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Research Article

Potential of *Moringa oleifera* Effervescent Granules as a New Antacid: Micronutrients, Formulation, and Evaluation

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Abstract

Moringa oleifera, a nutritionally rich plant widely distributed in tropical and subtropical regions, possesses a diverse array of medicinal properties. This study aimed to develop and evaluate effervescent granules from *M. oleifera* leaves and seeds, assessing their *in vitro* acid neutralization capacity (ANC) compared to a commercial antacid. Micronutrient content (calcium and magnesium) of both leaf and seed powders was quantified using flame photometry. Effervescent granules were formulated using wet granulation, and their physicochemical properties were evaluated. The ANC was determined in simulated gastric juice. Results revealed that *M. oleifera* leaves contained significantly higher calcium and magnesium levels than seeds. Two-way ANOVA demonstrated that both leaf and seed effervescent granules, at 5 and 10 g, exhibited significantly higher ANC than the negative control. Post-hoc Tukey's test further indicated that the leaf granules possessed superior ANC compared to seed granules, and equivalent efficacy to 5 g of the commercial antacid. These findings suggest that *M. oleifera* leaves and seeds can be effectively formulated into effervescent granules with potent antacid properties. The observed ANC, likely attributed to the high micronutrient content of the leaves, highlights a novel nutraceutical application for *M. oleifera* as a potential alternative to conventional antacids.

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INTRODUCTION

The therapeutic potential of natural compounds derived from plants has been extensively documented, offering valuable alternatives to conventional drug treatments. Plants represent a sustainable source for the synthesis of diverse phytoconstituents with applications in managing various diseases[1]. Historically, natural products from plants, animals, and minerals have formed the foundation of human disease treatment[2,3]. Among these natural resources, *Moringa oleifera*, often referred to as the "Miracle Tree," stands out due to its rich composition of nutrients, amino acids, antioxidants, and anti-inflammatory compounds, rendering it beneficial for both human nutrition and therapeutic purposes[4]. Traditional medicine ascribes to *M. oleifera* the ability to address over 300 ailments[5], including anti-diabetic[6], hepatoprotective and nephroprotective[7], as well as hypotensive effects[8]. Despite the availability of numerous synthetic antacids, which effectively neutralize stomach acid, their use is often associated with adverse effects such as rebound acid secretion, diarrhea, and constipation, alongside being potentially costly for vulnerable populations. Consequently, the identification of a highly effective and affordable natural medicine for managing gastric acidity is a pertinent area of research[9,10].

Effervescent granules, a mixture of acids and bases that produce a palatable, carbonated solution upon contact with water, represent a popular oral dosage form. They are widely utilized for various pharmaceutical products, including analgesics, antacids, and cough formulations[11]. The advantages of effervescent granules include rapid dissolution, enhanced solubility,

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taste masking of unpleasant active substances, improved stability, and ease of administration[12]. The effervescence, resulting from the interaction between acidic and basic components in the presence of water, further enhances drug dissolution and provides a refreshing sensation[13,14]. Effervescent granules are particularly suitable for plant extracts due to their simplified processing, rapid disintegration, good flow properties, and cost-effectiveness[15]. The *in situ* reaction between acidic ingredients (typically citric and tartaric acid) and basic bicarbonates (like sodium bicarbonate) upon addition to water releases carbon dioxide, facilitating drug dispersion and masking bitter tastes[16,17].

In contemporary society, disorders related to excessive gastric acid secretion are highly prevalent, affecting a significant portion of the global population. The persistent increase in gastric acid contributes to a spectrum of gastroesophageal disorders, dyspepsia, and heartburn, significantly impacting daily life. While conventional acid-reducing and neutralizing medications offer relief, they are often accompanied by undesirable side effects such as constipation, diarrhea, nausea, and headaches[18]. Furthermore, long-term use can lead to dependency and impaired nutrient absorption, while frequent dosing, high costs, and accessibility issues can hinder patient compliance. This context underscores the critical need for safer and more affordable alternatives[19].

