

Development and Characterization of a Natural Polymer from *Manilkara Zapota* Seed Gum with Phytochemical Evaluation of Leaf Extract for Sustained-Release Drug Delivery

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Abstract:

Background: Natural plant-derived polymers have gained increasing attention as alternatives to synthetic excipients in sustained-release (SR) drug delivery systems owing to their biocompatibility, safety, and renewability. *Manilkara zapota* (L.) P. Royen, recognized for its gastroprotective and antioxidant potential, is rich in bioactive flavonoids and phenolic compounds, while its seed gum exhibits desirable swelling and gel-forming properties suitable for controlled drug delivery. **Objective:** The present study aimed to extract and perform phytochemical and physicochemical evaluation of *Manilkara zapota* leaf extract and to assess *Manilkara zapota* gum as a natural polymeric excipient. **Methods:** Leaves and seed gum of *Manilkara zapota* were isolated and characterized. Physicochemical evaluations, including pH, viscosity, and swelling index, were conducted. Structural and thermal characterization was performed using Fourier-transform infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC). **Results:** The *Manilkara zapota* gum exhibited a **high swelling capacity (324 ± 8%)** and **viscosity (428 ± 12 cps)**, confirming its suitability as a **hydrophilic matrix-forming polymer**. The **total phenolic content** was found to be **87.6 ± 2.3 mg GAE/g**, while the **total flavonoid content** was **52.1 ± 1.8 mg QE/g**, indicating the presence of significant bioactive phytoconstituents. Overall, the gum isolated from *M. zapota* demonstrated **excellent swelling behavior, high viscosity, and good thermal stability**, which are **essential attributes for its application in sustained-release matrix drug delivery systems**.

Keywords: Gastroprotective; natural gum; *Manilkara zapota* leaf extract; sustained release

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1. Introduction

Manilkara zapota, referred to as sapodilla or chikko, is an evergreen tree indigenous to America and the Caribbean, currently cultivated in numerous tropical and subtropical climates throughout. It is a member of the Sapotaceae family and is celebrated for its sweet and delectable fruit, which has become popular both as a fresh produce and as an ingredient in diverse culinary applications. The fruit of *Manilkara zapota* is rich in carbohydrates, primarily consisting of simple sugars such as sucrose, fructose, and glucose^[1]. *Manilkara zapota* (L.) P. Royen (family Sapotaceae), commonly known as sapodilla or chico, has gained prominence in ethnomedicine owing to its wide spectrum of pharmacological activities^[2]. The leaf extract of *M. zapota* has demonstrated notable gastroprotective effects in experimental ulcer models. Reports indicate that ethanolic leaf extract significantly attenuates acid-pepsin secretion, enhances antioxidant enzyme activity, and increases mucosal glycoprotein levels in rat models of aspirin plus pylorus ligation and HCl-ethanol-induced gastric injury^[3]. Additionally, *M. zapota* leaves contain abundant phenolic and flavonoid compounds associated with strong antioxidant effects^[4]. These findings support the suitability of *M. zapota* leaf extract as the active phytoconstituent in gastroprotective formulations.

Parallel to this, the gum obtained from the seeds of *M. zapota* (hereafter “MZ seed gum”) presents a promising natural excipient for sustained-release matrix systems. Although limited studies have specifically examined MZ seed gum in pharmaceutical applications, extensive literature on other natural seed-derived gums—such as guar, xanthan, and tamarind seed gum—demonstrates their excellent gelling, swelling, and release-retarding properties^[5,6,7]. Despite the pharmacological potential of *M. zapota* leaf extract and the functional attributes of MZ seed gum, their combined application in a single sustained-release pharmaceutical system has not yet been reported. Integrating both components from the same plant species offers a novel, holistic, and plant-based formulation strategy in which the leaf extract serves as the gastroprotective agent while the seed gum functions as the natural matrix-forming polymer^[8,9,10].

