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Review Article

Antidiabetic Activity of *Aegle Marmelous* and Its Relationship with Its Antioxidant Properties

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ABSTRACT

Aegle marmelos, better known as bael, has long been celebrated in traditional medicine for its potential health benefits, especially when it comes to managing diabetes mellitus. This review sets out to dive into the latest findings on the antidiabetic properties of Aegle marmelos, paying special attention to how it works and its connection to antioxidant benefits. Numerous studies, both in the lab and in living organisms, have shown that extracts from various parts of the plant—like the leaves, fruits, and bark—can significantly lower blood sugar levels. This effect is linked to how it influences insulin secretion, boosts glucose uptake, and inhibits enzymes that break down carbohydrates. On top of that, A. marmelos is packed with antioxidants thanks to its high levels of polyphenols, flavonoids, and other beneficial compounds, which help reduce oxidative stress—a major player in the development and complications of diabetes. The way its antioxidant and antidiabetic effects work together hints at a dual therapeutic potential, positioning A. marmelos as a promising option for creating natural diabetes treatments. This review emphasizes the importance of conducting more clinical studies and standardizing its use to confirm its effectiveness and safety in diabetes management.

INTRODUCTION

Diabetes mellitus is a long-lasting metabolic condition marked by high blood sugar levels, which can stem from issues with insulin production, its effectiveness, or a combination of both. Over the past few decades, the number of people living with diabetes has surged, turning it into a significant public health issue due to its potential long-term complications like heart disease, kidney problems, nerve damage, and eye disorders. A key player in the development and worsening of diabetes and its related issues is oxidative stress, which arises from an imbalance between the production of reactive oxygen species

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(ROS) and the body's antioxidant defenses. Given the drawbacks and side effects of traditional diabetes medications, there's been a rising interest in plant-based treatments that provide safer and more comprehensive .One such plant is *Aegle marmelos* (L.), often referred to as bael or Bengal quince, which belongs to the Rutaceae family. This medicinal plant has a long history of use in Ayurvedic and traditional medicine for addressing various health issues, including diabetes. Various parts of the plant—especially the leaves, fruit, and bark—are known to contain bioactive compounds that boast impressive pharmacological benefits.(1)

Recent research has revealed that *Aegle marmelos*, commonly known as bael, shows impressive antidiabetic properties through various mechanisms. It helps improve insulin secretion, boosts glucose uptake in the body, and inhibits enzymes that break down carbohydrates. On top of that, this plant is packed with antioxidants, which may enhance its antidiabetic effects by lowering oxidative stress and protecting pancreatic β-cells(2). This review aims to take a deep dive into the antidiabetic potential of *Aegle marmelos* while also looking at its antioxidant benefits. By shedding light on the plant's pharmacological actions and its bioactive components, this paper hopes to lay a solid scientific foundation for considering *A. marmelos* as a complementary treatment in managing diabetes and to inspire more research into its clinical uses.(3)



Objective :

1. To quantify the blood glucose-lowering effect of *Aegle marmelos* extracts in diabetic models.
2. To measure antioxidant enzyme activity (e.g., SOD, catalase, glutathione) and free radical scavenging capacity.
3. To identify and analyze phytochemical constituents responsible for the observed antidiabetic and antioxidant activities.
4. To compare the efficacy of *Aegle marmelos* with standard antidiabetic drugs such as metformin or glibenclamide.
5. To explore the relationship between oxidative stress and hyperglycemia, and how *Aegle marmelos* mitigates these conditions.
6. To determine the dose-dependent toxicity and safety profile of *Aegle marmelos* extracts in experimental models.(4,5)

Biological discription :

- **Scientific Name:** *Aegle marmelos* (L.) Corrêa

- **Family:** Rutaceae
- **Common Names:** Bael, Wood Apple, Bilva (Sanskrit), Maredu (Telugu), Bel (Hindi)
- **Plant Type:** Medium-sized deciduous tree
- **Height:** Up to 12–15 meters
- **Leaves:** Trifoliate, aromatic, with a strong citrus scent
- **Flowers:** Greenish-white, sweet-scented, bisexual
- **Fruit:** Globular, woody shell, green to yellow when ripe, contains sweet, aromatic Pulp
- **Habitat:** Dry forests, hilly slopes, plains, cultivated in homesteads(6)