Moringa oleifera, with its traditional use in treating gastrointestinal issues and its documented array of beneficial properties, presents a scientifically promising yet underexplored option as a natural antacid. Its accessibility, affordability for local communities, historical use in traditional medicine suggesting safety and efficacy, and rich phytochemical profile position *M. oleifera* as a strong candidate for addressing hyperacidity disorders. Therefore, this research was undertaken to quantify the micronutrient content of *M. oleifera* (leaves and seeds) powder and to develop and evaluate an effervescent granule formulation incorporating this plant material. Specifically, this study aimed to determine the *in vitro* acid neutralization capacity (ANC) of the prepared *M. oleifera* effervescent granules in comparison to a commercially available antacid product.

MATERIALS AND METHODS

Materials

The following materials were utilized in this study: tartaric acid (analytical grade), sodium bicarbonate (analytical grade), starch (pharmaceutical grade), stevia, lactose monohydrate (pharmaceutical grade), Mango flavor (food grade), nitric acid (HNO_3, analytical Grade), pepsin, sodium chloride (NaCl, GRIFFEN, analytical grade), and Hydrochloric acid (HCl, 35% w/w, Labbox). The commercially available effervescent formulation ENO (GlaxoSmithKline) was used as a reference product. The equipment and instruments employed included: a laboratory blender (Hommer, 350 Watt), an analytical balance (Sartorius), a flame photometer (BWB type), a set of standard laboratory sieves (various mesh sizes), a tapped density tester (Pharma Test PT-TD1, US), a friability tester (Pharma Test PTF 20E, US), and a benchtop pH meter (PH 50 VioLab, Italy).

Methods

Collection and preparation of plants

Fresh leaves and seeds of *M. oleifera* Lam. were sourced from Al-Kumushi Farm, a recognized distributor located in Tajoura, Libya. The plant material was botanically authenticated by Prof. Mohammed Makhlouf at the National Herbarium of the Botany Department, Faculty of Science, University of Tripoli, Libya (voucher specimen number: 197615111), and a corresponding voucher specimen was deposited therein. Following collection, the *M. oleifera* leaves were thoroughly washed and air-dried under shade for one week until complete desiccation and attainment of a constant weight. Concurrently, the outer coats of the *M. oleifera* seeds were manually removed. Subsequently, both the dried leaves and the decoated seeds were separately pulverized into a fine powder using an electric blender. The resulting powders were then sieved to ensure uniformity in particle size and stored in airtight plastic bags under conditions protected from heat, humidity, and light to maintain their integrity prior to further experimentation.

Determination of micronutrients (Ca, Mg)

To determine the mineral content, 100 g of finely ground *M. oleifera* leaf and seed powder (analyzed separately) were subjected to controlled combustion in a muffle furnace. The temperature was gradually increased at a rate of approximately 50°C per hour until reaching 450°C, and this temperature was maintained until complete ashing was achieved. The resulting

ash was then dissolved in 6 N HCl, and the solution was carefully evaporated to dryness on a hot plate to ensure complete dissolution of the mineral components. The residue obtained was subsequently reconstituted in 0.1 N HNO_3 to a known volume. The concentration of specific minerals in the prepared solutions was then quantified using a flame photometer (BWB Technologies, UK). All measurements were performed in triplicate to ensure the reliability and reproducibility of the data (n=3 for each sample type)[20].

Moringa oleifera effervescent granule formulation

Two distinct effervescent granule formulations of *M. oleifera* were prepared in this study, utilizing both leaf and seed powders, based on a consistent formulation outlined in **Table I**. The effervescent granules were produced using a modified wet granulation method. Traditionally, this method involves separate wet granulation of the basic and acidic components. However, this study employed a streamlined approach involving a single wet granulation step after the initial mixing of all components. For the leaf powder formulation, a predetermined quantity of *M. oleifera* leaf powder was initially combined and homogenized with sodium bicarbonate using a mortar and pestle. Subsequently, starch, stevia, and lactose were added and thoroughly mixed to ensure uniformity. Deionized water was then carefully added dropwise to this powder blend, forming a cohesive dough mass. Similarly, for the seed powder formulation, *M. oleifera* seed powder was substituted for the leaf powder, and the same procedure was followed for mixing with sodium bicarbonate, excipients (starch, stevia, and lactose), and granulation with water. The resulting dough mass for both leaf and seed powder formulations was then passed through a 1.600 mm sieve to obtain granules. Finally, the granules were dried in a convection oven at 50°C until a constant weight was achieved, indicating complete removal of moisture. This modified single-step granulation process, adapted from previously described methods[21] but omitting the separate granulation of acidic and basic components, aimed to simplify the manufacturing process.

