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DEVELOPMENT AND CHARACTERIZATION OF A CAFFEINE-SHILAJIT (ASPHALTUM PUNJABIANUM) CHEWING GUM AS AN INNOVATIVE ORAL DELIVERY SYSTEM: ANXIOLYTIC AND COGNITIVE ENHANCER

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ABSTRACT
The present study was undertaken to develop and evaluate a natural medicated chewing gum containing caffeine and *Asphaltum punjabianum* using mastic gum as the gum base. Caffeine (50 mg) and Asphaltum punjabianum (150 mg) were incorporated into five formulations (MCGF1-MCGF5) prepared by a modified fusion method, with different proportions of mastic gum and olive oil. The prepared formulations were evaluated for their physicochemical and mechanical properties, including appearance, weight variation, thickness, elasticity, stickiness, softening point, and drug content uniformity. The raw materials and formulation components were also examined by UV-visible spectroscopy and FTIR spectroscopy to support their identification and compatibility. The λmax values of caffeine and *Asphaltum punjabianum* were found to be 272 nm and 221 nm, respectively, with good linearity over the selected concentration ranges. FTIR analysis showed retention of the characteristic absorption bands of the individual components without significant changes in the physical mixture, indicating compatibility between the active ingredients and mastic gum. The formulations showed satisfactory physical properties and uniform drug content, with caffeine content ranging from 98.42-99.11% and *Asphaltum punjabianum* content ranging from 98.15-99.02%. In-vitro drug release was evaluated using an in-house mechanical mastication simulator in phosphate buffer pH 6.8 at 37 ± 0.5 °C. Within 20 min, caffeine release ranged from 87.67-95.00%, whereas *Asphaltum punjabianum* release ranged from 79.07-89.47%. Among the prepared formulations, MCGF3 showed a suitable balance of chewability, mechanical properties, drug content, and release characteristics and was selected as the optimized formulation. Overall, the study demonstrates the feasibility of developing a natural medicated chewing gum containing caffeine and *Asphaltum punjabianum*, although further *in-vivo* and clinical studies are required to establish its pharmacokinetic and therapeutic potential.

KEYWORDS: Medicated chewing gum; Caffeine; *Asphaltum punjabianum*; Mastic gum; Buccal drug delivery; Cognitive enhancement; Dissolution kinetics.

1. INTRODUCTION

Anxiety disorders are one of the most common psychiatric disorders in the world, and are often accompanied by attention, memory and executive function deficits and reduced overall cognitive functioning [1]. The cognitive impairments have a substantial impact on academic performance, work productivity and the quality of life [2]. This has led to an increasing interest in therapeutic approaches that have the ability to treat anxiety symptoms while also improving cognitive function. However, many conventional oral dosage forms may lack the efficacy necessary to achieve a rapid effect on the central nervous system (CNS), may have significant bioavailability variations and may be metabolized by the liver in the first pass through the intestine [3].

The chewing gum has become a novel drug delivery system that overcomes some of the drawbacks of conventional dosage forms, and has proven to be an effective, patient-friendly drug delivery system known as medicated chewing gum (MCG). In the case of mastication, the active pharmaceutical ingredients are released and absorbed through the buccal mucosa partly, which results in a faster systemic availability and in a lower effect of the hepatic first-pass metabolism [4]. Medicated chewing gum offers the added benefits of convenience and enhanced patient compliance, and its fast onset of action is ideal for delivering CNS-active drugs that need to have an immediate effect on the brain for cognitive stimulating and stress management. In addition, chewing has been reported to have additional therapeutic effects, such as increasing alertness, decreasing perceived stress, and improving cognitive performance [5, 6].