2. Materials and Methods

2.1 Materials

Fresh, disease-free leaves and mature seeds of *Manilkara zapota* (L.) P. Royen was collected during the month of February–March 2024 from the Botanical Garden of Bhilai, Chhattisgarh, India. The plant material was taxonomically identified and authenticated by Vinay Ranjan, Scientist E, Department of Botany, Botanical survey of India, Allahabad and a voucher specimen no is 2024-25/041 dated 19/04/2024, was deposited in the institutional herbarium for future reference. The collected leaves were washed thoroughly with running water, shade-dried at room temperature (25–28 °C) for 10–12 days, and subsequently powdered using a mechanical grinder. Seeds were cleaned and stored for gum extraction.

All chemicals and reagents used were of analytical grade. Organic solvents, including ethanol, acetone, and petroleum ether (AR grade) were purchased from Merck Life Sciences. Double-distilled water was prepared in-house and used throughout the study for extraction. UV–Visible

spectrophotometer, and FTIR spectrophotometer, were used as required during the experimental procedures.

2.2 Extraction of *Manilkara zapota* Leaf Extract

2.2.1 Preparation of Plant Material

Fresh leaves of *Manilkara zapota* were collected, thoroughly washed under running tap water followed by rinsing with distilled water to remove dust and surface contaminants. The cleaned leaves were shade-dried for 10-12 days at 25 ± 2 °C to prevent degradation of heat- and light-sensitive phytoconstituents^[11]. The dried leaves were pulverised using a mechanical grinder and the resulting coarse powder was passed through a 60-mesh sieve to obtain uniform particle size, which enhances solvent penetration during extraction. The sieved powder was stored in airtight, light-resistant containers until further use^[12].

2.2.2 Extraction Procedure (Hydroethanolic Method)

Approximately 250 g of the powdered leaf material was subjected to continuous hot extraction using a Soxhlet apparatus. A 70% ethanol (v/v) mixture was selected as the extraction solvent owing to its efficiency in extracting a broad spectrum of polar and moderately polar phytochemicals, including phenolics, flavonoids, tannins, and glycosides. The extraction was carried out for 8 hours, ensuring complete siphoning cycles of the solvent. The obtained hydroethanolic extract was concentrated using a rotary evaporator under reduced pressure at 45 °C to prevent thermal decomposition^[12, 13]. The semi-solid concentrate was further dried in a vacuum desiccator to obtain a constant weight. The percentage yield of the extract was calculated using the formula:

$$\text{Yield (\%)} = \left(\frac{\text{Weight of dried extract (g)}}{\text{Weight of crude leaf powder (g)}} \right) \times 100$$

The dried extract was stored in amber-coloured vials at 4 °C until analysis.

2.2.3 Phytochemical Screening

The dried hydroethanolic extract was subjected to qualitative phytochemical analysis using standard phytochemical protocols to detect the presence of major secondary metabolites. The extract was screened for Alkaloids (Dragendorff's and Mayer's tests), Flavonoids (Shinoda and alkaline reagent tests), Phenolics and tannins (Ferric chloride and lead acetate tests), Saponins (Froth and emulsion tests) and Terpenoids (Salkowski and Liebermann–Burchard tests). The presence or absence of each class of phytochemicals was recorded^[14, 15].

2.2.4 Quantification of Total Phenolic Content and Total Flavonoid Content

Quantitative estimation of key antioxidant phytoconstituents was conducted as follows:

a. Total Phenolic Content (TPC)

TPC was determined using the Folin–Ciocalteu method. Aliquots of the extract were mixed with Folin–Ciocalteu reagent and a sodium carbonate solution, incubated for colour development, and the absorbance was measured at 765 nm. Results were expressed in mg gallic acid equivalents per gram of extract (mg GAE/g). A gallic acid calibration curve was used for quantification.

b. Total Flavonoid Content (TFC)

TFC was estimated using the aluminium chloride (AlCl₃) colorimetric method. The reaction mixture was prepared with extract, AlCl₃ reagent, and potassium acetate, and the absorbance was

recorded at 415 nm. Results were expressed in mg quercetin equivalents per gram of extract (mg QE/g). A quercetin standard curve was used for calculation.