Table I. Formula for preparing effervescent granules of *M. oleifera* leaf and seed powder.

Ingredients	F1: leaves (g)	F2: seeds (g)
Moringa oleifera powder	500	500
Sodium bicarbonate	1000	1000
Tartaric acid	500	500
Citric acid	500	500
Stevia	20	20
Starch	120	120
Lactose	1360	1360
Mango flavor	Q.S.	Q.S.

Q.S: Sufficient quantity

Evaluation of effervescent granules of M. oleifera leaves and seeds

Organoleptic evaluation: Effervescent granules were assessed for organoleptic properties, specifically shape, color, and odor, through visual examination[22].

Particle size distribution: The particle size distribution of the *M. oleifera* effervescent granules was determined using a standardized sieve analysis method. A stack of calibrated test sieves (Retsch GmbH, Germany) with aperture sizes of 1.600 mm, 1.400 mm, 0.750 mm, 0.355 mm, 0.250 mm, and 0.125 mm, arranged in descending order, was employed, with a collection pan positioned at the bottom. A 100.00 ± 0.01 g sample of the prepared *M. oleifera* (seed-derived and leaf-derived) granules was accurately weighed using a calibrated analytical balance (Sartorius, Germany). Each sieve and the collection pan were individually weighed prior to the analysis to establish their tare weights. The assembled sieve stack, with the granule sample carefully placed on the uppermost sieve, was then securely mounted onto a vibratory sieve shaker (Retsch AS 200 basic) and clamped to ensure proper sealing. The shaker was operated at a controlled frequency of 60 Hz for a duration of 20 minutes, allowing for effective particle separation based on size. Following the vibration period, each sieve and the collection pan were meticulously reweighed. The weight of the granules retained on each sieve was calculated by subtracting the previously recorded tare weight of the respective sieve and pan[23]. The resulting weight fractions for each sieve size were then used to construct particle size distribution curves for both the *M. oleifera* seed and leaf-derived effervescent granules, providing a quantitative profile of their particle size characteristics.

Angle of repose: The angle of repose of the prepared granules was determined using the fixed funnel method. A glass funnel with a standardized orifice was rigidly clamped with its tip positioned at a fixed vertical height (h) of 2.0 cm above a sheet of graph paper resting on a level horizontal surface. The granule sample was carefully poured through the funnel until a stable conical pile formed, with its apex just touching the tip of the funnel's outlet. The radius (r) of the base of the resulting conical pile was then precisely measured using the underlying graph paper. This procedure was meticulously performed in triplicate for each granule formulation (leaf and seed) to ensure the acquisition of statistically reliable and representative data. The angle of repose (θ) was subsequently calculated for both types of granules using the standard trigonometric relationship as shown in **Equation 1**, where 'h' represents the height of the conical pile (equal to the funnel tip height) and 'r' represents the radius of the base of the conical pile.

$$tan(\theta) = \frac{h}{r} \quad [1]$$

Bulk density: To determine the apparent bulk density, precisely 15.00 g of the prepared granules were carefully introduced into a dry 100 mL graduated cylinder, ensuring no manual compaction was applied during the transfer. Following the complete transfer of the sample, the powder bed was gently leveled without tapping or compression to obtain the unsettled apparent volume (V_0), as described by United States Pharmacopeia (USP)[22]. All measurements were performed in triplicate to ensure accuracy and reproducibility. The apparent bulk density (ρb) was subsequently calculated using the following **Equation 2**, where ρb is apparent bulk density (g/mL), M is weight of the granule sample (g), and Vo is unsettled apparent volume of the powder (mL).

