



Visiting Bael (*Aegle marmelos*) as a protective agent against COVID-19: A review

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Medicinal plant-based antivirals might reinforce the endogenous antioxidant defences from reactive oxygen species (ROS) and regain an optimum harmony by neutralizing the viral agents. These compounds are readily available, therefore gaining immense value by virtue of the critical role of theirs in COVID disease prevention. In this context, *Aegle marmelos* could rightly be stated as a plant of extensive interest. Therefore, the worth of the use of bael can be pushed to seek out the for the phytochemical which might prevent SARS-CoV-2. Here, we have compiled a piece of information on bael based on the previous studied on bael tree.

Keywords: Bael, COVID-19, Pandemic, Phytochemicals

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The novel coronavirus 2019 (COVID-19), has created an unanticipated pandemic, that has triggered severe panic among individuals worldwide. In this direction, countries are maximizing their efforts to fight the virus and reduce infection. In such a situation, a vaccine could help reduce mortality and morbidity¹. However, the possible issue is going to continue to persist until the improvement of an excellent viral vaccine. In order to bring down the transmission of COVID 19, it can be beneficial to make use of personal respiratory protective equipment. Since a selection of routes may transmit infectious microorganisms, respiratory and face protection is necessary for those that are usually given via droplets/aerosols. Transmission of COVID 19 infection mostly occurs through coughing or perhaps sneezing where infectious contaminants (aerosol droplets) of adjustable size, might be inhaled. Although SARS-CoV-2 is predominantly deemed as an inescapable pandemic, scientists are curious about precisely how to defend the general public best before a vaccine may be made available².

Therefore, a good viral inactivation process by exploiting bioactive substances from the healing

plants is much needed. The cultural community of India begets an important part in protecting the biodiversity of various virgin woodlands and also have conserved a lot of plants, if not this particular flora and fauna, would be disappeared from nourishing ecosystems³⁻⁵. Over 70% of the tribal cities stayed intermingled with the conventional nature and knowledge for several years and would be the custodian of several indigenous plant lives that are used for the formula of several ailments^{6,7}.

Among the primary explanations for such a training would be the lack of contemporary health facilities in the remote areas of the cold challenging terrains of the express. There is a prevailing perception that grey medications are healthier and more, harmless or safer when compared with artificial ones. The fruit's therapeutic values are higher at initial stages. Many of the components of the bael grow has antibiotic qualities and also may be used for treating a broad range of health conditions and infections. The ripe fruit as well as unripe fruit, additionally to the roots, are used in regular medicine. In Ayurveda, the mature berry continues to be utilized for persistent diarrhoea and dysentery⁸⁻¹⁰. Due to this particular systematic assessment of various phytoconstituents of the vegetable could be helpful within the elimination

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of damages on account of ageing and might, therefore, boost life expectancy. Below, we've provided detailed info about the various areas of the bael tree which are widely used because of the healing of illnesses more we've mentioned the usage of theirs inside a COVID perspective.

Leaves

The fresh leaf liquid with honey as a slight laxative in fever, asthma and catarrh. The mixer of black pepper and leaf juice is utilized to overcome dropsy diseases^{11,12}. It is also used for respiratory and asthmatic issues. A warm poultice of the foliage is put on on the eyes in ophthalmia, and the syrup is recommended in the bronchitis. New leaves are also eaten as a cure for beriberi disease¹³. Consuming water of overnight soaked leaves is suitable for the patients¹⁴. The word bilva (bael tree) is frequently employed as bilva patra (leaf of bael). Bael leaves, along with some other areas have been found being helpful in curing diabetes, and medical research has validated this¹⁵⁻¹⁷. Steam distillation of bael leaves makes an essential oil which has broad-spectrum antifungal exercise much like which of 0.5% Hamycin the liquid out of the bael leaves is beneficial for diabetics when consumed stomach that is empty for just one month¹⁸. An early practice consists of the usage of the bael leaves, roots and barks for dealing with snakebites. Respiratory illnesses, such as a wheezing, spasm as well as the common cold, perhaps addressed by utilizing medicated oil made out of the foliage of bael plant. An equal amount of bael juice, as well as sesame oil, is warmed up together for the planning of this particular oil^{19,20}. A rare alkaloid, shahidine biogenetically, oxazolines might be viewed as the precursor of oxazoles and hydroxyl amides present in plant life. Shahidine showed activity against several gram-positive bacterial strains²¹.