Traditional use of marmelous :

1. **Digestive Health**
- Unripe fruit (usually dried and powdered) is used to treat:
- Diarrhea
- Dysentery
- Irritable bowel syndrome (IBS)
- Ripe fruit pulp acts as a mild laxative, helping relieve constipation.
2. **Fever and Infections**
- The leaves and bark are used to reduce fevers and treat microbial infections, due to their antibacterial and antiviral properties(7)
3. **Diabetes Management**
- Leaf extracts are believed to help lower blood sugar levels and are used in Ayurvedic remedies for type 2 diabetes.
4. **Respiratory Conditions**
- Bael leaves and fruit are used in traditional remedies for asthma, bronchitis, and cold symptoms.
5. **Anti-inflammatory and Pain Relief**
- Paste made from leaves or bark is applied externally to relieve joint pain, swelling, and inflammation(8)

Soil Type :

Aegle marmelos is said to do best on rich well drained soil, but it has grown well and fruited on the oolitic Limestone of southern Florida. It also grows well in swampy, alkaline or stony soils having pH range from 5-8. In India it has a reputation of thriving where other fruit trees cannot survive(9)

Tree Management :

The tree has no exacting cultural requirements, doing well with minimum of fertilizer and irrigation. The Spacing in orchards is 6-9 m between trees. Seedlings begin to bear in 6-7 years vegetative propagated trees in 5 Years. Full production is reached in 15 years. Normally the fruit is harvested when yellowish-green and kept for 8 days while it loses its green tint. Then the stem readily separates from the fruit. A tree may yield as many as 800 fruits in a season(10)

Origin and Distribution :

The *Aegle marmelos* tree has its origin from Eastern Ghats and Central India. It is native to India and is found Growing wild in Sub-Himalayan tracts from Jhelum eastwards to West Bengal, in central and south India.(11)

Phytochemistry :

Aegle marmelos is a rich source of bioactive compounds, primarily secondary metabolites that contribute to its pharmacological effects. Various studies have identified the following groups of compounds:

Alkaloids: Alkaloids like aegeline have been isolated from the plant, which shows antihyperglycemic and antioxidant properties.

Flavonoids: Flavonoids such as rutin and quercetin contribute to the antioxidant,

antiinflammatory, and cardioprotective properties of the plant.

Tannins: The fruit pulp contains significant amounts of tannins, which have astringent and antimicrobial properties.

Coumarins: Coumarins such as imperatorin and marmelosin have been shown to exhibit anti-inflammatory, antimicrobial, and antidiabetic effects.

Essential Oils: The volatile oils found in the leaves and fruit include limonene, citronella, and linalool, which contribute to antimicrobial and antioxidant effects.

Other Compounds: Terpenoids, sterols, saponins, and phenolic acids have also been identified, contributing to the plant's broad range of biological activities (12).

Antidiabetic activity:

Diabetes mellitus, especially type 2, is marked by high blood sugar due to insulin resistance, poor insulin secretion, or both. Current synthetic diabetes drugs can cause serious side effects. This has led to more interest in plant-based treatments. *Aegle marmelos* (L.) Corrêa, known as bael, is a well-known medicinal plant in traditional Indian medicine, including Ayurveda and Siddha. It has been used for a long time to help manage diabetes.

Several studies have shown the antidiabetic effects of *Aegle marmelos* using both laboratory and live models. Different parts of the plant, including leaves, fruits, bark, and seeds, have shown blood sugar-lowering activity through various mechanisms (13)

Mechanism of antidiabetic activity :

1. **Increasing Insulin Secretion**: It has been demonstrated that extracts from *A. marmelos* stimulate pancreatic β-cells, increasing insulin secretion and lowering blood glucose levels, particularly in animal models of diabetes induced by streptozotocin (STZ) or alloxan.