$$\rho b = \frac{M}{Vo} \quad [2]$$

Tapped density: The tapped density of the powder sample was determined using a tapped density tester apparatus. Following the method outlined in USP[22], a known weight (M) of the powder was carefully transferred into a graduated cylinder. The cylinder was then subjected to an initial 500 taps, followed by an additional 750 taps, until the difference between successive volume readings was less than 2%. The final tapped volume (Vf) was recorded to the nearest graduated unit. All measurements were performed in triplicate. The tapped density (ρtap), expressed in g/mL, was calculated using the following **Equation 3**, where ρtap is tapped density (g/mL), M is weight of the powder sample (g), and Vf is final tapped volume of the powder (mL).

$$\rho tap = \frac{M}{Vf} \quad [3]$$

Carr's index: The compressibility index, commonly known as Carr's index, was employed to quantitatively assess the compressibility of the granules, a crucial parameter indicative of their flowability. This index was determined by measuring both the bulk density (ρb) and the tapped density (ρtap) of the granular material. The principle underlying this measurement is that granules exhibiting lower compressibility tend to possess superior flow characteristics. This phenomenon arises from the weaker interparticulate interactions within less compact granular systems. In free-flowing materials, these interactions are less pronounced, resulting in closer values between the bulk and tapped densities. Conversely, poorly flowing materials typically exhibit stronger interparticulate forces, leading to a more significant difference between their bulk and tapped densities[24]. The Carr's index (%) was calculated using **Equation 4**, as previously described[25].

$$\text{Carr's index} = \frac{\rho tap - \rho b}{\rho tap} \times 100 \quad [4]$$

Hausner's ratio: The flowability of the powder was quantitatively assessed using Hausner's ratio, a widely recognized index for predicting powder flow characteristics[24]. This dimensionless parameter provides an indication of the ease with which a powder will flow under gravity. Hausner's ratio was calculated according to **Equation 5**[25]. The resulting Hausner's ratio provides a numerical value indicative of powder flow behavior, with lower values generally correlating with better flowability.

$$\text{Hausner's ratio} = \frac{\rho tap}{\rho b} \quad [5]$$

Evaluation of granules friability: The friability of the granules was determined using a friability apparatus. Precisely 10.00 g of the granule sample was accurately weighed and carefully placed into the rotating drum of the apparatus, along with a

specified number of glass beads. The drum was then attached to the apparatus and subjected to rotation at a speed of 25 rpm for a duration of 4 minutes. Following the completion of the rotation period, the granule sample was quantitatively removed from the drum and gently sieved using a sieve of appropriate mesh size. The granules retained on the sieve, representing those that withstood the friability testing, were accurately weighed to determine the final weight[26]. The percentage friability was subsequently calculated using the following **Equation 6**, where the initial weight was 10.00 g, and the final weight represents the mass of the granules retained after the friability test. All tests were performed in triplicate, and the mean percentage friability along with the standard deviation was calculated and reported. The acceptance criterion for granule friability was set at not more than 1.0%.

$$\%\text{friability} = \frac{\text{initial weight} - \textit{final weight}}{\text{initial weight}} \times 100 \qquad [6]$$

Moisture contents: The moisture content of both *M. oleifera* seed and leaf granules was determined using the gravimetric method with oven drying, adhering to established protocols. Briefly, for each sample type, three replicates of precisely weighed granules (5 g) were transferred to pre-weighed, clean, and dry petri dishes. These dishes, containing the samples, were immediately covered and placed in a laboratory oven maintained at 105°C. The drying process was conducted for 3 to 4 hours, or until a consistent weight was achieved, indicating complete moisture removal. Following the drying period, the petri dishes were carefully removed from the oven and allowed to cool to room temperature in a desiccator to prevent moisture reabsorption before the final weight measurement. The weight measurements were performed using a calibrated digital analytical balance[27]. The percentage of moisture content was subsequently calculated for each replicate using **Equation 7**, where W_1 is weight of petri dish and granules before drying (g), W_2 is weight of petri dish and granules after drying (g), and W_3 is weight of the granules (g).

$$\%\text{moisture content} = \frac{W_1 - W_2}{W_3} \times 100 \qquad [7]$$

Effervescent time: To assess the effervescence properties of the granule formulation, a standardized procedure was employed. For each trial, precisely 5 g of the effervescent granule sample were slowly and uniformly introduced into a 250 mL beaker containing 150 mL of distilled water maintained at room temperature (25±1°C). The effervescence time, defined as the interval from the initial contact of the granule particles with the water surface until the complete cessation of bubbling and gas evolution, was accurately recorded using a calibrated digital stopwatch. This measurement was meticulously replicated two additional times under identical experimental conditions to ensure the reliability and reproducibility of the data, resulting in a total of three independent determinations for each sample.

