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Review Article

Formulation and Evaluation of Effervescent Anti-Diabetic Tablets Using Aegle marmelos Extract for the Management of Type 2 Diabetes Mellitus

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Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin action, or both. Type 2 diabetes mellitus is the most prevalent form and is associated with insulin resistance, obesity, sedentary lifestyle, and genetic predisposition. Conventional anti-diabetic drugs effectively control blood glucose levels but are often associated with adverse effects such as hypoglycemia, gastrointestinal disturbances, and weight gain. Herbal medicines have gained increasing attention as safer alternatives due to their therapeutic efficacy and minimal side effects. Aegle marmelos (Bael or Belpatra), a medicinal plant widely used in Ayurveda, possesses significant anti-diabetic activity owing to the presence of flavonoids, alkaloids, tannins, phenolic compounds, and coumarins. These phytoconstituents exert hypoglycemic effects through stimulation of insulin secretion, inhibition of α-amylase and α-glucosidase enzymes, enhancement of glucose uptake, and reduction of oxidative stress. Effervescent tablets offer advantages such as rapid dissolution, improved bioavailability, enhanced patient compliance, and ease of administration. This review discusses diabetes mellitus, pharmacological properties of Aegle marmelos, formulation strategies for effervescent anti-diabetic tablets, evaluation parameters, and future prospects of herbal effervescent formulations in diabetes management.

Keywords: Diabetes Mellitus, Type 2 Diabetes, Aegle marmelos, Belpatra, Effervescent Tablets, Herbal Formulation, α-Amylase Inhibition, Anti-diabetic Activity.

INTRODUCTION

Diabetes mellitus is a group of metabolic disorders characterized by elevated blood glucose levels due to abnormalities in insulin secretion, insulin action, or both. The disease has emerged as one of the most significant public health challenges worldwide. Persistent hyperglycemia leads to disturbances in carbohydrate, lipid, and protein metabolism and may result in severe complications affecting the cardiovascular system, kidneys, eyes, nerves, and blood vessels. Insulin, secreted by pancreatic β-cells, plays a crucial role in maintaining glucose homeostasis. Deficiency of insulin or resistance to its action results in impaired glucose utilization and accumulation of glucose in the bloodstream. The increasing prevalence of Type 2 diabetes has been attributed to sedentary lifestyles, unhealthy dietary habits, obesity, stress, and genetic factors. Although several synthetic anti-diabetic drugs are available, their long-term use may produce undesirable effects. Therefore, researchers are focusing on medicinal plants as alternative therapeutic agents. Among various medicinal plants, *Aegle marmelos* has attracted considerable attention because of its proven anti-diabetic, antioxidant, anti-inflammatory, and hepatoprotective activities. Incorporation of *Aegle marmelos* extract into an effervescent dosage form may provide rapid drug release, better absorption, improved patient compliance, and enhanced therapeutic effectiveness.

❖ Diabetes Mellitus

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels resulting from impaired insulin secretion, insulin resistance, or both.

Classification

1. Type 1 Diabetes Mellitus (IDDM)

Type 1 diabetes mellitus is an autoimmune disorder characterized by destruction of pancreatic β-cells leading to complete insulin deficiency.

Causes

- Autoimmune destruction of β-cells
- Genetic predisposition
- Viral infections
- Environmental factors

Symptoms

- Polyuria
- Polydipsia
- Polyphagia
- Weight loss
- Fatigue
- Blurred vision

Treatment

- Insulin therapy
- Dietary management
- Physical exercise

2. Type 2 Diabetes Mellitus (NIDDM)

Type 2 diabetes mellitus is characterized by insulin resistance and gradual decline in insulin secretion.

