography), the amount of taxol generated by this endophytic fungus was determined to be approximately 188 lg/L. According to Gangadevi V *et al*, this parasite is likely responsible for the production of a significant amount of taxol [33].

Lupeol extracted from *A. marmelos* is effective as opposed to a variety of human cancer stem cell lines (human melanoma 451 Lu cells, WM 35 cells, and B162F2 cells). Lupeol prevents cells from progressing from the G1 stage to the S stage by preventing the formation of cyclin D1 and D2 proteins and increasing the expression of the p21 protein, which plays an important role in cell cycle regulation [35].

In Various cell types, lupeol stimulates the expression of proapoptotic proteins such as Erythroblastoma2, cyclin D1, Fas-associated death domain and lattice metalloproteinase (MMP)- 2 characteristics, and 14-3-3 qualities [24]. It lowers the activity of PI3K/Akt, the activity of the MAPK proteins p38 and Erk1/2, and the phosphorylation of IkBa and NF-kB/p65, passing receptor 3 (DR3), cyclin B, cdc25C, and plk1. Lupeol can fulfill its function by increasing apoptotic protein expression and decreasing anti-apoptotic protein expression. In PC-3 cells, treatment with lupeol leads to the disintegration of DNA, an increase in reactive oxygen species, and a loss of integration of the membrane of mitochondria [35].

Eugenol, also known as 2-methoxyphenol, is a phenolic chemical that may be found predominantly in aromatic plants. Both salivary gland cancer cell lines and normal human gingival fibroblasts are susceptible to the cytotoxic effects of eugenol. The cancerous cell lines like HepG2 hepatoma cells, Caco-2 colon cells line, and the benign human VH10 fibroblast line are all susceptible to the cytotoxic effects of eugenol [34].

Studies conducted with the human invasive cell line WM1205Lu have also shown that eugenol causes the death of cells arrested incell cycle at S phase, induces cell death and that dysfunctioning of E2F1 may be a critical element in eugenol-mediated melanoma growth inhibition[34]. These results were obtained by examining the effects of eugenol on melanoma cells[28]. In the study of a nontreated group with the treated group, research conducted with mice that had B16 melanoma found that eugenol treatment inhibited cell multiplication, slowed the kinetics of tumor growth, reduced the size of the tumor by almost 40 percent, nearly 20 percent increase in the median survival time, and blocked invasion and metastasis in almost half of the animals [34]. The crucial oil that may be obtained from *A. marmelos* is abundant in sesquiterpene, particularly beta-caryophyllene. Sesquiterpenes are being looked at as potentially useful chemicals due to their anticancer properties. Analyses of the action of sesquiterpenes are performed on a number of cell lines, including ovarian cells and pancreatic, Colon, and lung cells [57].

Some hematological cancer cell lines were induced to undergo apoptosis by citral, a phytochemical isolated from Bael; the anticancerous activity was equivalent to that of staurosporine, an antineoplastic anti-infection determined by Streptomyces staurosporine. Citral, as recently postulated by Chaouki, inhibits the proliferation of cells in the cell cycle from G2 to M, induces apoptosis in the MCF-7 cell line (human breast cancer), and reduces PgE(2) synthesis [34].

Therapeutic Effects of Diabetes: Chronic metabolic illness such as diabetes is a danger to human health and the global economy [58]. The International Diabetes Federation (IDF) predicts that 463 million people will have diabetes in 2019 [59]. Insulin deficiency is recognized to be the cause of diabetes in humans, which is why getting insulin from an outside source is essential for the treatment of diabetes. In a similar manner, bael can substitute insulin by improving the body's ability to take in glucose from the outside source. Serum glucose levels in rodents with elevated amounts were significantly reduced after treatment with a 75% methanolic concentrate of *A. marmelos* [60].

