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Review

A Systematic Review of the Pharmacological and Formulative Potential of Bael (*Aegle marmelos*)

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Abstract

Aegle marmelos (L.) Correa, popularly known as Bael, is a mid-sized slender aromatic tree belonging to the Rutaceae family. It holds a preeminent position in the Indian traditional systems of medicine, including Ayurveda, Siddha, and Unani. This review synthesizes current research regarding the phytochemical profile of Bael, its significant pharmacological activities specifically antidiabetic and anti-ulcerative properties and its emerging role as a versatile pharmaceutical excipient. By examining its application in sustained-release matrix tablets, mucoadhesive systems, and specialized oral care formulations, this article highlights *Aegle marmelos* as a sustainable, biocompatible, and efficacious resource for modern drug delivery and therapeutic intervention.

Keywords: *Aegle marmelos*, Antidiabetic, Bael gum, Mucoadhesion, Neuroprotective, Natural polymers, Phytochemistry Sustained-release.

1. INTRODUCTION

The global pharmaceutical industry is currently witnessing a paradigm shift toward "Green Pharmacy." This movement prioritizes the use of plant-derived materials over synthetic polymers and chemicals due to their inherent advantages: biodegradability, low toxicity, cost-effectiveness, and local availability. *Aegle marmelos*, a tree indigenous to the Indian subcontinent, serves as a quintessential example of this shift [1,2,3]. Historically, every part of the Bael tree leaves, fruit, stem, bark, and roots has been utilized to treat various ailments such as diarrhea, dysentery, constipation, and respiratory infections. Modern scientific inquiry has now validated these traditional uses, uncovering a complex chemical landscape that allows Bael to function both as an active therapeutic agent and a functional pharmaceutical aid [3].

2. BOTANICAL AND PHYTOCHEMICAL PROFILE

Aegle marmelos is characterized by its trifoliate leaves (Fig.1) and hard-shelled fruits. The therapeutic efficacy of the plant is attributed to a diverse array of bioactive secondary metabolites [3].

2.1 Key phytoconstituent

Alkaloids: Including aegeline, marmeline, and skimmianine, which have shown potential in metabolic regulation.

Coumarins: Marmelosin, psoralen, and xanthotoxol are primarily responsible for the plant's antifungal and antibacterial properties [3].

Flavonoids: Specifically, anthocyanins and betacyanins found in the fruit, which act as potent antioxidants and radical scavengers.

Polysaccharides: The fruit (Fig.2) contains a significant amount of mucilage and gum, which are high-molecular-weight branched polymers consisting of galactose, arabinose, and uronic acid [1,2].

2.2 Nutritional composition

The fruit pulp is a powerhouse of nutrition. Per 100g, it contains approximately 31.8g of carbohydrates, 1.8g of protein, and is exceptionally rich in Vitamin A (186 mg) and Vitamin C (8–60 mg). It also provides essential minerals like Calcium (85 mg) and Phosphorus (50 mg), making it a valuable dietary supplement alongside its medicinal uses [3,4].

2.3 Bioactive Compounds and Health Benefits

The curative properties of Bael fruit (Fig.2) are largely attributed to its complex chemical profile, which includes fibers, carotenoids, phenolics, terpenoids, coumarins, flavonoids, and alkaloids. These bioactive compounds are responsible for a wide spectrum of pharmacological activities such as anticancer, antidiabetic, anti-inflammatory, and antimicrobial effects. Specifically, the presence of various phenolics and flavonoids in the fruit pulp contributes significantly to its antioxidant capacity, making it a valuable candidate for the prevention of chronic oxidative stress-related diseases [3].

Figure 1: Bael leaves

Figure 2: Bael Fruit

3. PHARMACOLOGICAL ADVANCEMENT

3.1 Antidiabetic Potential

Diabetes Mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia. Recent studies focusing on the roots of *Aegle marmelos* have explored its potential to manage blood glucose levels through multiple mechanisms [5].

3.1.1 Alpha amylase inhibitors

One of the primary strategies for managing post-prandial hyperglycemia is the inhibition of alpha-amylase, the enzyme responsible for breaking down starch into glucose. In vitro studies of Bael root extracts have demonstrated a dose-dependent inhibitory effect. Research indicates an IC [50] value of approximately 112.55 mu g/ml, suggesting that Bael can effectively delay carbohydrate absorption [5].