One of the most commonly used psychoactive substances is caffeine, commonly referred to as 1,3,7-trimethylxanthine, and is known to possess CNS stimulant properties. Its main effect is through antagonism of the

adenosine receptors A1 and A2A, which boosts neuronal activity and the release of neurotransmitters like dopamine, norepinephrine, and acetylcholine [7,8]. These can lead to better alertness, attention, concentration, reaction time and cognitive functioning [9,10]. Caffeine is rapidly absorbed, has excellent safety, and can easily penetrate the blood brain barrier making it a promising individual to include in a fast-acting drug delivery system [11,12]. *Asphaltum Punjabianum* is exudate that naturally occurs in rock and is used in traditional Ayurvedic medicine for its rejuvenating properties "Rasayana" [13,14]. It is a complex mixture of bioactive components, such as fulvic acids, humic substances, dibenzo-α-pyrones and essential minerals, that is responsible for its multiple pharmacological properties [15,16]. Experimental and clinical research has proven that *Asphaltum punjabianum* is anti-oxidant, adaptogenic, neuroprotective, anxiolytic and anti-fatigue. Furthermore, it has been demonstrated to promote learning, memory, neuronal activity and stress resistance, and thus, it is a potential natural nootropic and psychotropic substance [17].

Caffeine and *Asphaltum punjabianum* can be used together for a complementary pharmacological strategy to tackle anxiety-related cognitive dysfunction. Increased vigilance, attention and mental performance has been reported for caffeine's modulation of central neurotransmitter systems [18]. On the contrary, the adaptogenic and neuroprotective effect of *Asphaltum punjabianum* has been shown, which can help increase the tolerance to stress and maintaining cognitive function [19]. Additionally, the fulvic acid content of *Asphaltum punjabianum* has been linked to supporting the health of the neurons, as well as enhancing the functioning of them, which could help complement the quick stimulatory effects that caffeine offers. It is therefore possible that the co-administration of these agents in a single dose may yield benefit in two areas: cognition and resistance to anxiety induced impairments. Choosing the right gum base is also crucial for the formulation of medicated chewing gum. Natural gum that was used as gum base was mastic gum, which is extracted from Pistacia lentiscus, because of its biocompatibility, biodegradability, elasticity, and good mechanical properties [20,21].

The above characteristics make mastic gum an attractive natural excipient for medicated chewing gum formulation due to its desirable chewing properties, formulation stability and patient acceptability. While the specific effect of caffeine and *Asphaltum punjabianum* have been widely studied, there were only a few studies investigating their simultaneous incorporation into a medicated chewing gum delivery system for both anxiolytic and cognitive-enhancing properties. This is an important gap in the current knowledge and an indication of the need for the development of new formulations that can offer the patients fast therapeutic effect with ease in compliance. Hence, the present study was designed to formulate and evaluate the medicated chewing gum with the required active ingredients, caffeine, and *Asphaltum Punjabianum* with the natural gum base mastic gum. The developed formulation was evaluated for physicochemical property, mechanical properties and in vitro drug release evaluation for fast release dosage form for the anxiolytic and cognitive enhancement application.

2. MATERIALS AND METHODOLOGY:

2.1 Materials:

Caffeine anhydrous, beeswax, olive oil, and sucrose were purchased from Central Drug House (P) Ltd. (Gujarat, India). *Asphaltum punjabianum* was sourced from Bionest Herbals Pvt. Ltd. (Mohali, Punjab, India), while mastic gum was acquired from Gaur Ayurvedic Store (Punjab, India). Fresh lemons were obtained from a local market in Bareilly, Uttar Pradesh, India. High purity distilled water was generated in-house using a laboratory distillation unit. All additional chemicals, reagents, and solvents utilized throughout the investigation were of analytical reagent (AR) grade and were used directly as received without any further purification.

2.2 Pre-formulation Studies:

2.2.1 Organoleptic properties:

Visual and sensory examination of the raw materials was carried out under standard laboratory conditions prior to formulation development. The procured caffeine sample appeared as a white, odourless, crystalline powder, consistent with the macroscopic description in the Indian Pharmacopoeia. *Asphaltum punjabianum* was characterised as a dark brown to blackish, sticky, viscous mass with a characteristic bituminous odour, matching the diagnostic profile reported for authentic purified specimens [14, 22].

2.2.2 Preliminary Phytochemical Screening of *Asphaltum punjabianum*

A small quantity of purified *Asphaltum punjabianum* was dissolved in distilled water and subjected to standard qualitative tests for alkaloids, flavonoids, terpenoids, phenolic compounds and tannins. Colour changes or precipitate formation were recorded as evidence of the respective phytoconstituents [23].