2. **Enhanced Uptake and Utilization of Glucose:** By upregulating GLUT4 expression and triggering insulin signaling pathways, leaf and fruit extracts enhance peripheral glucose uptake in muscle and adipose tissues.

3. **Inhibition of Enzymes That Digest Carbohydrates:** Some *Aegle marmelos* extracts reduce postprandial blood sugar spikes by inhibiting the enzymes α-amylase and α-glucosidase, which delays the digestion of carbohydrates and the absorption of glucose.

4. **Pancreatic β-Cell regeneration:** Histological research indicates that administering *A. marmelos* leaf extract to diabetic animals may help them regain their ability to produce insulin by partially regenerating damaged β-cells.

5. Lowering Inflammation and Oxidative Stress Because antioxidant (14)

Antioxidant activity :

Oxidative stress, caused by free radicals, plays a key role in aging and the pathogenesis of various chronic diseases. *Aegle marmelos* has been shown to possess significant antioxidant activity, primarily due to its high content of flavonoids (quercetin, rutin) and phenolic compounds.

These compounds scavenge free radicals and protect cells from oxidative damage. Studies have demonstrated that extracts from the leaves and fruit exhibit potent antioxidant capacity, making

them effective in reducing oxidative stress-related damage to the liver, heart, and brain(15).

1. Free Radical Scavenging :

Aegle marvelous contains various , such as flavonoids, isofevonce, anthocyanins, coumarins, lignans, catechins, and isocatechins, which are known for their free radical scavenging properties.

These compounds can directly interact with and neutralize harmful free radicals like superoxide, hydroxyl, and nitric oxide radicals, preventing them from damaging cells and tissues.

The antioxidant activity is often dose-dependent, meaning that higher concentrations of the plant extract led to greater free radical scavenging.

2. Prevention of Free Radical Formation:

Antioxidants can also play a role in preventing the formation of free radicals in the first place. example, some enzymes like superoxide dismutase (SOD) and catalase, which are present in plants, can help convert harmful free radicals (like superoxide and hydrogen peroxide) into less damaging molecules (like water).

3. Enhancement of Antioxidant Enzymes:

The extracts of *A. marmelos* enhance the activity of endogenous antioxidant defense enzymes, including:

- Superoxide dismutase (SOD) – converts superoxide radicals into hydrogen peroxide.
- Catalase (CAT) – decomposes hydrogen peroxide into water and oxygen.
- Glutathione peroxidase (GPx) – reduces lipid hydroperoxides and hydrogen peroxide.
- Glutathione reductase (GR) and Glutathione-S-transferase (GST) – maintain and utilize reduced glutathione (GSH)(16)

Fecture prospective:

1. Bioactive Compound Isolation and Characterization: Although previous research has identified a number of phytochemicals with antidiabetic and antioxidant properties, it is still essential to fully isolate and elucidate the structures of these compounds. Advanced analytical techniques such as LC-MS/MS, NMR, and metabolomics could provide a deeper understanding of the active ingredients and their mechanisms of action.

2. Molecular Mechanisms and Pathway Analysis: It is essential to comprehend the precise molecular targets and signaling pathways that *Aegle marmelos* influences. In order to clarify the ways in which its compounds affect insulin secretion, glucose uptake, oxidative stress, and inflammation, future research should concentrate on gene expression studies, proteomics, and molecular docking.

3. Synergistic Effects and Polyherbal Formulations: *Aegle marmelos* could be studied in combination with other antidiabetic herbs to explore synergistic effects, potentially reducing doses and side effects of conventional drugs.Development of standardized polyherbal formulations with proven efficacy and safety could be a promising future direction.

4. Nanotechnology and Drug Delivery Systems: Nanoformulations (e.g., nanoparticles, liposomes) of *Aegle marmelos* extracts could improve bioavailability, stability, and targeted delivery of its active compoundsSuch advances might enhance therapeutic efficacy while minimizing dosage and side effects.