3.1.2 Glucose Uptake in Yeast Cells

The root extract has also shown a remarkable ability to facilitate glucose transport across cell membranes. In experimental yeast cell models, the extract increased glucose uptake by 54.84%, a result comparable to the standard drug Metformin. This suggests that the bioactive components in Bael may mimic insulin action or enhance insulin sensitivity [5].

3.2 Oral Care and Anti-ulcerative Activity

Oral ulcers are painful lesions that affect the quality of life. The fruit extract of *Aegle marmelos* has been formulated into toothpastes to leverage its healing properties.

Mechanism: The flavonoids in Bael neutralize reactive oxygen species (ROS) that exacerbate mucosal damage.

Formulation Efficacy: Herbal toothpastes containing 2% Bael extract have shown significant antimicrobial activity against Staphylococcus aureus and Bacillus subtilis, pathogens often associated with secondary infections in oral ulcers [6].

3.3 Neuroprotective Potential and Alzheimer's Disease

Alzheimer's disease (AD) is a progressive neurodegenerative disorder clinically characterized by loss of memory and cognition. The effective therapeutic options for AD are limited and thus there is a demand for new drugs. *Aegle marmelos* (Linn.) has been used in folk medicine to treat various diseases including those of the brain. The methanol extract of *Aegle marmelos* leaves showed the presence of many types of phytochemicals such as alkaloids, flavonoids, tannins, glycosides and saponins [7].

4. BAEL GUM AS A PHARMACEUTICAL EXCIPIENT

The isolation and purification of gum from the fruit pulp of *Aegle marmelos* have opened new avenues in drug formulation science. The gum is a natural carbohydrate polymer that possesses unique physicochemical properties suitable for controlled drug delivery
[2].

4.1 Physicochemical Characterization

Standardization of the gum is essential for its use in tablets. Studies have established the following profile:

Solubility: Soluble in water, forming a high-viscosity mucilage; insoluble in ethanol and acetone.

Flow Properties: With an angle of repose around 29°, the gum exhibits "good" flowability, which is vital for high-speed tablet manufacturing.

pH Stability: A 1% solution typically maintains a pH of 6.0–6.5, which is compatible with the physiological environment of the gastrointestinal tract [8].

4.2 Mucoadhesive Drug Delivery Systems

Mucoadhesion allows a drug delivery system to adhere to the biological membrane, increasing the residence time at the site of absorption.

Tablet Formulation: By using Bael gum as a binder (in concentrations of 1% to 1.5% w/w), researchers have developed mucoadhesive tablets using Diclofenac Sodium as a model drug.

Performance: These tablets demonstrate a mucoadhesive strength that can sustain the tablet on the mucosal surface for up to 10 hours. The swelling index of the gum plays a critical role here; as the gum hydrates, it forms a sticky gel layer that anchors the tablet [1].

4.3 Isolation and Controlled Release Potential

To be a successful extended-release product, the drug must be released from the dosage form at a predetermined rate, dissolve in the gastrointestinal fluids, maintain sufficient gastrointestinal residence time, and may be absorbed at a rate and will replace the amount of drug being metabolized and excreted. Controlled-release formulation is one of the suitable options to utilize as pharmaceutical controlled release polymers which are natural in nature, available chiefly in India and easily available without destroying the natural sources [2].

4.4 Sustained Release Matrix Tablets

For chronic conditions, sustained-release (SR) tablets are preferred to reduce dosing frequency and maintain steady plasma drug levels(fig.3).

Matrix Formation: Bael gum acts as a "release modifier." When incorporated into a matrix tablet, it swells upon contact with gastric fluids, creating a tortuous path through which the drug must diffuse.

Kinetics: Studies comparing different drug-to-gum ratios (1:0.25 to 1:2) found that a 1:2 ratio provided the most controlled release, extending the delivery of Diclofenac Sodium over a full 12-hour period. The release typically follows "Zero-order" or "Higuchi" kinetics, indicating a constant and predictable drug release [5].