Evaluation of preparation PH: The pH of the reconstituted effervescent preparation was determined using a calibrated digital pH meter. Specifically, 5 g of the effervescent powder was accurately weighed and dissolved in 150 mL of distilled water at room temperature. Prior to each measurement, the pH meter underwent a two-point calibration using standard buffer solutions of pH 4.0 and pH 7.0, following the manufacturer's instructions[28]. Once calibration was confirmed, the electrode of the calibrated pH meter was carefully immersed into the prepared effervescent solution. To ensure accurate readings, pH measurements were initiated only after the complete cessation of gas bubble formation, indicating the full dissolution and equilibration of the sample. The resulting pH value was then recorded for each replicate.

Determination of the ANC of the prepared M. oleifera leaf and seed granules against synthetic gastric juice

Preparation of synthetic gastric juice: Synthetic gastric juice (SGJ) was prepared by dissolving 2 g of NaCl and 3.2 mg of pepsin in 500 mL of distilled water. Subsequently, 7 mL of HCl was added, and the solution was brought to a final volume of 1,000 mL with additional distilled water. The resulting SGJ solution was then thoroughly mixed to ensure homogeneity prior to use in subsequent experiments[29].

Preparation of test solutions: Effervescent granules of *M. oleifera* leaves and seeds were prepared and subsequently used to generate test solutions at varying concentrations. Specifically, doses of 5 g, 10 g, and 15 g of both leaf and seed granules were individually dissolved in 250 mL of distilled water to create fresh aqueous solutions. These solutions were prepared immediately prior to experimentation. As a positive control, a commercially available antacid (ENO) solution was prepared by dissolving one 5 g sachet of its dispersible granules in 250 mL of distilled water, following the manufacturer's instructions[29]. For each experimental condition, 90 mL aliquots of the *M. oleifera* leaf solutions, *M. oleifera* seed solutions, the

positive control solution, and distilled water (negative control) were separately added to 100 mL of SGJ. The pH of each resulting mixture was then meticulously measured to assess the neutralizing effect on the SGJ. All experimental conditions were performed in triplicate to ensure the reliability and reproducibility of the results.

Data analysis

All quantitative data are presented as the mean ± SD of triplicate measurements (n = 3). Statistical analysis was performed using IBM SPSS Statistics version 20. To determine statistically significant differences between group means, a two-way ANOVA was employed, followed by Tukey's post hoc test for pairwise comparisons. A probability (P) value of less than 0.05 was considered statistically significant for all analyses.

RESULTS AND DISCUSSION

Determination of Micronutrients (Ca, Mg)

Previous research has indicated a positive correlation between calcium content and antacid efficacy in natural sources[9]. Given the notably high calcium content reported in *M. oleifera*, reaching up to four times that of milk[30], it is plausible that this substantial mineral presence contributes to an antacid effect through direct acid neutralization. Our micronutrient analysis of *M. oleifera* leaf and seed powder samples revealed a significantly higher calcium concentration in the leaf powder (2528.9 ± 44.6 mg/100 g) compared to the seed powder (**Figure 1**), a trend mirrored by magnesium levels. Notably, the calcium content observed in our samples surpassed values reported in prior investigations of *M. oleifera*. However, the magnesium content in our samples was found to be lower in comparison to some previous findings[5,31]. While the high calcium content likely plays a role in the observed antacid properties, it is probable that other phytochemical constituents present in *M. oleifera* contribute synergistically through alternative acid-reducing mechanisms. It is important to note that previous studies have identified calcium in *M. oleifera* primarily in the form of calcium oxalate crystals, present in significant amounts in both leaves and seed[32]. Therefore, future research should investigate the specific contribution of calcium oxalate and other phytochemicals to the overall antacid activity of *M. oleifera* extracts, considering potential bioavailability and mechanisms beyond simple neutralization.