Causes

- Obesity
- Sedentary lifestyle
- Genetic factors
- Unhealthy diet
- Stress
- Aging

Symptoms

- Frequent urination
- Excessive thirst
- Fatigue
- Delayed wound healing
- Obesity
- Recurrent infections

Treatment

- Oral anti-diabetic drugs
- Lifestyle modification
- Insulin therapy in severe cases

❖ **Symptoms and Complications of Diabetes Mellitus**

Symptoms

1. **Polyuria:** Frequent urination due to osmotic diuresis caused by excess glucose in urine.
2. **Polydipsia:** Excessive thirst resulting from dehydration.
3. **Polyphagia:** Increased hunger because cells fail to utilize glucose effectively.
4. **Fatigue:** Reduced cellular energy production causes weakness and tiredness.
5. **Weight Loss:** Common in uncontrolled diabetes due to breakdown of fats and proteins.
6. **Blurred Vision:** High blood glucose affects the eye lens leading to visual disturbances.
7. **Slow Wound Healing:** Poor circulation delays tissue repair.
8. **Recurrent Infections:** Increased susceptibility to bacterial and fungal infections.

Complications

1. Microvascular Complications

- Diabetic neuropathy
- Diabetic nephropathy
- Diabetic retinopathy

2. Macrovascular Complications

- Hypertension
- Coronary artery disease

- Stroke
- Peripheral vascular disease

3. Other Complications

- Diabetic foot ulcers
- Delayed wound healing
- Diabetic ketoacidosis

❖ **Plant Profile**



Fig no 1: Aegle marmelos

Botanical Description

Aegle marmelos (L.) Corr., commonly known as Bael or Belpatra, belongs to the Rutaceae family and is extensively used in traditional medicine.

Parameter	Details
Scientific Name	*Aegle marmelos* (L.) Corr.
Family	Rutaceae
Common Name	Belpatra, Bael
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Sapindales
Genus	Aegle
Species	Marmelos
Part Used	Leaves
Geographical Source	India, Nepal, Sri Lanka, Bangladesh

Phytochemical Constituents

The leaves of *Aegle marmelos* contain several bioactive compounds including:

- Flavonoids
- Alkaloids
- Tannins
- Phenolic compounds
- Coumarins
- Marmelosin
- Essential oils

Pharmacological Activities of Aegle marmelos

1. **Anti-Diabetic Activity:** The anti-diabetic activity is attributed to:

   - Stimulation of insulin secretion
   - Enhancement of glucose utilization
   - Reduction of oxidative stress
   - Inhibition of α-amylase enzyme
   - Inhibition of α-glucosidase enzyme

2. **Antioxidant Activity:** Phenolic compounds and flavonoids neutralize free radicals and protect pancreatic β-cells from oxidative damage.

3. **Anti-Inflammatory Activity:** The plant suppresses inflammatory mediators and reduces tissue inflammation.

4. **Antimicrobial Activity:** Effective against various bacterial and fungal pathogens.

❖ **Effervescent Tablets**

Effervescent tablets are solid dosage forms that release carbon dioxide when dissolved in water due to reaction between acids and bicarbonates.

Effervescence Reaction

Citric Acid + Sodium Bicarbonate → Carbon Dioxide + Water + Sodium Citrate

The generated carbon dioxide promotes rapid disintegration and dissolution of the tablet.

Advantages of Effervescent Tablets

- Rapid dissolution
- Improved bioavailability
- Faster onset of action
- Better patient compliance
- Pleasant taste
- Suitable for geriatric and pediatric patients
- Easy administration

❖ **Objectives**

1. To formulate and evaluate effervescent anti-diabetic tablets containing *Aegle marmelos* leaf extract for the management of Type 2 diabetes mellitus.
2. To collect, identify, and authenticate *Aegle marmelos* leaves.
3. To prepare and standardize the leaf extract using a suitable extraction method.
4. To formulate effervescent tablets using appropriate pharmaceutical excipients.
5. To improve drug dissolution and patient compliance through an effervescent dosage form.
6. To evaluate pre-compression parameters such as angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio.
7. To evaluate post-compression parameters including weight variation, hardness, thickness, friability, drug content, pH, and effervescence time.
8. To assess the in-vitro anti-diabetic activity of the formulation using the α-amylase inhibition assay.
9. To investigate the mechanism of anti-diabetic action of *Aegle marmelos* extract.
10. To perform stability studies according to ICH guidelines.
11. To develop a stable, safe, effective, and patient-friendly herbal anti-diabetic formulation with minimal side effects.