2.3 Isolation and Purification of *Manilkara zapota* Gum

2.3.1 Isolation of Seed Gum

Mature seeds of *Manilkara zapota* were collected and thoroughly washed with distilled water to remove adhering pulp and impurities. The cleaned seeds were then shade-dried until the moisture content was sufficiently reduced to facilitate removal of the seed coat. After dehulling, the cotyledons were used as the gum-containing material. The dehulled seeds were soaked in distilled water at a seed-to-water ratio of 1:10 (w/v) for 24 hours to allow hydration and swelling of the mucilage. Following hydration, the soaked seeds were subjected to controlled heating at 60–70 °C for 2 hours, which facilitated the release of the mucilaginous gel from the seed matrix and resulted in viscous slurry.

The slurry was filtered through several layers of muslin cloth to separate the soluble gum fraction from insoluble seed residues. The filtrate was then subjected to non-solvent precipitation using three volumes of acetone, which caused the gum to flocculate and separate from the aqueous phase. The precipitated gum was collected, air-dried and subsequently oven-dried at 40 °C until a constant weight was achieved. The dried gum mass was milled gently, passed through a 60-mesh sieve, and stored for subsequent purification [16, 17].

2.3.2 Purification of Seed Gum

The crude gum powder obtained from the isolation step was subjected to further purification to remove associated proteins, pigment residues, lipids, and other insoluble plant materials.

For purification, the crude gum was dissolved in hot distilled water to yield a 1% w/v gum solution, with continuous stirring to ensure complete dispersion and solubilization. The solution was maintained at 70–80 °C for 30–45 minutes for maximum extraction of the hydrophilic polysaccharide components.

The hot solution was filtered through muslin cloth followed by filtration through Whatman No. 1 filter paper to obtain a clear gum extract. The filtrate was again precipitated by the gradual addition of acetone (in a 1:3 ratio), under continuous agitation. This step effectively removed proteins and other low-molecular-weight impurities that remain dissolved in the aqueous phase.

The purified gum precipitate was collected and dried in a hot-air oven at 40 °C, then powdered and sieved to obtain a uniform particle size. The final purified gum was stored in airtight, moisture-resistant containers and protected from light and humidity to prevent degradation and microbial growth.

2.4 Characterization of *Manilkara zapota* Gum

To evaluate its suitability as a natural excipient for sustained-release matrix tablets, the isolated *M. zapota* seed gum was subjected to comprehensive physicochemical characterization. All tests were performed in accordance with standard pharmacopeial and analytical procedures [17, 18].

2.4.1 Organoleptic Properties

The gum was examined visually and manually to assess its basic sensory characteristics. Parameters such as colour, odour, appearance, and texture were recorded. These properties help

indicate preliminary purity, presence of contaminants, and general acceptability as a pharmaceutical excipient.

2.4.2 Solubility

Solubility studies were carried out to determine the gum's behaviour in different solvents and its potential for hydration or swelling. Approximately 1 g of gum was tested for solubility or dispersibility in the following media like; Distilled water, Ethanol (95%), Acetone and Chloroform. Observations included solubility, partial solubility, swelling, or insolubility. Solubility characteristics are crucial for predicting gel formation, hydration kinetics, and release-controlling behaviour in tablet matrices.

2.4.3 pH Determination

The pH of 1% w/v gum mucilage prepared in distilled water was measured using a calibrated digital pH meter. The pH value provides information about the gum's compatibility with acidic or neutral drugs and indicates the presence of acidic or alkaline groups that may affect stability.