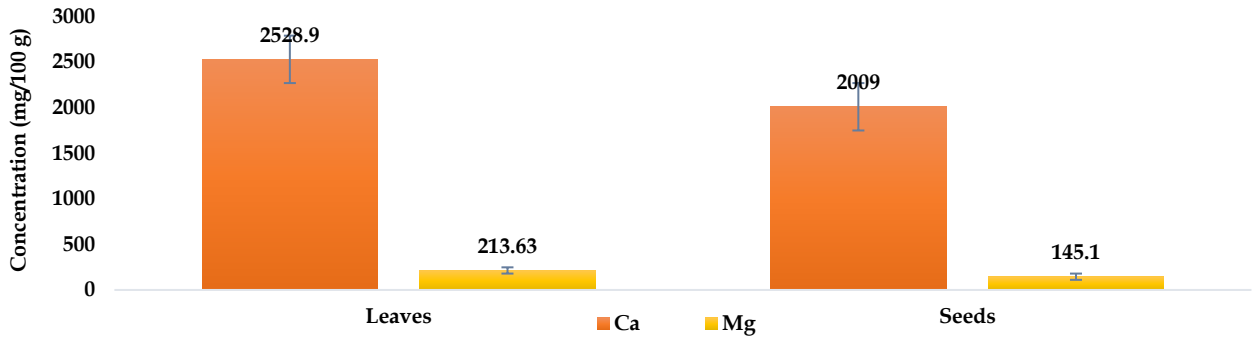

Figure 1. Micronutrient of *M. oleifera* seed and leaf powder.

Evaluation Results of Prepared Effervescent Granules

The effervescent granules were successfully manufactured using the wet granulation method, a technique known for its simplicity, speed, and ability to produce homogeneous granules (**Figure 2**). As a critical step to prevent premature acid-base reactions during the wet mixing process, the acidic and alkaline components were processed separately[21]. Organoleptic evaluation of all formulations revealed distinct visual characteristics: dark green granules for the leaf extract formulations and white granules for the seed extract formulations, each exhibiting a characteristic aroma profile of mango combined with the typical *M. oleifera* scent. All formulations displayed a visually homogeneous appearance.

Particle size distribution analysis, conducted using a vibratory sieve, aimed to determine the range and uniformity of granule sizes. This parameter is crucial as particle size significantly influences the flowability of the granules; finer particles tend to exhibit lower flow rates due to increased inter-particle cohesive forces. A narrow particle size distribution indicates good granule quality and uniformity[33]. The results of the sieve analysis indicated maximum granule retention within the

size range of 1400 to 1600 µm. These particle size distribution data are visually represented as a frequency distribution curve in **Figure 3**. This controlled particle size range suggests favorable flow properties, which are essential for consistent dispensing and dissolution of the effervescent product.

Figure 2. Prepared *M. oleifera* leaf (**left**) and seed (**right**) effervescent granules.

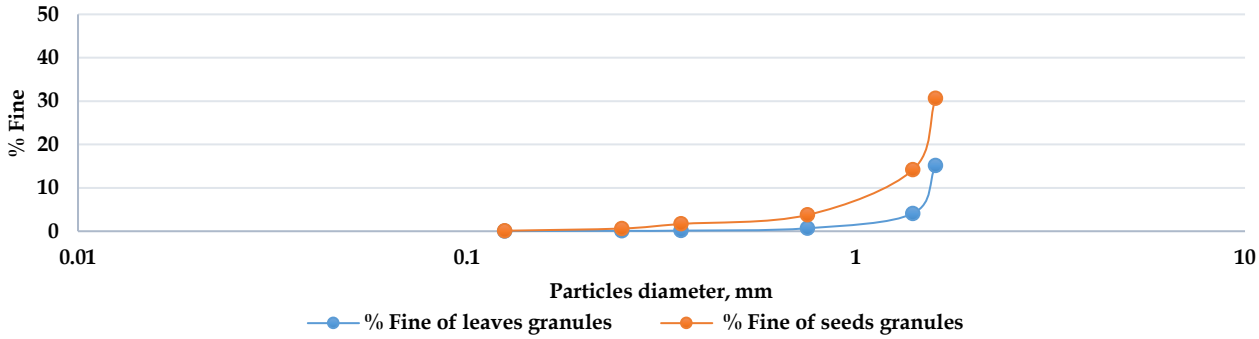

Figure 3. Particle size distribution curve of *M. oleifera* seed and leaf granules.