2.2.3 Melting Temperature Determination:

Melting behaviour was determined using the capillary-tube method in a calibrated digital melting-point apparatus, used to verify raw material identity and purity. For crystalline caffeine, a finely packed capillary tube was heated, and the temperature range from initial collapse to complete liquefaction was recorded per official protocol. For the amorphous *Asphaltum punjabianum* complex, thermal screening was carried out over a 50-150 °C gradient, with the onset of volumetric shrinkage, particle aggregation, and phase transition closely monitored and documented [14, 22].

2.2.4 Partition coefficient:

The partition coefficients of Caffeine and *Asphaltum punjabianum* were determined by the shake-flask method using a chloroform–water solvent system. Primary stock solutions were formulated by precisely dissolving 100 mg of each individual compound into 100 mL of pure chloroform using volumetric flasks to yield a final concentration of 1 mg/mL. From these prepared stock solutions, 25 mL aliquots were transferred into dedicated separating funnels, followed by the addition of 25 mL of purified distilled water to establish a 1:1 phase ratio with a combined volume of 50 mL.

To facilitate mass transfer across the liquid-liquid interface, the biphasic mixtures were agitated vigorously for 30 minutes. Following agitation, the separating funnels remained completely stationary to allow the system to reach equilibrium and ensure complete separation of the two immiscible layers. The denser, lower organic (chloroform) phases were systematically collected and diluted where necessary. Quantification of Caffeine and *Asphaltum punjabianum* retained in the organic fractions was carried out using a UV-Visible spectrophotometer at their respective maximum absorption wavelengths (λ_{max}).

The partition coefficient was calculated as:

$$P = \frac{C_{organic}}{C_{aqueous}}$$

where P is the partition coefficient, and $C_{(organic)}$ and $C_{(aqueous)}$ represent drug concentrations in the respective layers [24].

2.2.5 Calibration Curves:

λmax and calibration curves for caffeine and *Asphaltum punjabianum* were established to enable quantitative determination. Standard stock solutions were serially diluted to obtain a range of working standards, scanned across the UV-visible spectrum, and absorbance at λmax plotted against concentration to construct calibration curves [25].

Unknown sample concentrations were determined using the linear regression equation:

$$y = mx + c$$

where y is absorbance, m is the slope, x is concentration, and c is the intercept, rearranged as:

$$x = \frac{(y-c)}{m}$$

2.2.6 Fourier Transform Infrared (FTIR) Spectroscopy:

FTIR spectroscopy was performed to evaluate physicochemical compatibility between caffeine, *Asphaltum punjabianum*, and the compounding excipients. Spectra of the pure actives, the formulated gum base, and their physical mixtures were recorded using the KBr pellet technique over 4000-400 cm^{-1}, as part of a standardised drug-excipient screening protocol. Spectra were compared for retention of characteristic peaks, and for wave number shifts, intensity changes, or new absorption bands indicating possible solid-state interaction [26, 27].

2.2.7 Formulation Development:

Formulations (MCGF1-MCGF5) were prepared by the fusion method with minor modifications. Weighed quantities of mastic gum and beeswax were heated at 60-70 °C until molten and uniform. Sugar syrup was added gradually under continuous stirring, followed by caffeine and *Asphaltum punjabianum*, incorporated with constant stirring to ensure uniform distribution. Lemon juice and olive oil were then added to improve palatability and mechanical properties, and the mixture stirred for 10-15 min to obtain a homogeneous mass.

The mass was cooled slightly, rolled into a uniform sheet, and cut into pieces of suitable size, each adjusted to approximately 3.2 g containing 50 mg caffeine and 150 mg *Asphaltum punjabianum* [28, 29].

2.3 Formulation Design and Dose Selection:

The medicated chewing gum (MCG) formulations were developed to achieve fast delivery of caffeine via the oral route and the possible adaptogenic and neuroprotective effect of *Asphaltum punjabianum*. The aim of the formulation strategy was to achieve the desired mechanical properties, chewable formulation acceptable chewability, efficient drug release, and formulation stability.

The doses of caffeine and *Asphaltum punjabianum* used in the formulation of MCG were based on published pharmacological data, safety, patent literature and the proposed application for cognitive enhancement. The dose of 50 mg/unit of chewing gum was chosen because it is in the reported therapeutic range for alertness, attention and cognitive function and at a low enough level to avoid dose-related adverse effects, such as nervousness, tachycardia, or sleep disturbances [9, 30].