2.4.4 Swelling Index

The swelling index reflects the hydration capacity and potential to form viscous gels-key mechanisms in sustained-release systems. The approximately 1 g of gum was placed in a graduated cylinder and distilled water was added than allowed to hydrate for 24 hours with intermittent shaking. The swelling index was calculated as the volume increase per gram of gum. Higher swelling index values suggest stronger gel-forming ability and better suitability as a release-retarding polymer.

2.4.5 Viscosity Measurement

A 1% w/v aqueous dispersion of the gum was prepared and evaluated using a Brookfield viscometer at controlled temperature and spindle speed. The viscosity indicates rheological behaviour, hydration properties, and the ability of the gum to form viscous diffusion barriers in matrix tablets, directly affecting release kinetics.

2.4.6 Loss on Drying (LOD)

LOD was determined to estimate the moisture content of the gum, which can influence stability, microbial susceptibility, and flow properties. 1 g of gum was dried at 105 °C until a constant weight was achieved.

LOD (%) was calculated using:

$$\text{LOD (\%)} = \frac{\text{initial weight of sample} - \text{final weight after drying}}{W_1 \text{ initial weight of sample}} \times 100$$

2.4.7 Ash Values

Ash values were determined according to Indian Pharmacopoeia (IP 2022) guidelines to quantify inorganic impurities and purity of the gum. The total ash (% w/w) indicates overall inorganic residue, acid-insoluble ash (% w/w) represents siliceous or soil-related impurities and water-soluble ash (% w/w) indicates the amount of inorganic salts and water-soluble minerals.

2.4.8 FTIR Spectroscopy of GUM

Fourier Transform Infrared (FTIR) spectroscopy was performed using a shimadzu 8400S instrument to identify functional groups present in the gum. FTIR spectral range: 4000–400 cm⁻¹ and sample preparation by KBr pellet method. The characteristic peaks corresponding to

polysaccharides (e.g., hydroxyl, carboxyl, ether groups) were identified. FTIR helps determine chemical structure, confirm purity, and compare batch consistency^[19,21].

2.4.9 Differential Scanning Calorimetry (DSC)

Thermal analysis was performed using a Mettler-Toledo DSC-1 system. It maintained heating rate 10 °C/min, temperature range 30-300 °C and environmental nitrogen gas was purge. DSC thermograms were evaluated for endothermic and exothermic transitions, glass transition temperature (T_g), and degradation behaviour. These data aid in assessing thermal stability and compatibility with other formulation components^[20, 22].

2.5 Compatibility Studies

To evaluate the physicochemical compatibility between the *Manilkara zapota* leaf extract (drug) and *M. zapota* gum (natural polymer excipient), a 1:1 (w/w) physical mixture was prepared by gently triturating both components in a mortar and pestle. Compatibility studies were performed using Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC), as these techniques provide sensitive indicators of potential interactions.

2.5.1 FTIR Analysis for compatibility

FTIR spectroscopy was conducted to identify possible chemical interactions at the molecular level. The spectra of pure leaf extract, pure *M. zapota* gum and 1:1 extract-gum for physical mixture were recorded and compared.

The following parameters were examined; Shifts in characteristic peaks indicate significant movement (typically >10–15 cm⁻¹) in functional group absorption bands may indicate intermolecular interactions. Disappearance or attenuation of peaks are losses or weakening of signature peaks can reflect chemical modification or interaction and appearance of new peaks indicates formation of new chemical bonds or degradation products and broadening of bands suggests hydrogen bonding or physical interactions.

2.5.2 DSC Analysis

DSC thermograms of pure leaf extract, pure *M. zapota* gum and 1:1 extract-gum mixture were obtained to investigate thermal behaviour. The following features were analyzed; Melting point (endothermic) transitions of the extract a distinct melting endotherm in the pure extract serves as a fingerprint for its crystalline/thermal identity. Shifts in melting point in the mixture indicate a significant reduction or broadening of the drug's melting peak may suggest interaction, partial solubilization, or amorphization within the gum matrix. The presence or absence of new endothermic/exothermic events may indicate thermal incompatibility or formation of degradation/interaction products and Changes in enthalpy (ΔH) is a large alteration in peak area can imply modifications in crystallinity or stability due to interaction.

