A Natural Remedy for Diabetes Management from Aegel Marmelos

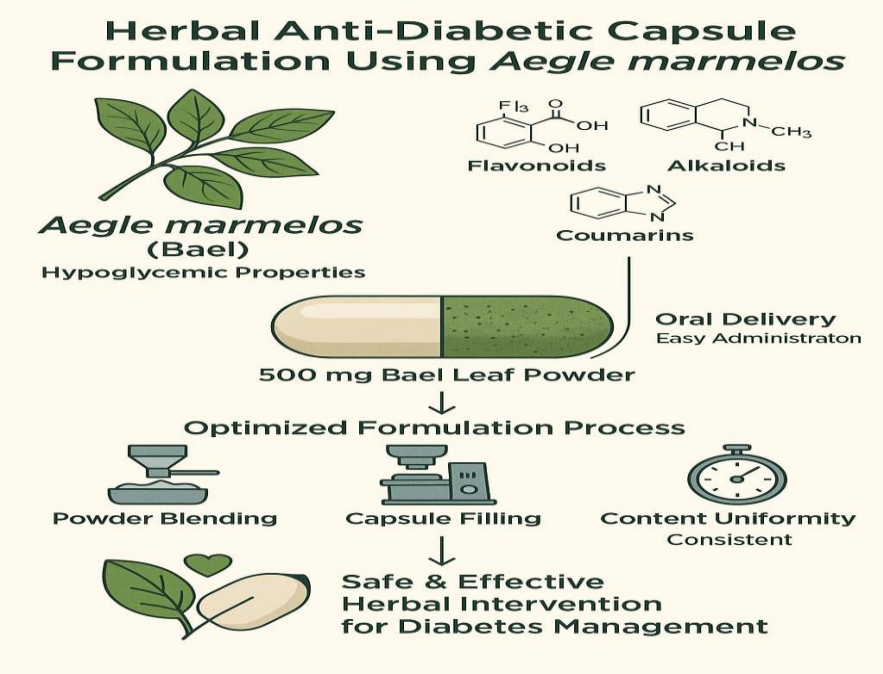
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ABSTRACT

The current research seeks to create and test an herbal anti-diabetic capsule with Aegle marmelos (Bael) leaf powder as the active pharmaceutical component. Due to its high phytochemical content, including flavonoids, alkaloids, and coumarin, Aegle marmelos has been historically known for its hypoglycemic benefits. With an emphasis on simplicity of administration and increased patient compliance, the capsule formulation was created to provide a 500 mg dosage of Bael leaf powder in each unit. Choosing the right excipients was a key part of the process for maintaining consistent capsule fill weight and flow characteristics. Several quality criteria, including weight fluctuation and disintegration time, were tested for the completed capsules. The capsule's promise as a natural and efficient therapy for diabetes management was highlighted by the fact that it satisfied pharmacopeial criteria, as shown by the findings. The usage of bael leafbased capsules as a promising herbal intervention with few adverse effects is supported by this study.



KEYWORDS: Aegle Marmelos, Herbal Anti-diabetic Capsule, Hypoglycemic Properties, Minimal side effects.

Introduction

1. Bael plant

Scientifically known as Aegle marmelos, the plant that is widely referred to as "Bael" in Marathi is a member of the Rutaceae family. Aegle marmelos (L.) Corrêa, often known as the stone apple, golden apple, or Bengal quince, is one of the most medicinally valuable tree species among the 250,000 terrestrial plant species that are now recognized. It has great cultural and religious significance in India and is frequently considered sacred by Hindu people. Devotees worship Bael trees, which are frequently found close to temples devoted to Lord Shiva. Ayurvedic treatment in India and other South Asian nations has historically relied heavily on bael. The classic literature of Ayurveda, the Charaka Samhita, emphasizes the use of bael in conventional treatments. The fruit, leaves, bark, roots, and seeds of the bael tree are all utilized extensively in traditional and Ayurvedic medicine because of their well-known therapeutic qualities. [(1)]