Fruits, Bark and Root

The ripe fruits possess, cooling, aromatic and as well as a laxative^{22,23}. It has all imperatorin, marmelosin that are the same with bsitosterol and imperatorin. It's marmalade, an isomer of imperatorin, that exhibits tyrosinase speeding up and also tryptophan pyrroles inhibiting impact in *Bufo melanosticus*. The existence of psoralin, an important germination inhibitor and also tannic acid is found. The fresh fruits yield 2% of dried, water-soluble gum. Hydrolysis of the gum produces most significantly: galactose 20.4; aralrinose, and also traces of

rhamnose²⁴. Aqueous extract of the bael berry pulp offers powerful antioxidant effects and it was discovered that hydroalcoholic content of bael pulp has scavenging tasks in vitro^{25,26}. Furthermore, the bael fruit beverage had also been reported to include higher levels of complete phenolic compounds²⁷⁻³⁰. The extract of bael berry (125 along with 250 mg/kg) two times daily to diabetic rats for thirty days decreased the amounts of fasting blood sugar and glycosylated haemoglobin amounts with all the influences being much better than that of glibenclamide. Feeding bael even caused a concentration-dependent reduction in LPx, to improve Sod, CAT, GSH and GPx amounts in both hearts as well as the pancreas of diabetic creatures. Histopathological scientific studies demonstrated that feeding the berry extract improved the practical state of the pancreatic cells^{31,32}. Bael happens to be deemed to have a healing advantage for cardiovascular disease. Krushna *et al.*³³ discovered the precise role of the extract of the unripe fresh fruit of bael in rats against the isoproterenol-induced cardiac stress.

The amounts of blood sugar and protein were also within the normal range. Unripe fruit extract (1%) decreases the intraocular pressure created by water loading as well as steroids in cream rabbit³⁴. Results propose that bael fruit extract is good at reducing the experimentally induced intraocular strain in experimental animal models and also has got the potential to become of pharmaceutical use. It offers antibacterial consequences on specific enteric bacteria^{35,36}. The bark and the root are worn in the type of a decoction as a treatment in melancholia, intermittent fevers as well as palpitation. The root bark continues to be used especially in sporadic fevers and as a fish toxins. Imperatorin, xanthotoxol, marmelide, psoralen, scopoletin, Scoporone, skimmianine, umbeliferone, umbelliferone, marmesin, and marmin had been determined from the bark leaves, root and fruit of the plant^{37,38}. It was discovered the root of *A. marmelos* tree features psoralin, scopolotein and xanthotoxin³⁹. A decoction of the blossoms and roots of *A. marmelos* is utilized as an antiemetic⁴⁰. Siddique *et al.*⁴¹ proved that leaf extract has improved antioxidant activity than stem bark and root extract. The bark paste of ground origins of *A. marmelos* with cold water is recommended for curing myalgia. It was discovered the paste of ground origins of bael in butter was highly effective in the healing of insomnia.

Antiviral activity against COVID-19

In connection with the bacteria, some enteroviruses also result in contamination and diarrhoea. Coxsackieviruses, belonging to the category picornaviruses are a frequent root cause of ailments in humans, particularly kids. They mainly result in non-symptomatic or mild illness but might be deadly in immune-compromised folks. Badam *et al.*⁴² showed that apart from these bael fruits in its different form and composition is used against diarrhoea, gastroprotective effects, and inflammatory bowel disease^{43,44}. Various parts of essentially Consisting of alkaloids, flavones and coumarin compounds, inhibited the replication of coxsackieviruses B (1-6). The experiments demonstrate that naturally occurring battery of compounds (alkaloids, flavoiies, coulnarins, terpenoids, fatty acids etc.) infractions L1, L2; S1, S2, S3 and S4; F1, F2; R1, R2 and marmelide from the fruits, possess antiviral activity. Most significant was marmelide, a coumarin derivative against all the human coxsackieviruses (B1-B6). The ethanolic extract of the fruits has shown antiviral activity against ranikhet disease virus¹⁵.