3. Results and Discussion

3.1 Extraction Yield and Phytochemical Screening

Ethanol extraction of *Manilkara zapota* leaves yielded 12.4% w/w, producing a dark brown semisolid mass upon concentration. Preliminary phytochemical screening confirmed the presence of flavonoids, tannins, saponins, glycosides, and phenolic compounds, consistent with previously reported gastroprotective phytoconstituents.

Table 1. Preliminary phytochemical profile of hydroethanolic extract of *M. zapota* leaves

Phytochemical class	Test performed	Observation	Inference
Alkaloids	Mayer's / Dragendorff's	Cream ppt / orange ppt	++
Flavonoids	Shinoda / Alkaline reagent	Reddish-pink / yellow color	+++
Tannins	Ferric chloride	Blue-black coloration	+++
Saponins	Froth test	Stable foam formation	++
Steroids	Liebermann–Burchard	Green ring at junction	+
Terpenoids	Liebermann–Burchard	Brownish-red ring	++
Glycosides	Keller–Killiani	Reddish-brown ring	++

Note: (+ = trace, ++ = moderate, +++ = abundant)

The high phenolic/flavonoid levels suggest strong antioxidant potential, supporting their role in gastroprotection and sustained-release applications.

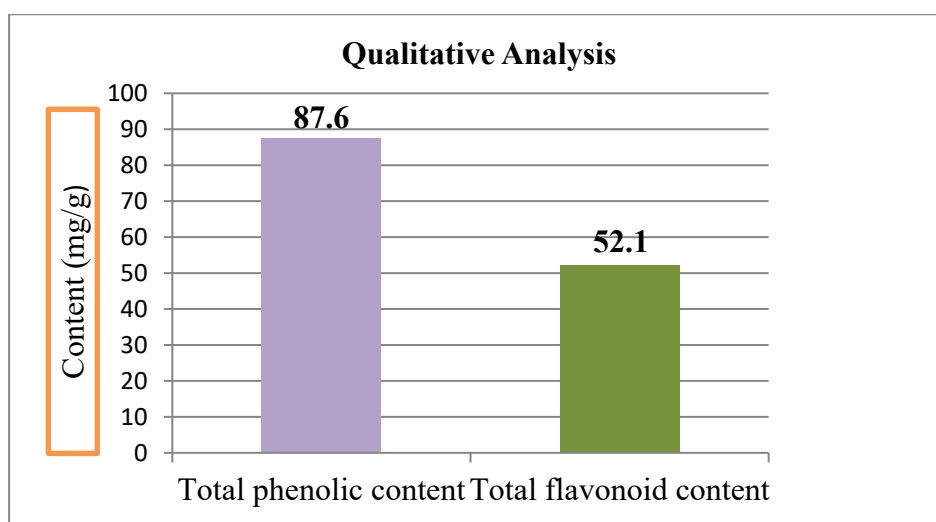


Figure 1: Total phenolic and flavonoid contents of EEMZ.

3.2 Evaluation of *Manilkara zapota* Gum

3.2.1 Physicochemical Properties

The isolated gum appeared light brown, odourless, and tasteless with smooth texture. It was freely soluble in warm water and insoluble in organic solvents. The pH of a 1% aqueous dispersion was 6.8 ± 0.2 , indicating suitability for oral formulations. The loss on drying was $7.2 \pm 0.4\%$, within acceptable limits ($<10\%$), ensuring low moisture content. The high swelling index and viscosity indicate strong water absorption and gel-forming capacity, desirable for sustained drug release.