Based on its reported properties of antioxidant, adaptogenic and neuroprotective effects, a 150 mg dose of *Asphaltum punjabianum* was chosen. *Asphaltum punjabianum* is rich in active components like fulvic acid, dibenzo-α-pyrones, humic substances and minerals, which have been linked to the function of mitochondria, metabolic processes of cells and neuronal health. In addition, patent literature on functional chewing gums containing *Asphaltum punjabianum* indicates that the amount of *Asphaltum punjabianum* can be in the range of 50-400 mg per unit dosage, which is consistent with the amount selected in the proposed formulation. Therefore,

150 mg was found as appropriate for incorporation into the chewing gum as long as it was formulation feasible and compatible [31,32].

The doses used for caffeine and *Asphaltum punjabianum* were chosen based on their complementary pharmacologic properties. Caffeine is believed to offer quickened central nervous system stimulation via adenosine receptor antagonism, while *Asphaltum punjabianum* is thought to support cognitive functions due to its adaptogenic, antioxidant, and neuroprotective effects. The medicated chewing gum delivery system was therefore designed to deliver the drug in a rapid manner during chewing and to be a convenient and patient friendly dosage form.

The five formulations (MCGF1-MCGF5) were made by adjusting the amounts of mastic gum and olive oil while preserving the levels of beeswax, sugar syrup, lemon flavor, caffeine, and *Asphaltum punjabianum*. The use of mastic gum as a natural gum base was favored due to its elasticity, chewability and good mechanical properties, while beeswax was used as a stiffener to increase the resistance of the chewing gum matrix. The use of olive oil as a plasticiser was added to improve flexibility and chewing texture. Sugar syrup was used as a sweetener and binder and lemon was used for flavoring to enhance palatability. The average weight of a unit is 3.2 g, and the amount of caffeine and *Asphaltum punjabianum* per unit is 50 mg and 150 mg, respectively. The composition of the five medicated chewing gum formulations (MCGF1-MCGF5) is presented in Table 1.

Table 1 Composition of Different Medicated Chewing Gum Formulations (MCGF1–MCGF5)

Ingredient	**Formulation code**				
	MCGF1	**MCGF2**	**MCGF3**	**MCGF4**	**MCGF5**
Mastic Gum	51%	52%	53%	54%	55%
Bees wax	1%	1%	1%	1%	1%
Sugar Syrup	35%	35%	35%	35%	35%
Lemon	5%	5%	5%	5%	5%
Olive Oil	8%	7%	6%	5%	4%

2.4 Preparation of Medicated Chewing Gum:

A modified fusion method was used to create the formulation of the medicated chewing gums. First, the lipophilic gum base material was prepared by melting beeswax in a water bath at 60-70 °C and then adding the olive oil immediately to the water bath and stirring evenly and continuously to form a blended phase. This molten mixture was then progressively loaded with increasing amounts of mastic gum while vigorously agitated in a high shear mixer until a uniform gum matrix was obtained, according to a classic "naturally derived" structure. Thereafter, sugar syrup and lemon juice was well mixed with the matrix. In order to ensure the thermal stability of the active compound and to prevent chemical degradation, whole molten mass was cooled to about 40°C before addition of caffeine and *Asphaltum punjabianum* in geometric fraction. The medicated mass was kneaded uniformly to ensure uniform distribution of the drug in the matrix according to the following medicated chewing gum processing parameters. Finally, the prepared formulation was rolled into uniform thickness sheets, cut into individual structural units, left to solidify at room temperature and stored in an airtight container in a desiccated environment until further evaluation [28,33]. The prepared medicated chewing gum formulations obtained after the fusion process are shown in Figure 1.

Figure 1: Prepared Medicated Chewing Gums

3. Evaluation of Medicated Chewing Gum:

3.1 Organoleptic Evaluation:

Formulations were evaluated for colour, odour, and texture. Colour and appearance were assessed visually under normal daylight, odour was evaluated manually, and texture was assessed by gently pressing the gum between thumb and finger to judge softness and smoothness.