MATERIAL AND METHOD

MATERIALS:

Aegle marmelos leaf extract, sodium bicarbonate, citric acid, tartaric acid, mannitol, PVP K30, sodium saccharin, magnesium stearate, orange/lemon flavour, ethanol and distilled water.

Extraction Process (Soxhlet Method)

1. Fresh *Aegle marmelos* leaves were collected and authenticated.
2. Leaves were washed thoroughly with water to remove dirt and impurities.
3. The leaves were shade-dried for 7–10 days.
4. Dried leaves were powdered using a grinder.
5. The powder was passed through sieve No. 60 to obtain uniform particle size.
6. About 50 g of leaf powder was packed into a Soxhlet thimble.
7. Ethanol was added to the round-bottom flask.
8. Extraction was carried out for 6–8 hours using a Soxhlet apparatus.
9. The obtained extract was filtered.
10. The solvent was evaporated to obtain a concentrated extract.
11. The extract was dried and stored in a desiccator until further use.

Formulation Process (Direct Compression Method)

1. All ingredients were accurately weighed according to the formulation.
2. Sodium bicarbonate, citric acid, tartaric acid, mannitol, and *Aegle marmelos* extract were dried separately to remove moisture.
3. All dried ingredients were passed through sieve No. 60.
4. The ingredients were mixed uniformly in a mortar.

5. PVP K30 was added as a binder and blended thoroughly.
6. Sodium saccharin was added as a sweetener.
7. Orange/lemon flavour was added and mixed uniformly.
8. Magnesium stearate was added as a lubricant and blended gently.
9. The prepared powder blend was evaluated for pre-compression parameters.
10. The blend was compressed into tablets using a tablet compression machine.
11. The prepared effervescent tablets were stored in airtight containers to protect them from moisture.

EVALUATION PARAMETER

Pre-Compression evaluation

1. Repose

Angle of repose is the maximum angle formed between the surface of powder heap and horizontal plane. It indicates flow property of powder blend.

❖ **Procedure**

1. Funnel was fixed at a suitable height.
2. Powder blend was allowed to flow through the funnel freely onto graph paper.
3. Powder formed a cone-shaped heap.
4. Height (h) and radius (r) of heap were measured.
5. Angle of repose was calculated.

❖ **Formula**

$$\tan\theta = \frac{h}{r}$$

Where:

- θ = Angle of repose
- h = Height of powder cone
- r = Radius of cone

❖ **Interpretation**

Angle of Repose	Flow Property
<25°	Excellent
25–30°	Good
30–40°	Passable
>40°	Poor

2. Bulk Density

Bulk density is the ratio of mass of powder to bulk volume before tapping.

❖ **Procedure**

1. Accurately weighed powder blend was transferred into graduated cylinder.
2. Initial volume occupied by powder was noted.
3. Bulk density was calculated.

❖ **Formula**

$$\text{Bulk Density} = \frac{\text{Mass of powder}}{\text{Bulk volume}}$$

Where:

- ρb = Bulk density
- M = Mass of powder
- V b = Bulk volume

3. Tapped Density

Tapped density is the ratio of mass of powder to tapped volume after mechanical tapping.

❖ **Procedure**

1. Measuring cylinder containing powder was tapped mechanically for 100 taps.
2. Final volume was recorded.
3. Tapped density was calculated.

❖ **Formula**

$$\text{Tapped Density} = \frac{\text{Mass}}{\text{Tapped volume}}$$

Where:

- ρt = Tapped density
- M = Mass of powder
- Vt = Tapped volume

4. Carr's Compressibility Index

Carr's index indicates compressibility and flow behavior of powder blend.

❖ **Procedure**

Calculated using bulk density and tapped density values.

❖ **Formula**

$$\text{Carr's Index} = \frac{(TD-BD)}{TD} \times 100$$

Where:

- TD = Tapped density
- BD = Bulk density

❖ **Interpretation**

Carr's Index	Flow Character
5–15%	Excellent
16–20%	Good
21–25%	Fair
>25%	Poor

5. Hausner's Ratio

Hausner's ratio indicates interparticle friction and flowability of powder.