5. Clinical Trials and Human Studies: Robust, randomized controlled trials in diabetic patients are essential to validate preclinical findings and

establish standardized dosages.Long-term safety and efficacy data are required before widespread clinical use.

6. Antioxidant Role in Preventing Diabetic Complications: The strong antioxidant activity of *Aegle marmelos* may help prevent or mitigate diabetes-associated complications like neuropathy, nephropathy, and retinopathy.Future studies can focus on its role in reducing oxidative stress markers and inflammation in diabetic patients.

7. Personalized Medicine and Genomics: Exploring genetic variations in patients may help tailor *Aegle marmelos*-based therapies for better outcomes.Integration with personalized medicine approaches could optimize its use in managing type 2 diabetes.(17)

Nutritional value:

The fruit is eaten fresh or dried. The leaves and small shoots are eaten as salad greens in many Asian countries. The young shoots and leaf are used as vegetable in Thailand and used as seasonal food in Indonesia. These are Used to reduce appetite16 Various studies have been done to know the proximate composition of the leaves, pulp of fruit and seed powder Of *Aegle marmelos*. A study was conducted to analyze values for proximate composition of *Aegle marmelos*Leaf, pulp and seed powder using standard methods found that bael leaf, pulp and seed powder are good source Of protein, fat, minerals, crude fiber and energy, rich source of available carbohydrates, dietary fiber and also Contain antinutrient content which help in controlling blood sugar. Another study reported that *Aegle marmelos* leaf powder has 10.3g ash, 0.14µg zinc, 2.67µg iron and 1.73µg of chromium in leaf powder(18).The proximate composition of wild variety of *Aegle marmelos* leaves (Gir forest) and cultivated variety (Gomayasi from Vejalpur Research Station, Panchmahals, Godhra, Gujarat, India) was studied and it was found That both the varieties had good nutritional components however, the wild variety was superior to the cultivated Variety in nutrients like carbohydrates, protein, fiber, moisture, ash content and many of the trace elements like Cu, Fe, Mn, Zn, Ca, Vanadium, Gold etc. Also heavy metals like lead, arsenic, mercury and cadmium were not Detected in either of the variety proving it to be nontoxic(19)

TABLE- PROXIMATE COMPOSTION OF *AEGLE MARMELOS* LEAF

Parameter	A M Leaf (wild) (%)	A M Leaf (cultivated) (%)
Moisture	54.0	52.4
Crude Protein	7.6	2.22
Crude Fat	8.18	12.7
Crude Fiber	30.14	25.1
Carbohydrate	10.3	5.4
Zinc (ppm)	0.067	0.026
Chromium (ppm	49	38
Iron (ppm)	181	169

Toxicity and safety profile of *Aegle marmelos*:

1. Acute Toxicity-

LD50 (Lethal Dose 50%) Studies: Acute toxicity studies in rodents show that *Aegle marmelos* extracts have a high safety margin. For instance, when administered orally, aqueous or ethanolic extracts of the leaves, fruits, or roots in mice and rats revealed an LD50 greater than 2000 mg/kg body weight. This indicates low acute toxicity.

Signs of Toxicity: At high doses, there were no reports of mortality or severe clinical signs, such as behavioral changes, convulsions, or respiratory distress, in animal models within 24 to 72 hours after administration.

2. Subchronic and Chronic Toxicity-

Hematological and Biochemical Parameters: When rats received repeated doses of *Aegle marmelos* extracts over 28 to 90 days, there were no significant adverse effects on hematological parameters (RBC, WBC, hemoglobin) or biochemical markers (liver enzymes ALT, AST, ALP; kidney function markers urea, creatinine).

Histopathology: Examination of vital organs, like the liver, kidney, heart, and spleen, after chronic treatment showed no major pathological changes. This supports the extract's safety.

Dose-Dependent Effects: Some studies noted mild changes in liver or kidney tissues only at very high doses (above 1000 mg/kg), which do not reflect therapeutic doses.