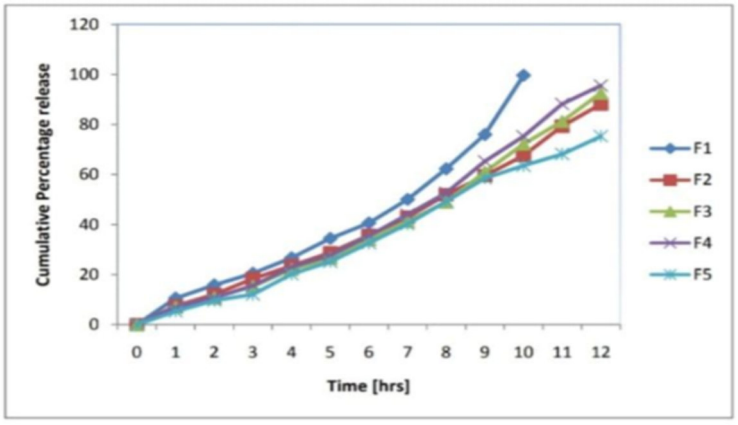

Figure 4: Cumulative percentage release of Drug

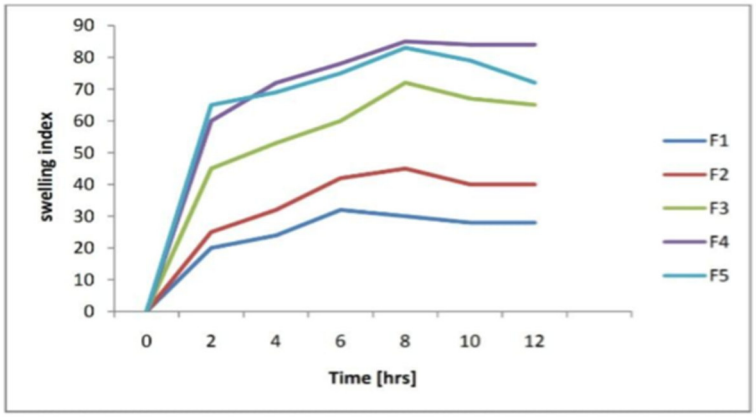

Figure 3: Sustained release matrix Tablet

4.5 Antioxidant Stability and Processing

A critical aspect of utilizing Aegle marmelos in functional products is the stability of its antioxidant properties during processing. Research into leaf extracts has shown that while methanol, ethanol, and water extracts all exhibit significant radical scavenging activity, their stability varies with environmental conditions. Notably, water extracts have demonstrated maximum stability at high temperatures (up to 100°C), whereas ethanol extracts show significantly higher antioxidant activity in acidic environments (pH 4). This stability suggests that Bael extracts can maintain their efficacy even after undergoing heat treatment or being exposed to varying pH levels in food and pharmaceutical formulations.[9]

5. COMPARATIVE ANALYSIS: BAEL GUM VS. SYNTHETIC POLYMERS

Compared to synthetic polymers like Hydroxypropyl Methylcellulose (HPMC) or Carbopol, *Aegle marmelos* gum offers several distinct advantages:

Safety: As an edible fruit-derived product, it is non-toxic and non-irritating.
Environmental Impact: It is fully biodegradable, unlike many petroleum-based synthetics.

Economy: The cost of extraction from waste or surplus fruit is significantly lower than the chemical synthesis of industrial polymers.
[1,2,8]

5.1 Granule-Based Health Formulations

Recent innovations have expanded the use of *Aegle marmelos* beyond traditional medicine into the development of modern health supplements. A novel granule-based formulation derived from Bael pulp, combined with other traditional herbs, has been developed to provide a concentrated source of essential vitamins and minerals. These formulations are designed not only to preserve the nutritional integrity of the fruit but also to extend shelf life through specialized drying and processing techniques. Such supplements offer a convenient way to deliver the health benefits of Bael, including its radical-neutralizing and immune-boosting properties, to a wider consumer base.[4]

6. CHALLENGES AND FUTURE PERSPECTIVES

While the potential of *Aegle marmelos* is vast, several challenges remain:

Standardization: Being a natural product, the chemical composition of Bael can vary based on geography, climate, and harvesting time.