The aqueous preparation of *Aegle marmelos* leaves has hypoglycemic action (decreased glucose level in the blood). Upadhya S *et al.* (2004) used alloxan-induced diabetes in male, microbe rats to indicate that *A. marmelos* leaf extract may play a vital role in the long-term treatment of diabetes and therefore altered cellular support [61]. Glucose transporter GLUT2, which is expressed in -cells, is regulated by phenolic acids in a manner that increases GLUT 4 movement *via* PI3K/Akt and the AMP-activated protein kinase (AMPK) pathway. Both ferulic acid and chlorogenic acid, which are both types of phenolic acid, operate in the same way and are thus powerful antidiabetic medicines [62]. In their investigation of the impact of Alloxan on diabetes, Kuttan and Sabu (2004) identified the

potency of *Aegle marmelos* leaf extract on diabetic patients and found that its use alone was sufficient to reduce oxidative stress by monitoring lipid peroxidation and trying to adjust specific antioxidant potential [60]. *A. marmelos* reduces insulin sensitivity, making it effective against type 2 diabetes [63]. Another research found that treating rats with an extract of unripe bael fruit significantly reduced the amount of stomach mucosal damage caused by 100% ethanol [64]. Linolenic acid was found to dramatically lower the incidence of diabetes and increase insulin sensitivity, according to a study by Belurey *et al.* [65] Oxidative, immunomodulatory, and hypolipidemic properties of linolenic acid were also described [66].

AFEAM (alkaloid-free hydroalcoholic extract of A. marmelos) demonstrated excellent cytotoxic activity and cytoprotective capability against hyperglycemia-induced oxidative stress in HepG2 cells. Ingestion of AFEAM greatly improved the blood glucose level in serum, the condition of dyslipidemia, the level of pro-inflammatory markers like TNF, interleukin-1, and interleukin 6, and the antioxidant note in diabetic mice. Histological assessment of in-drug treatment providing mice group revealed improved pancreatic, liver, and kidney tissue damage. In conclusion, AFEAM supplementation may benefit prediabetics and diabetics as an adjuvant to contemporary therapy [67].

Aegeline, Citral, Marmesinin, Auraptene, and Bisabolene are the five phytochemicals found in the *A. marmelos* plant. *In-silico* studies revealed that these phytochemicals have the potential to act as more effective candidates for antidiabetic drugs against DPP-4(Dipeptidyl peptidase-4). These phytochemicals may also be beneficiary for the treatment of type 2 diabetes [38].

Chemoprevention: Several case-control and cohort studies have shown that chemoprevention may be an effective strategy as an anticancerous[68]. Gupta et al. demonstrated that DMBA (1,2-Dimethylbenzoyl anthracene) induced carcinoma in mice and that A. marmelos fruit juice had a chemopreventive effect against this mechanism [69]. Hepatocarcinogenesis in Wistar rats induced by diethylnitrosamine and 2-acetyl aminofluorene was inhibited by a methanolic concentrate of *A. marmelos* by Khan *et al.* at dosages ranging from 25.5 to 50.5 milligrams per kilogram of body weight. Phytochemicals like eugenol, lupeol, citral, rutin, limonene, and anthocyanins seen as in *A. marmelos* have all been displayed to make a chemopreventive difference [34]. Pretreatment with 25 or 50 milligrams for each kilogram of body weight of Bael extricates alleviated the impacts of 2-acetyl aminofluorene on oxidative pressure. This was achieved by normalizing the grouping of cancer prevention agent impetus and detoxification impetus, as well as stifling the action of the compound ornithine decarboxylase (ODC) and the combination of DNA.

Antipyretic or Anti-inflammatory Activity: Shukla *et al.,* demonstrate the action in lowering the fever, of *A. marmelos* was evaluated using Brewer's fermentation fever in rats with pale skin. They discovered that the ethanolic elimination, at a concentration of 200 mg/kg body weight and 400 mg/kg body weight, brought about a relevant depletion in the increased internal heat level in a somewhat subservient manner. Similar to the effects of paracetamol on fever reduction, concentrates were shown to be effective in treating fevers [22]. The phytochemicals in A. marmelos, specifically lupeol, citral, and Skimmianine, give the plant its anti-inflammatory properties.