The flow properties of the formulated effervescent granules, crucial for consistent processing and dosage uniformity, were evaluated based on the angle of repose, Hausner ratio, and Carr index. According to established pharmacopoeial standards[34], an angle of repose ≤30° indicates free-flowing material, while values ≥40° suggest poor flow. Our findings revealed angles of repose of 24.3° for leaf extract granules and 22.9° for seed extract granules, both falling within the 25-30° range indicative of excellent flow characteristics. Similarly, a Hausner ratio below 1.25 is associated with good flow, whereas values exceeding 1.5 suggest poor flow[35]. The calculated Hausner ratios for the leaf and seed extract granules were 1.14 and 1.15, respectively, further supporting their good flowability. The Carr index, a measure of compressibility, suggests good suitability for granulation within the 12-16% range and sufficient compressibility between 16-23%. In this study, the Carr index values (**Table II**) indicated sufficient compressibility for both leaf and seed extract granules. Collectively, these parameters confirm that the formulated effervescent granules, irrespective of the plant part, exhibited favorable flow properties, essential for uniform filling and handling during pharmaceutical processing.

Beyond flow properties, other critical physicochemical characteristics were assessed. The moisture content of the dried granules was found to be 1.5% for leaves and 1.4% for seeds. While these values are slightly higher than the reported optimal range of 0.4-0.7% for herbal effervescent granules[34], they are likely within acceptable limits for stability, though further optimization might be considered. The pH of the reconstituted effervescent solutions was 5.85 for the leaf formulation and 5.38 for the seed formulation. These near-neutral pH values (optimal range generally considered 6-7 for minimizing gastric irritation and unpleasant taste) suggest good patient acceptability. The disintegration time, a critical factor for rapid drug release, was less than 5 minutes for both formulations (2-3 minutes), meeting the criteria for good soluble time in effervescent granules. This rapid dissolution is attributed to the effervescent reaction between the incorporated acid and alkali upon water penetration, generating carbon dioxide that accelerates granule breakdown. Finally, friability testing, an indicator of granule strength during handling, yielded a weight loss of 1% for leaf extract granules, well within the USP limit of ≤1%. However, seed extract granules exhibited a slightly higher friability of 1.3%, potentially due to their inherent starch content which might render them more susceptible to abrasion. The bulk density of the formulations ranged from 0.41 to 0.5 g/mL (**Table II**), suggesting suitability for unit dosage packaging.

Table II. Parameters of the prepared effervescent granules.

Parameters	Leaf granules	Seed granules
Bulk density (g/mL)	0.5±0	0.41±0
Tapped density (g/mL)	0.57±0.017	0.47±0.012
Compressibility index (%)	12.2	12.8
Hausner's ratio	1.14	1.15
Friability (%)	1.0±0.3	1.3±0.5
Angle of repose (°)	24.3±1.3	22.9±0.28
Moisture content (%)	1.5±0.4	1.4±0.28
Effervescent time (minutes)	2-3	2-3
PH	5.85	5.38

The ANC of the Prepared M. oleifera Leaf and Seed Granules against Synthetic Gastric Juice