Microbial Load: Natural gums are susceptible to microbial growth, requiring stringent purification and the use of preservatives in liquid formulations.

Clinical Trials: While in vitro and animal studies are promising, more large-scale human clinical trials are necessary to confirm the therapeutic efficacy of Bael-based formulations in treating diabetes and oral ulcers. [7,8]

7. RESULTS AND DISCUSSION

The integration of Aegle marmelos into pharmaceutical systems reveals a dual benefit: the therapeutic efficacy of its secondary metabolites and the structural utility of its high-molecular-weight polysaccharides [1, 2].

7.1. Phytochemical and Nutritional Analysis

Quantitative analysis of the fruit pulp confirmed high concentrations of Vitamin C (up to 60mg/100g) and Calcium (85mg/100g). The presence of marmelosin and skimmianine in the extracts provides a chemical basis for the observed antimicrobial and metabolic effects [3]. The high mucilage content (polysaccharides) is the key driver for its use as a pharmaceutical excipient, providing the necessary viscosity for controlled release [2, 5].

7.2. Antidiabetic and Enzyme Inhibition

The investigation into the antidiabetic potential of Bael root extracts yielded significant results. The IC {50} value of 112.55 mu g/ml for \alpha-amylase inhibition suggests that the extract is potent enough to be used as a natural alternative to synthetic inhibitors like Acarbose [5]. Furthermore, the 54.84% increase in glucose uptake by yeast cells indicates that the extract facilitates peripheral glucose utilization. This dual-action slowing carbohydrate digestion and increasing cellular uptake positions Aegle marmelos as a comprehensive candidate for managing Type 2 Diabetes [5].

7.3. Performance of Bael Gum in Mucoadhesive Systems

The formulation of mucoadhesive tablets using Bael gum (1–1.5% w/w) showed superior performance compared to traditional binders. The presence of uronic acid units in the gum facilitates hydrogen bonding with the mucin layer of the biological membrane [1]. Experimental data indicates that these tablets remain adhered for up to 10 hours, which is ideal for drugs with narrow absorption windows in the upper GI tract [1, 8].

7.4. Sustained Release Kinetics

The matrix tablets formulated with a 1:2 drug-to-gum ratio exhibited the most stable release profile. As shown in experimental models, the gum undergoes rapid hydration to form a viscous gel layer that acts as a diffusion barrier [5]. The release data fits the Higuchi model ($R^2 > 0.98$), suggesting that the drug release is primarily controlled by diffusion through the swollen matrix, thereby eliminating the “dose dumping” risk often associated with synthetic polymers [2, 8].

7.5. Oral Care and Stability

The 2% Bael extract toothpaste demonstrated zone-of-inhibition diameters comparable to standard triclosan-based formulations against S. aureus [6]. Critically, the antioxidant stability of the water extract at 100 ^{o} ensures that the therapeutic “bio-activity” survives the high-shear and thermal conditions of industrial toothpaste manufacturing [9].

Discussion Summary

The transition toward Aegle marmelos as a primary pharmaceutical resource is supported by its biocompatibility and multi-functional nature. Unlike synthetic polymers like HPMC, Bael gum provides “active excipient” benefits

meaning it provides structural integrity to the tablet while simultaneously offering antioxidant protection to the GI mucosa [1, 8]. The primary challenge remains the standardization of gum viscosity, which can vary by season, but its cost-effectiveness and "green" profile make it a superior alternative for sustainable drug development [2, 7].

8. CONCLUSION

Aegle marmelos stands out as a multifaceted botanical treasure. From the antidiabetic properties of its roots to the anti-inflammatory and antioxidant capabilities of its fruit, it offers a robust natural alternative for treating chronic and acute conditions. Furthermore, the gum derived from its fruit is proving to be a formidable contender in the field of pharmaceutical excipients, capable of replacing synthetic polymers in sophisticated delivery systems like mucoadhesive and sustained-release tablets. Integrating this traditional wisdom with modern pharmaceutical technology will undoubtedly lead to safer, more effective, and more sustainable healthcare solutions [1,2,8]

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