❖ **Formula**

$$\text{Hausner Ratio} = \frac{TD}{BD}$$

❖ **Interpretation**

Hausner Ratio	Flow Property
1.00–1.11	Excellent
1.12–1.18	Good
1.19–1.25	Fair
>1.25	Poor

❖ **Significance**

- Indicates flow efficiency
- Predicts powder handling property

Post-compression evaluation

1. Weight Variation Test

❖ **Principle:** This test ensures uniformity of tablet weight and dose.

❖ **Procedure**

1. Twenty tablets were selected randomly.
2. Individual tablet weights were measured using digital balance.
3. Average weight was calculated.
4. Individual weights were compared with average weight.

2. Thickness Test

❖ **Principle:** Thickness determines uniformity in tablet size.

❖ **Procedure**

1. Thickness of tablets was measured using Vernier caliper.
2. Average value was calculated.

3. Hardness Test

❖ **Principle:** Hardness indicates mechanical strength of tablets

❖ **Procedure**

1. Tablets were placed between jaws of Monsanto hardness tester.
2. Pressure required to break tablet was recorded.

4. Friability Test

❖ **Principle:** Friability determines resistance of tablets to abrasion and shock.

❖ **Procedure**

1. Preweighed tablets were placed in Roche friabilator.
2. Apparatus rotated at 25 rpm for 4 minutes.
3. Tablets were dedusted and reweighed.

❖ **Formula**

Percentage Friability (F) = (Iw – Fw) / Iw x 100

Where:

- F = Friability
- W1 = Initial weight
- W2 = Final weight

5. Disintegration Test

❖ **Principle:** Determines time required for tablet to break into small particles.

❖ **Procedure**

1. Tablets were placed in disintegration apparatus containing distilled water at 37±0.5°C.
2. Time required for complete disintegration was recorded.

6. Effervescence Time

❖ **Procedure:**

- One tablet was added to 200 mL of water at room temperature.
- Time required for complete cessation of effervescence was recorded.

❖ **Acceptance Range:**

- Usually less than 5 minutes.

7. pH Determination

❖ **Procedure:**

- One tablet was dissolved in 200 mL distilled water.
- pH of resulting solution was measured using a calibrated pH meter.

8. In-Vitro Dissolution Study

❖ **Procedure:**

1. Dissolution study was performed using USP Dissolution Apparatus II (Paddle Method).
2. Dissolution medium: 900 mL phosphate buffer (pH 6.8).
3. Temperature maintained at 37 ± 0.5°C.
4. Paddle speed: 50 rpm.
5. Samples were withdrawn at predetermined intervals and analyzed spectrophotometrically.

9. Anti-Diabetic Activity Evaluation

α-Amylase Inhibition Assay

Principle:
The anti-diabetic activity was assessed by measuring inhibition of α-amylase enzyme responsible for carbohydrate digestion.

Procedure:

1. α-Amylase enzyme solution was prepared.
2. Different concentrations of extract were mixed with enzyme solution.
3. Starch solution was added as substrate.
4. Mixture was incubated at 37°C for 10 minutes.
5. DNSA reagent was added and heated.
6. Absorbance was measured at 540 nm using a UV spectrophotometer.

❖ **Formula:**

$$\%\ Inhibition = \frac{A_c - A_s}{A_c} \times 100$$

Where:

- Ac = Control absorbance
- As = Sample absorbance

10. Stability Studies

Conditions (ICH Guidelines):

- 25 ± 2°C / 60 ± 5% RH
- 40 ± 2°C / 75 ± 5% RH

Duration:

- 3 Months

Parameters Evaluated:

- Appearance
- Hardness
- Friability
- Drug content
- Effervescence time
- pH
- Dissolution profile

CONCLUSION

Aegle marmelos is a valuable medicinal plant with significant anti-diabetic potential due to its rich phytochemical composition and multiple mechanisms of action. Development of effervescent tablets containing *Aegle marmelos* extract combines the therapeutic advantages of herbal medicine with the pharmaceutical benefits of effervescent dosage forms. Such formulations provide rapid dissolution, enhanced patient compliance, improved bioavailability, and effective glycemic control. Therefore, effervescent anti-diabetic tablets of *Aegle marmelos* represent a promising herbal alternative for the management of Type 2 diabetes mellitus.

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