Most of these plant compounds block the histamine receptor. This research aimed to assess whether or not extracts of dried and fresh *Aegle marmelos* (L.) pulp have anti-inflammatory properties. Denatured Systemic illness, glomerulonephritis, autoimmune disorders, and systemic lupus erythematosus are caused by the protein generated as antigens and a Type III allergic reaction.

Beta-Caryophyllene and caryophyllene oxide, both present in bael extract, have been demonstrated to have an anti-inflammatory impact on lymphoma and neuroblastoma cells. This response is consistent with down-regulating anti-apoptotic genes while up-regulating pro-apoptotic ones. Bael pulp extract demonstrates anti-inflammatory, mast cell stabilizing, and antioxidant properties, as well as a rise in superoxide dismutase and a drop in malondialdehyde concentration, which protects mast cells from inflammatory mediators. When tried with carrageenan-actuated paw edema, the

outer layer of the bael tree root section shows a strong mitigating effect. A concentrate on the youthful underlying foundations of the bael tree uncovers significant calming impacts in cyclooxygenase (COX-2) restraint and limitation of favorable to provocative cytokine. In contrast, an in vitro study with bael leaf remove uncovers a mitigating influence at 100 g/mL. Marmelosin confined from bael organic product has a mitigating activity joined by a diminishing in nitric oxide (NO) and supportive of provocative cytokine TNF-Alpha.

Anti-obesity Impact: The research was carried out to examine the efficacy of phytochemical components found in *Aegle marmelos* leaf extracts for combating obesity. *A. Marmelos* foliage dichloromethane, ethyl acetate, and butanol extracts exhibit lipid breakdown potential. Maximum vitality Dichloromethane extract phytochemicals produced a wide variety of compounds. The impacts of the isolated compounds on lipid hydrolysis have been measured at varying doses. Umbelliferone and esculetin, two of the most active compounds, have also been studied for their potential to combat obesity in a rat model which consumes a high-fat diet.

The lipolytic effects of umbelliferone and esculetincause body weight reduction. The lipid breakdown in adipose cells is one mechanism by which the *A. marmelos* DCM extract and chemicals derived from it may combat obesity [36]. In a test using streptozotocin-promoted rodents, it was shown that the fat composition of the serum could be regulated by adding aqueous bael extract. The hydrolysis of triglycerides has begun, which leads to a drop in serum cholesterol levels. The transfer of fat from adherent adipose tissue may cause this decrease in serum cholesterol levels. Based on the study's findings, one may conclude that the umbelliferone found in bael possesses antihyperglycemic action. The bael leaf extract contains saponins and coumarins, which have been shown to lower cholesterol levels. Both the free cholesterol and ester cholesterol concentrations have been lowered by using bael fruit powder. Diabetic rats with fasting blood glucose, also known as FBG, are treated with a watery concentrate of based at a dosage of 250 mg/kg, which leads to a lowering of 60.87 percent in their blood glucose level.

Radio-protective Effects: When radiotherapy is used to treat cancer, it can also cause damage to healthy cells due to the cytotoxicity generated by the radiation. Developing radio-protective chemicals that can shield common materials from radiation damage is highly desirable. When exposed to radiation, our bodies produce free radicals and antioxidant chemicals, which are highly reactive and can potentially harm bodily cells in a variety of ways [38]. For example, Jagetia et al. (2004) found that injecting hydroalcoholic leaves extract of *Aegle marmelos* into the abdomen region of mice increased their lifespan when subjected to greater doses of gamma radiation [76]. The leaf extract stands out more clearly than the fruit extract and the control (2-mercapto propionyl glycine). Extracts from leaves protect against gastrointestinal and marrow damage [38]. Radiation is harmful because it ionizes DNA, creates free radicals, and can damage other parts of cells. Cell cycle regulation can be disrupted by DNA damage, leading to either uncontrolled cell division or cell death. Both diseases are extremely dangerous, and death is a real possibility due to either one of them [71]. After extensive research, scientists have established that *A. marmelos* leaves may be used to scavenge reactive oxygen and nitrogen species. Additionally, antioxidant and free-radical-foraging capabilities may be found in fruit. *A. marmelos* fruit drink was shown to be rich in phenolic content and a strong antioxidant in another study [72].