Table 2. Physicochemical Properties of *Manilkara zapota* Gum

Parameter	Result
Appearance	Light brown amorphous powder
pH (1% w/v)	6.8 ± 0.2
Loss on drying (%)	7.2 ± 0.4

Swelling index (%)	324 ± 8
Viscosity (1% w/v, cps)	428 ± 12
Total ash (%)	4.9 ± 0.3
Acid-insoluble ash (%)	0.7 ± 0.1
Water-soluble ash (%)	3.8 ± 0.2

3.2.2 FTIR and DSC Characterization

FTIR Analysis

Fourier Transform Infrared (FTIR) spectroscopy was performed to identify the major functional groups present in *Manilkara zapota* seed gum and to confirm its polysaccharide nature. The FTIR spectrum exhibited several characteristic absorption bands corresponding to structural features commonly observed in natural plant-derived gums. A broad and intense peak around 3421 cm^{-1} was attributed to O–H stretching vibrations, representing the abundant hydroxyl groups present in the polysaccharide backbone. This broadness typically arises from extensive hydrogen bonding within the gum matrix, which is consistent with hydrophilic biopolymers. A medium-intensity band near 2920 cm^{-1} corresponded to C–H stretching of aliphatic –CH and –CH₂ groups, confirming the presence of carbohydrate-chain functionalities. The peak at 1653 cm^{-1} was assigned to C=O stretching, which may indicate uronic acids, amide groups from residual proteins, or bound water molecules contributing to slight carbonyl characteristics—commonly reported in natural seed gums.

A prominent band at 1042 cm^{-1} represented C–O–C stretching vibrations of glycosidic linkages, further confirming the polysaccharide backbone and the presence of pyranose ring structures. This region is typically regarded as a “fingerprint zone” for natural gums and supports the identity of the isolated material as a carbohydrate-rich polymer.

Overall, the FTIR profile demonstrated all the essential functional groups associated with natural hydrophilic gums, indicating suitability for application as a release-modifying excipient in sustained-release matrices.

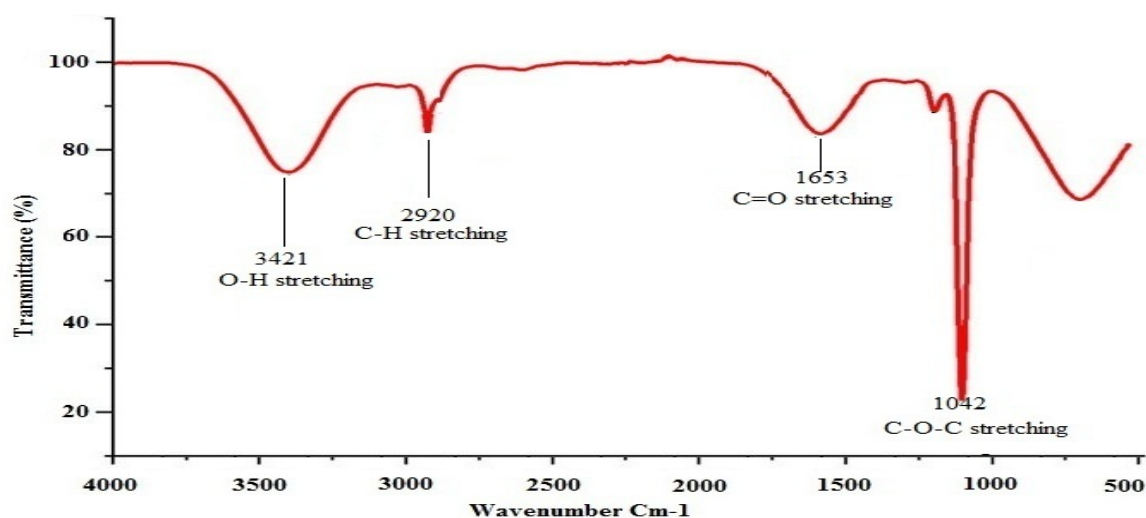


Figure 2: FTIR Spectrum of the *Manilkara zapota* (sapodilla) seed extract (EEMZ)