Throughout history, numerous bioactive chemicals have been isolated from different portions of the bael tree and used to treat a wide range of illnesses. In ethnotherapy, several plant parts—including the leaves, roots, stem, bloom, and fruit—have been used to harness the medicinal properties of chemicals that have been isolated from bael and demonstrated to have biological action against a range of ailments. Analgesic, anticancer, antifungal, antiviral, antibacterial, antiulcer, antipyretic, anti-dycentric, anti-diarrheal, and redioprotective are some of these. Crude extracts from different portions of the bael plant are used in folklore medicine in many Indian traditional systems to cure a wide range of ailments. While the unripe fruit helps treat dysentery and the leaves have digestive, febrifuge, astringent, and laxative properties, the ripe fruit is used as an appetizer, laxative, tonic, restorative, and astringent. Roots are used to treat heart malfunction, fever, melancholy, hypochondriasis, abdominal pain, and urinary problems. Along with the fruits, the root is known as "dasmula," or "ten roots," in Ayurvedic medicine. Depression, intermittent fever, and heart palpitations are all treated using a decoction prepared from the bark and roots. Moreover, root contains hypoglycemic and anti-amoebic qualities. Fever is treated with the bitter leaves. A leaf poultice is used to cure ophthalmia and ulcers.[(2)]



Fig.No.2: Bael Tree

1.2 Diabetes mellitus (DM):

It affects about 537 million individuals worldwide, making up 10.5% of the population, making it the most prevalent endocrine illness. It is brought on by insufficient or inefficient insulin production by the pancreas, which causes blood glucose levels to rise or fall. It has been shown to harm numerous bodily systems, including the nerves and blood vessels. In addition to synthetic medications, a variety of plant-based treatments are used in its treatment, especially for non-insulin-dependent diabetic mellitus (NIDDM). Bael is a widely used plant with a global spread. It has numerous therapeutic benefits, including antifungal, antibacterial, antiprotozoal, and hypoglycemic effects. Its leaves have been shown to have an insulin-like effect on hyperglycemia, and their mode of action has been documented.[3]

MATERIAL AND METHODS [7,8,9,10]

2.1 Material

Formulation of Granules:

Sr. No	Material	F1 (mg)	F2 (mg)	F3 (mg)*
1.	Bael Leaf Powder	500	500	500
2.	Microcrystalline cellulose (MCC)	45	50	60
3.	Starch	45	40	30
4.	Starch Paaste (10 %)	65	70	70
5.	Magnesium Stearate	8	8	8
6.	Talc	12	12	12

Table No.1: Composition of Bael Leaf

2.2 Collection of Plant Material:

The leave of plant (Aegel marmelos) was collected from the farm. The Plant material were identified and authenticated by **(Botanist)** Arts, Commerce and Science College, Maregaon. Empty hard gelatin capsules were purchased from online source and all other materials were obtained through college.

2.3 Preliminary Phytochemicals Analysis of Leave Powder: [5, 6]

The powdered bael leaves underwent initial phytochemical screening to identify secondary metabolites such coumarin, flavonoids, and alkaloids.

2.4 Formulation and Development:

Bael leaf powder granules were made using the wet granulation method. Weighing and carefully blending a predetermined amount of starch, microcrystalline cellulose, and bael leaf powder will be done. Drop by drop, the required amount of binder must be added to the mixture. After passing through a sieve, the wet granules will be dried in a hot air oven for fifteen minutes. The granules will be run through a sieve once they have dried. The appropriate concentrations of magnesium stearate and talc were added to the granules. The prepared granules were then placed inside the size #00, empty hard gelatin capsule. Table No. 1 displays the bael leaf powder granule formulation.

3. UV SPECTROSCOPY STUDY: [11,12]

3.1 Isolation of Compound: A portion of the plant (the leaves) was air-dried and crushed. Methanol was used to sequentially extract the powdered specimens.