Reproductive Dysfunction: It has been shown that marmelos can have a detrimental effect on male fertility. Bael's ethanolic bark extract is capable of fully inhibiting sperm activity. It leads toan increase in germinal epithelium degeneration, epididymal sperm density, and acrosomal integrity. In the preimplantation stage, bael extract works, and preimplantation failure results in sterility. Bael effects negatively to sperm activity due to blockage of the calcium channel. It has been demonstrated that fagarine and marmin, which both exist in a larger amount in the stem bark of A. marmelos, inhibit male fertility. The *A. marmelos* methanolic extract causes infertility in a dosage amount and time-dependent approach.

This is because the extract lowers testosterone hormone levels and the weight of reproductive organs. The researchers also noted that once the extract therapy was discontinued, all morphological and physiological indications in the rats given the extract returned to normal [73]. According to these findings, the extract of A. marmelos shows significant potential for use as a birth control pill. It has been demonstrated to eliminate the possibility of a pregnancy occurring, but if treatment is stopped, fertility typically returns within a few months [74].

Diuretic Action and Protective Effects on the Kidneys: Analysis of the *in-vivo* diuretic impact of several natural concentrates and their minute amounts of *A. marmelos* organic product is conducted. Rats and mice were given intraperitoneal injections of the concentrates of varying strengths for testing purposes. They calculated the volume and osmotic pressure of the urine to evaluate the diuretic effect. They discovered that the ethanolic extract significantly increases sodium excretion at greater concentrations. There are also usable derivatives of oil ether, chloroform, and ethyl acetic acid [75]. Extraction of the leaves of *A. marmelos* has been shown to have nephron protective effects. The most obvious signs of renal impairment are increases in blood urea nitrogen concentration, serum creatinine, and malondialdehyde (MDA). A. marmelos leaf extract was found to considerably reduce the increased amount of MDA, blood urea nitrogen (BUN), and serum creatinine in a study investigating the neurotoxic effects of gentamicin. Protection against cisplatin-induced renal damage may also be achieved with *A. marmelos* extract from leaves.

Antiulcer Activity: Sharma *et al*. A. decipher the anti-ulcer effect of marmelos seeds in aqueous and methanolic concentrates. Both the methanolic separate and the fluid concentration exhibit an anti-ulceration effect. Reducing gastric juice volume, acidity, and pH while increasing the effects of flavonoids like quercetin has been linked to decreased ulcers. According to another review, mucosal thickness, superoxide dismutase activity, catalase activity, and glutathione levels are significantly reduced in white-haired mice treated separately with *A. marmelos* organic pumpkin [9].

In a 1997 study, researchers found that the pyranocoumarin class belonging compound Luvangetinisolated from the seeds of *A. marmelos* Correa significantly improved the survival rates of rats given, that the ulcer is caused by aspirin/ pylorus-ligated, as well as rats and guinea pigs, were underwent cold-induced stress-induced ulcers. According to another study, pre-treatment with an extract of unripe bael fruit dramatically reduced stomach mucosal damage caused by absolute ethanol in mice [31].