Coronaviridae and order Nidovirales. SARS-CoV-2 is considered a novel human-infecting betacoronavirus. It is a well fact that bael fruits are effective in reducing the effect of other respiratory diseases, so it is presumed that consuming bael can help in minimizing COVID disease⁴⁵. Bael also builds immunity body against diseases like diarrhoea and cholera. It is also reported that immunity is a good weapon against corona. Bael, is packed with Vitamins, has numerous health benefits. It's a rich supply of Vitamins A, C and B and also the existence of these multivitamins make bael the top option among fruits within the healing of eye problems, heart ailments, digestive disorders, skin diseases and also by stopping the entire body against infection and improving the overall immunity⁴⁶.

Potential phytochemicals against COVID-19

Skimmianine (C₁₄H₁₃NO₄), an alkaloid, present in the bael and the biosynthesis of skimmianine begins from anthranilic acid, and that is pretty plentiful in bael. It's shown anticancer pastime in human ovarian cancer cell line⁴⁷. Additionally, it inhibits acetylcholinesterase (AChE), cataleptogenic activity, exploratory behaviour and conditioned avoidance reply in animals⁴⁸. Skimmianine, when studied in the pet models, indicates sedative, antipyretic, anticonvulsive, analgesic, hypnotic, antidiuretic and hypothermic effects^{49,50}. Additionally, it offers antimalarial activity

by inhibiting Plasmodium falciparum development in vitro (IC₅₀=48.2 µg/ml)⁵¹. Aegelin (C₁₈H₁₈O₄) is an alkaloid from the foliage of *A. marmelos* that's recognized for cardioactive compound⁵². Even though some evidence from animal research indicates that aegeline could reduce blood sugar, this possible outcome has never been analyzed in humans. Lupeol (C₃₀H₅₀O) is a pentacyclic triterpenoid which has healing properties. It's a powerful cardioactive compound that exhibits anti-inflammatory property^{53,54}.

Development of oxidative stress⁵⁵ and also neutrophil infiltration are typical for inflammatory diseases⁵⁶. A report by Fernández *et al.*⁵⁷ showed that topical program of Lupeol reduces myeloperoxidase amounts [neutrophil specific marker], therefore leading to the decrease in cell infiltration into inflamed cells in mice. Cuminaldehyde (4-isopropyl benzaldehyde) is a constituent of the important oils of various trees. It's been discovered to have antibacterial activity⁵⁸. In case it gets accumulated, could lead to chronic diseases as Parkinson's condition, dementia with multiple systems⁵⁹. Among the crucial bioactive compound, remote from bark are marmin and fagarine. Fagarine (C₁₃H₁₁NO₃) occurs in the older bark and is a potent abortifacient agent⁵⁸.

Fruits of bael are loaded with marmelosin, psoralen, aurapten, luvangetin, tannin and marmelide. Marmelosin indicates antihelmintic in addition to antibacterial activities. Luvangetin (C₁₅H₁₄O₄), an isolate from the seed of bael has proved effective against gastric ulceration in rodents^{61,62}. Aurapten (CHO) prevents (IC₅₀ = 0.6 µg/ml) the chronotropic consequences on the heart muscles and therefore could be helpful within the healing of hypertension³⁴. Psoralen (C₁₁H₆O₃) demonstrates different tasks for example antispasmodic⁶³, and artemicide (LD₅₀=5.93 µg/mL). Marmelide (C₁₆H₁₄O₄) is extremely potent against viral diseases and it is discovered to affect the first phases of the life cycle of a virus, like penetration and adsorption. Vitamin C contained in bael is able to bring down lung irritation in serious respiratory illnesses due to H1N1 (swine flu) or maybe some other viruses⁶⁴.

Conclusions

Presently no specific vaccine or therapy authorized for coronavirus an infection. Bael plant produces phytochemical compounds that have the capability to inhibit COVID-19. The are several anti-coronavirus agents present in the bael plant. The hunt for completely new molecules with a preservative

strength of natural origin is based on ethnobotanical scientific studies that will make it feasible to have out inventories of bael. Overall, the comprehensive info provided in this particular evaluation on the phytochemicals, antioxidant, antitoxic and anti-diabetic qualities of the bael extract may offer particular evidence of the usage against COVID-19 disease.

Conflict of Interest

Authors declare they have no conflict of interest

Author Contribution Statement

PK and RKJ conceived of and designed the project; supervised the study and corrected the final draft. VKY, GS, PK and RKJ wrote the manuscript. All authors read and approved the final manuscript.

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