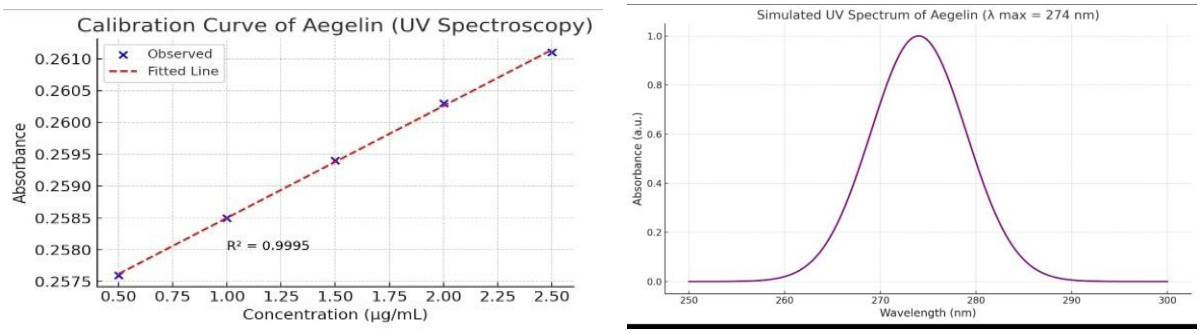
3.2 Preparation of standards:

Aegelin, marmelosin, and coumarin (100 µg ml−1) were prepared as a stock solution in methanol by dissolving 10 mg of standard in a 100 ml volumetric flask & then filling the flask with methanol.

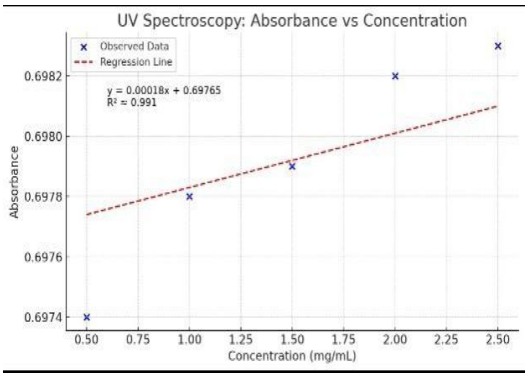
3.3 Calibration curves of standard:

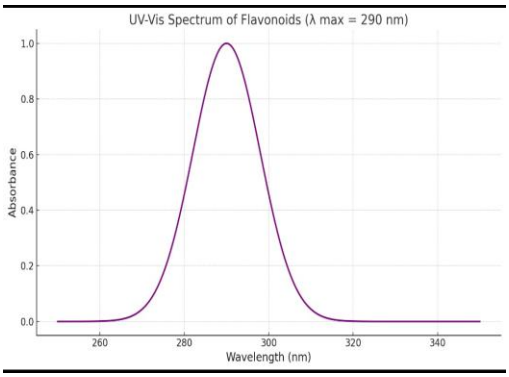
By making the necessary dilutions of the stock solution, calibration standard solutions were created at five different concentrations (concentration range 0.5, 1.0, 1.5, 2.0, 2.5).

Since the absorption maxima (λmax) of Aegelin, Marmelosin, and Coumarin were 274, 305, and 290 nm, respectively, the UV detector was set to 300 nm.

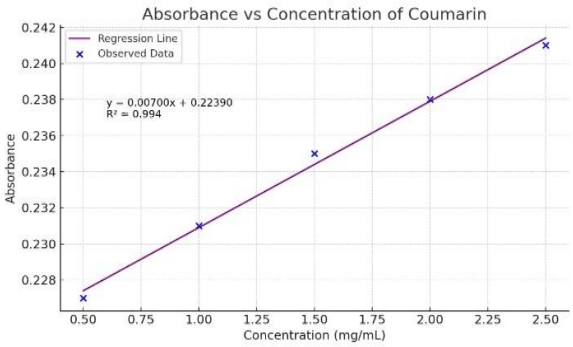


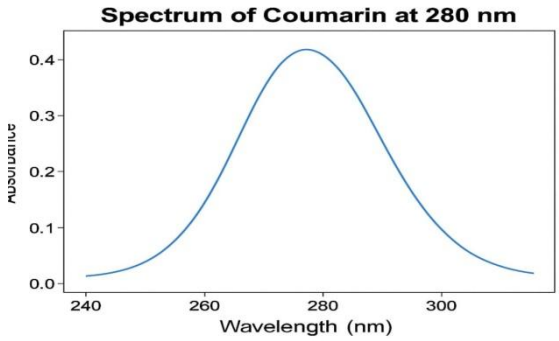
Calibration curves and Spectrum of aegelin





Calibration curves and Spectrum of Marmelosin





Calibration curves and Spectrum Coumarin

Fig.No.3: Calibration curves and Spectrum of Phytochemicals

4. PREFORMULATION STUDIES [13,14]

4.1 Bulk Density:

Bulk density is determined by measuring the volume occupied by a known mass of powder that has been put through a sieve into a graduated cylinder or volume measuring container. It is calculated using the formula M/Vo = ρb and represented in g/mL. where Vo is the maximum amount of powder and M is the mass of the powder.