Hepatoprotective Influence: Studies were conducted on the effects of alcohol on the livers of pale-yellow mice. They found that an extract of the leaves of an *Aegle marmelos* had outstanding hepatoprotective properties. In addition, Ramnik demonstrated that a fluid extract of bael organic product mash and seeds is efficient in treating CCI4-induced hepatic harmfulness and preventing this type of damage. Eugenol isolated from the bael leaf has demonstrated hepatoprotective properties. The hepatoprotective action of bael has been substantiated by a study revealing the presence of rutin in bael, which may be the cause of this activity. In this case, the elevated TNF level has decreased, and its efficiency is comparable to that of silymarin. Piperine and bael extract in aggregated form has been found to be effective against CCl4-induced hepatic problems. Aqueous alcohol bael extract increases liver glutathione peroxidase, glutathione reductase, glutathione-S-transferase-catalase, and glutathione-S-transferase basal levels, beside acid-soluble cytochrome P450 and sulfhydryl (SH) levels.

Thyroid Activity Contradictions: Panda S. extracted scopoletin, also known as 7-hydroxy-6-methoxy coumarin, from the leaves of *Aegle marmelos* and investigated the compound's potential for reducing the levels of thyroid hormone in the body. In rats given levothyroxine, the administration of scopoletin administered 1 milligram per kilogram in a day, followed by seven days, was observed to lower thyroid hormone levels. It has also been demonstrated that scopoletin is more effective than the traditional antithyroid medicine known as propylthiouracil. Another research came to the same conclusions, which was encouraging [37].

Wound Healing Activity: There are several stages involved in the healing of wounds, including inflammation, the multiplication of cells, and stiffness during the development of a collagen matrix. Reddening, soreness, and swelling are some of the most common symptoms linked with wounds, and they are also present when inflammation is present. It has been discovered that one defense mechanism involves the emission of reactive species.

Aegle marmelos fruit extract decreased wound size and enhanced tissue regeneration in beta-catenin, Akt signaling and ERK (extracellular signal-regulated kinase) pathway-regulated keratinocyte migration in *Aegle marmelos* fruit extract-treated rats. *A. marmelos* fruit extract and its active ingredient stimulate mRNA expression, decrease nitric oxide and PGE2 production, and encourage the movement of HaCaT keratinocytes during rat wound healing in culture [52]. When applied to the wounds of rats, A. marmelos fruit extract significantly reduced the wound sizes. Re-epithelialization of skin lesions occurred more quickly than expected. A further investigation into the effects of bael extract using an evacuation and an incisions model demonstrates that bael has a positive effect on wound healing. Essential oils, bioflavonoids, and nitrogenous-containing organic compounds like alkaloids and sterols are some phytochemical compounds found in bael. These phytoconstituents are responsible for the wound-healing properties of bael, the accelerated epithelization, tightening of the wound, flexible power, and hydroxyproline composition. The capacity of bael to promote wound healing is comparable to that of the medication nitrofurazone.

CONCLUSION: A. marmelos is a member of the Rutaceae family and is used in ayurvedic and traditional medicine to treat diseases like diarrhea, obesity, ulcer healing, chemopreventive, radioprotective, antiulcer, antibacterial, antiviral, cancer, SARS-CoVID 2, etc. This is because it contains many phytochemical compounds, such as aegelenine, fragrine, halfordinol, marmelide, marmelosin, marmesin, marmin, psoralen, umbelliferone, limonene, rutin, skimmianine, lupeol, quercetin, esculetin, scopoletin, aurpene, seselin. The Seselin compound that was taken from this plant works against SARS-Covid-2. Research shows how much work has been done on this plant, but not all of its properties are known yet. The goal was to put together all the known information about the *A. marmelos* plant, including its traditional and medical uses. This review contains all of the information about the *A. marmelos* plant; this review will be of tremendous use to scholars interested in researching this plant.

ACKNOWLEDGMENT: Nil

CONFLICTS OF INTEREST: The author declares no conflict of interest.

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How to cite this article:
Nevedita and Kumar A: A critical review on the medicinal herb *Aegle marmelos* (Linn.) correa. Int J Pharm Sci & Res 2023; 14(5): 2087-03. doi: 10.13040/IJPSR.0975-8232.14(5).2087-03.