The ANC of *M. oleifera* leaf and seed granules was evaluated in SGJ, and the results are presented in **Table III**. Two-way ANOVA revealed a significant and dose-dependent increase in pH ($p < 0.05$) over a 120-minute period for *M. oleifera* leaf granules at concentrations of 5 g and 10 g, indicating a sustained acid-neutralizing effect. Similarly, *M. oleifera* seed granules demonstrated a significant pH-elevating effect from baseline across all tested concentrations ($p < 0.05$). However, post-hoc Tukey's tests indicated that the leaf granules induced a significantly greater elevation in pH compared to the seed granules ($p < 0.05$). Notably, the 5 g and 10 g doses of leaf granules exhibited optimal ANC, achieving mean pH values of 5.91 and 5.90, respectively, at the 120-minute endpoint. These values were comparable to and slightly exceeded the efficacy of the standard antacid positive control, ENO (5 g), which reached a pH of 5.77 at 120 minutes. In contrast, the negative controls (water and baseline SGJ) maintained acidic pH values ranging from 3.2 to 3.54 throughout the experiment, confirming the significant pH-increasing effects of the *M. oleifera* granules ($p < 0.05$). While *M. oleifera* leaf powder (1.75 g) also demonstrated a pH-increasing effect over time, suggesting that the ANC is attributed to the presence of *M. oleifera*, the effervescent granules exhibited faster dissolution and activity, highlighting the advantages of the granule formulation and granulation process. Considering the comparable ANC observed between the 5 g and 10 g doses of leaf granules, the 5 g dose is proposed as the recommended dose, offering similar efficacy with potentially improved safety and patient compliance.

Table III. The ANC of the prepared *M. oleifera* leaf and seed granules against SGJ.

Dose (formulation)	Time (minutes)	pH	
		Leaf	Seed
5 g (granules)	5	5.70 ±0.03[a]	5.31 ±0.07[c]
	30	5.72 ±0.04[a]	5.36 ±0.11[c]
	60	5.73 ±0.04[a]	5.38 ±0.08[c]
	90	5.82 ±0.07[a]	5.51 ±0.21[c]
	120	5.91 ±0.11[a]	5.52 ±0.20[c]
10 g (granules)	5	5.75 ±0.05[a]	5.27 ±0.11[c]
	30	5.76 ±0.04[a]	5.25 ±0.13[c]
	60	5.77 ±0.13[a]	5.29 ±0.15[c]
	90	5.81 ±0.03[a]	5.28 ±0.17[c]
	120	5.90 ±0.07[a]	5.31 ±0.17[c]
15 g (granules)	5	5.50 ±0.24[a]	5.13 ±0.16[c]
	30	5.50 ±0.26[a]	5.24 ±0.26[c]
	60	5.50 ±0.29[a]	5.20 ±0.22[c]
	90	5.51 ±0.33[a]	5.30 ±0.32[c]
	120	5.63 ±0.32[a]	5.33 ±0.31[c]
1.75 g powder	5	5.60 ±0.00[a]	5.21 ±0.00[c]
	30	5.67 ±0.00[a]	5.13 ±0.00[c]
	60	5.73 ±0.00[a]	5.00 ±0.00[c]
	90	5.93 ±0.00[a]	5.24 ±0.00[c]
	120	6.02 ±0.00[a]	4.89 ±0.00[c]
Water + SGJ	5	3.54 ±0.02[b]	
	30	3.52 ±0.02[b]	
	60	3.53 ±0.01[b]	
	90	3.51 ±0.07[b]	
	120	3.48 ±0.03[b]	
SGJ	5	3.2 ±0.00[b]	
	30	3.2 ±0.00[b]	
	60	3.2 ±0.00[b]	
	90	3.2 ±0.00[b]	
	120	3.2 ±0.00[b]	

5 g ENO®	5	5.64 ±0.05[a]
	30	5.66 ±0.13[a]
	60	5.72 ±0.11[a]
	90	5.75 ±0.10[a]
	120	5.77 ±0.12[a]

Values mean±SD (n=3). Values with different superscript letters are significantly different (P <0.05) by Tukey's post hoc test.

CONCLUSION

The formulated granules demonstrated a significant capacity for neutralizing SGJ, effectively reducing acidity, which suggests their potential to alleviate acid-related symptoms. This substantial acid-neutralizing activity can be attributed to the elevated levels of calcium and magnesium present in the *M. oleifera* leaves and seeds powder. The findings of this study indicate that *M. oleifera* possesses promising antacid properties, positioning it as a potential natural alternative to conventional antacids, further supported by the observed short disintegration time. Moreover, the formulated granules met the established official monograph requirements, complying with the standards outlined in the British Pharmacopoeia and the International Pharmacopoeia. These results suggest the feasibility of developing a natural antacid formulation based on *M. oleifera* with acceptable pharmacopoeial standards.

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DATA AVAILABILITY

None.

CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this study.

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