4.2 Tapped Density:

The flow characteristics of a powder are also influenced by interparticle forces that have an impact on its bulk properties. By comparing the bulk density to the tap density, which also indicates the flowability of the powder, one can ascertain the extent of these interactions. A graduated cylinder's tap density is determined by mechanically tapping it to quantify the amount of powder inside. The cylinder is repeatedly tapped until the volume is stable after the first measurement. The cylinder is often tapped in this manner by raising and lowering it from a predetermined height. The tapped density, measured in g/mL, is determined by the last volume following compression.

The formula is: $\rho t = M/Vt$

where M is the powder's mass, Vt is the amount of tapping that has occurred.

4.3 Compressibility index: (CI)

The ability of a powder to reduce in size when compressed is known as its compressibility. Their compressibility was assessed by the quantity of space they occupy. After that, the cylinder is tapped 500, 750, and 1250 times. There should be less than 2% of difference between tabs. The system is used to determine the Compressibility Index %. determined by attention to density. A 50 ml graduated cylinder is filled with the weighed granules, and the volume is measured.

CI is equal to Vo-Vi multiplied by 100 over Vo. Vi is the taped density; Vo is the untapped density.

4.4 Hausner’s Ratio:

It is the amount of frictional resistance of the granular substance. The calculated bulk density to tapped density ratio should be in the range of 1.2 to 1.5. Vi / Vo is the Hausner's Ratio formula. Vi represents the untapped density, while Vo represents the tapped density.

4.5 Angle of Repose:

The coefficient of friction between the particles is equal to the tangent of the attitude of rest. Therefore, the more rough and uneven the particle floor, the more likely the rest position is. When the lower tip of the funnel was precisely 2.0 cm above a stiff surface, the attitude of repose (θ) stabilized after the mixes were poured down the funnel's partitions. Until the top of the pile floor reached the bottom of the funnel, the drug or combination had been poured. The following formula is used to determine the angle of repose.

where $\tan \theta = h/r$,

where h is the height and r is the radius. $\theta = \tan^{-1} (h/r)$, where r is the radius in centimeters, h is the peak in centimeters, and θ is the attitude of rest.

The compressibility index, Hausner's ratio, and angle of repose can all be used to ascertain the particles' physical characteristics.

Preformulation studies:

Sr. No.	Parameters	Trial 1	Trial 2	Trial 3*
1.	Bulk Density (gm/ cm^2)	0.43	0.45	**0.49**
2.	Tapped Density (gm/cm^2)	0.50	0.48	**0.50**
3.	Compressibility Index (% w/w)	14	6.25	**9**
4.	Hausners Ratio	1.16	1.06	**1.02**
5.	Angle of Repose	32.9	30.2	**27.6**

Table No.2: Preformulation Studies of Bael Leaf Granules.

5. EVALUATION PARAMETER: [14,15,16]

The nutraceutical capsule was evaluated for several factors after taking pre-formulation into consideration to avoid errors during the production process. These are some of the factors to consider: weight change, appearance, breakdown time, and dissolving tests.

5.1 General Appearance:

A capsule's overall appearance, identity, and elegance are essential for obtaining customer acceptance and ensuring batch-to-batch and capsule-to-capsule consistency. Controlling general appearance involves measuring characteristics such as size, form, color, taste, and the presence or absence of odor.