3. Genotoxicity and Mutagenicity -

Limited studies have looked at the genotoxic potential of *Aegle marmelos*, but the available evidence suggests it is non-mutagenic and does not cause DNA damage in standard tests like the Ames test or micronucleus assay. This indicates a low risk of cancer(20)

Clinical Safety Observations -

Although comprehensive clinical trials are limited, *Aegle marmelos* has been traditionally used in Ayurvedic medicine for centuries with minimal reports of toxicity.Small human studies and anecdotal evidence suggest good tolerability when used at therapeutic doses. Mild gastrointestinal discomfort has been occasionally noted but resolves without intervention.No major adverse drug interactions have been documented, but caution is advised when combined with other antidiabetic medications due to possible additive effects(21)

Safety Considerations -

- **Dose Dependency:** While generally safe, high doses may cause mild side effects such as nausea or diarrhea.
- **Pregnancy and Lactation:** Safety data are insufficient for pregnant or breastfeeding women; thus, use is not recommended in these populations without medical supervision.
- **Drug Interactions:** Potential exists for additive hypoglycemic effects when used concomitantly with conventional antidiabetic drugs; monitoring is advisable.(22).

Traditional use *Aegle marmelos* in ayurveda:

In Ayurveda, *Aegle marmelos*, commonly known as Bael, has been a go-to for managing diabetes thanks to its promising therapeutic qualities. Let's break down some important aspects:

Traditional Uses: -

- **Blood Sugar Control:** *Aegle marmelos* is thought to help keep blood sugar levels in check and boost insulin sensitivity.
- **Digestive Health:** This plant is known for its digestive benefits, which can ease gastrointestinal issues often linked to diabetes.
- **Antioxidant Activity:** The antioxidant properties of *Aegle marmelos* may offer protection against oxidative stress and inflammation related to diabetes.

Ayurvedic Preparations: -

- **Leaf Decoctions**: These are commonly used to create medicinal brews.
- **Fruit Pulp:** The pulp can be eaten raw or cooked to help manage blood sugar levels.
- **combination Therapies:** It's frequently combined with other herbs to amplify its health benefits.(23)

Potential Benefits: -

- **Regulation of Blood Sugar Levels:** *Aegle marmelos* might assist in controlling blood sugar and enhancing insulin sensitivity.
- **Prevention of Diabetic Complications:** Thanks to its antioxidant and antiinflammatory properties, it may help ward off complications associated with diabetes.

Aegle marmelos has been a staple in Ayurvedic medicine for centuries, and researchers are now delving into its potential advantages for diabetes management.(24)

CONCLUSION :

The rising challenge of diabetes mellitus, along with Its oxidative stress-related complications, has sparked a growing interest in exploring plant-based treatment options. One such plant, *Aegle marmelos*, has been a staple in traditional Ayurvedic medicine and is known for its impressive antidiabetic properties, largely due to its antioxidant capabilities. Research from various in vivo and in vitro studies shows that extracts from different parts of A. marmelos—particularly the leaves and fruits—can effectively lower blood sugar levels, boost insulin secretion, improve lipid profiles, and decrease markers of oxidative stress. These beneficial effects are mainly due to the presence of phytochemicals like flavonoids, phenolic acids, coumarins (such as umbelliferone), and essential fatty acids, all of which play a role in both antioxidant activity and enhancing insulin sensitivity.

The plant's knack for scavenging reactive oxygen species (ROS) and boosting the activity of natural antioxidant enzymes like SOD, catalase, and glutathione peroxidase really highlights its dual role in managing blood sugar levels and protecting cells. These insights back up the traditional use of *Aegle marmelos* in treating diabetes and show its promise as a natural source for creating new antidiabetic medications. That said, even with some encouraging preclinical results, we still need well-structured clinical trials to nail down the right dosages, effectiveness, and safety for people. Future studies should also aim to isolate and identify specific bioactive compounds and dig into how they work at the molecular level. In short, *Aegle marmelos* presents a comprehensive and versatile approach to managing diabetes, thanks to its combined antidiabetic and antioxidant benefits, making it a strong candidate for further pharmacological exploration and integrative treatment options.

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