DSC Analysis

Differential Scanning Calorimetry (DSC) is used to study the thermal behaviour of sapodilla seed gum and to assess its suitability as a pharmaceutical excipient. The DSC thermogram of sapodilla seed gum shows a broad endothermic event rather than a sharp melting peak. This behaviour is characteristic of natural polysaccharide gums, which are generally amorphous in nature. The observed endothermic peak at approximately 138.5 °C is attributed to loss of bound or adsorbed moisture, Relaxation or glass transition-like behaviour of polymer chains. It does not represent true melting, confirming the non-crystalline (amorphous) structure of the gum. Such amorphous nature is desirable for controlled/sustained drug release, as it allows better swelling and gel formation. During heat flow gradual increase in higher temperatures may indicate thermal degradation and polymer chain breakdown. Thermal Stability of Sapodilla seed gum remains thermally stable up to ~130–140 °C. This confirms its suitability for wet granulation and dry granulation of tablet manufacturing. So it possesses adequate thermal stability and it is suitable as a natural polymer excipient for sustained-release and gastroprotective pharmaceutical formulations.

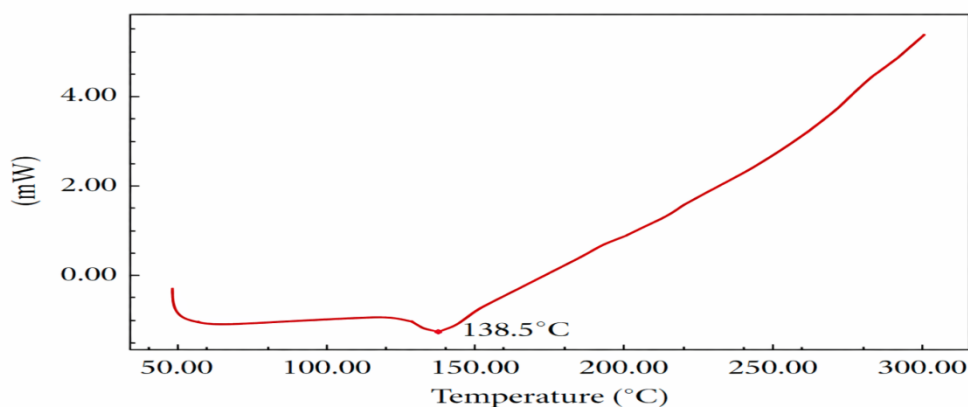


Figure 3: DSC Thermogram of the *Manilkara zapota* (sapodilla) seed extract (EEMZ)

3.3 Compatibility Studies

FTIR and DSC analyses of the physical mixture of *M. zapota* extract and gum showed no significant shift or disappearance of characteristic peaks, suggesting the absence of chemical interaction between extract and gum. The DSC thermogram of the mixture exhibited only minor changes in endothermic peak intensity, confirming compatibility between the extract and the excipient.

3.4 Discussion Summary

The results collectively demonstrate that *Manilkara zapota* gum possesses excellent swelling and gel-forming ability, enabling controlled and reproducible release of *M. zapota* leaf extract over 12 hours. The gum's potential as a natural, cost-effective, and biocompatible excipient for sustained-release formulations.

The findings support the feasibility of employing *M. zapota* gum in future phytopharmaceutical and nutraceutical product development aimed at gastroprotection and controlled release delivery systems.

4. Conclusion and Future Perspectives

The gum isolated from *M. zapota* was characterized by good swelling capacity, high viscosity, and thermal stability, essential features for sustained-release matrix systems. The physicochemical characterization confirmed its polysaccharide nature and absence of extract–excipient (gum) incompatibility.

Its use not only enhances the natural origin of the dosage form but also aligns with the increasing global demand for green excipients in pharmaceutical manufacturing.

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AUTHORS CONTRIBUTIONS

Dhanush Ram was involved in investigation, data collection, and manuscript writing. Hemant Badwaik was involved in supervision, manuscript review, and editing.

CONFLICT OF INTERESTS

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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