5.2 Moisture content: Moisture content of capsules was determined by using desicator apparatus.

5.3 Dissolution test:

The IP Dissolution Test Apparatus Type II (basket type) was used to measure the rate at which bael leaf powder was discharged from granules. Granules were initially added to an empty hard

gelatin capsule of size #00 at the start of each trial, and the capsule was then put in a dry basket. For the dissolution experiment, 900 cc of phosphate buffer with a pH of 6.8 was employed at 37±0.5°C and 50 rpm. After inserting the basket into the dissolution media, run the apparatus at 50 rpm. Five milliliters were taken out every five minutes for sixty minutes. Following this addition, the mass was maintained at the same temperature. Whatman filter paper number 41 was used to filter the samples. An ultraviolet-visible spectrophotometer was used to measure the absorbance of these solutions at 274 nm. A formula based on a standard curve was used to determine the cumulative percentage of medication release.

5.4 Weight variations test:

The average weight was calculated by weighing 20 randomly selected capsules. Each capsule was also weighed individually. The deviation from the average weight in each instance was calculated and expressed as a percentage. From the sample size ton, not a single capsule varies in weight from the average by more than 2%, and none of the capsules vary by more than twice that amount.

5.5 Disintegration test:

The capsule's disintegration time was determined in accordance with the British Pharmacopoeia 1998. Six capsules were put into each compartment of the disintegration instrument, and the medium was water kept at a temperature of 37 ± 1 °C. The capsule had passed the test, as evidenced by the fact that six capsules had made it through the device's mesh in fifteen minutes.

Evaluation Test:

General Apperance:

Sr. No.	Parameters	Observation
1.	Description	00 size and transparent body (ovul)
2.	Colour	Greenish
3.	Odour	Characteristic Odour
4.	Taste	Bitter Taste

Table No. 3: General Apperance

Other evaluation test:

Sr. No.	Parameters	Trial 1	Trial 2	Trial 3*
1.	Moisture content	3.27%	3.76%	**1.07%**
2.	Weight variations test	740±5%	710±5%	**711±5%**
3.	Disintegration test	9:21 min	9.39 min	**8:45min**

Table No.4: Other Evaluation Test

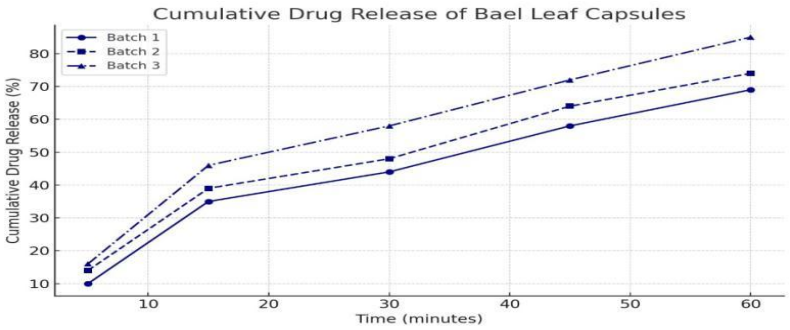


Fig.No.4: Calibration curves of bael leave powder in phosphate buffer pH

6. RESULT AND DISCUSSION:

In this work, three batches of antidiabetic hard gelatin capsules containing Bael leaf powder granules were made using the wet granulation process. Drug and excipient blends were created for each batch, and their micromeritic qualities were assessed, as indicated in Table 4. The F3 batch's angle of repose was determined to be 27.6°. For F3 formulations, the tapped density was 0.50 gm/cm3 and the bulk density was 0.49 gm/cm3. The percentage of compressibility that was determined from density data was 9%. It was determined that Hausner's ratio was 1.02. We performed chemical test for detection of phytochemicals that are present in bael leaves which are responsible for antidiabetic activity. Granules were made utilizing the wet granulation method since the F3 batch demonstrated good micromeritic characteristics for this process.

6.1 Disintegration Time: It was discovered that the hard gelatin capsule took 8:45 minutes to dissolve.

6.2 Drug Release in Vitro: The cumulative medication release percentage for each batch was displayed. Figure No. 4 displayed the in-vitro drug release data.

7. CONCLUSION:

The study successfully demonstrated the formulation of an anti-diabetic capsule using Aegle marmelos (Bael) leaf powder. The capsule were prepared via wet granulation and evaluated for various physicochemical parameters such as moisture content, weight variation, and disintegration time. The results indicated that the F3 batch met standard quality specifications and showed potential anti-diabetic activity. This supports the traditional use of Bael leaves in managing diabetes and highlights the feasibility of developing herbal formulations for therapeutic use.

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