3.2 Weight Variation:

Ten units from each formulation were randomly selected and weighed individually using a digital balance. Mean weight and standard deviation were calculated to assess dosage-unit uniformity.

3.3 Content Uniformity:

Content uniformity was assessed to confirm even distribution of caffeine and *Asphaltum punjabianum* across dosage units. Ten randomly selected units per batch were weighed, minced, and extracted in 100 mL pH 6.8 phosphate buffer via sonication (20-30 min) to ensure complete drug release. Solutions were filtered through Whatman No. 1 paper and appropriately diluted.

Drug content was determined by UV-visible spectrophotometry at the pre-verified λmax, with concentrations derived from the standard calibration curves and expressed as a percentage of the labelled dose. Batch acceptability was assessed against standard pharmacopeial thresholds for dosage-unit uniformity [34].

3.4 Other Physical Properties:

The formulations were evaluated for key mechanical properties that influence performance during mastication and drug release [35,36]:

- **Elasticity:**

Assessed manually by stretching the gum between two fingers and observing its recovery to original shape, a standard preliminary method for evaluating chewing gum mechanical properties, and an important determinant of both patient compliance and release behaviour.

- **Stickiness:**

Evaluated using a modified compression method, in which each sample was struck by a 250 g cylindrical hammer at ~30 cycles/min for 10 minutes, with surface adhesion visually observed and recorded. Lower stickiness is preferred for comfortable chewing and handling.

- **Thickness:**

Measured using a Vernier caliper, with the average value recorded for each unit.

- **Softening Point:**

Determined by gradual heating, noting the temperature at which softening began an important indicator of thermal stability and storage suitability.

3.5 *In-vitro* Study of Medicated Chewing Gum

An in-house mechanical mastication simulator was developed to evaluate the *in vitro* drug release of the medicated chewing gum. The apparatus was designed based on the chewing gum dissolution principles described in the European Pharmacopoeia (Ph. Eur.) and consisted of a chewing chamber with a reciprocating piston assembly. The chewing gum was subjected to repeated compression and relaxation at approximately 60 strokes min^{-1} to simulate mastication.

The chewing chamber was immersed in a dissolution vessel containing 900 mL of phosphate buffer (pH 6.8), which was maintained at 37 ± 0.5 °C under continuous stirring to ensure uniform distribution of the released drug. Drug release samples were collected at predetermined intervals and analysed using the appropriate analytical method [37].

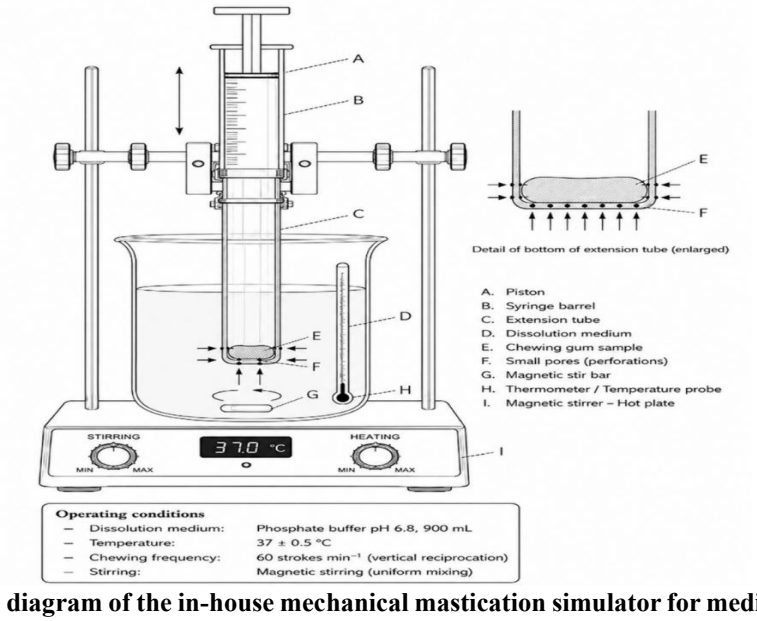

Figure 2: Schematic diagram of the in-house mechanical mastication simulator for medicated chewing gum

The fabricated system provided a simple, cost-effective means of evaluating drug release under simulated mastication conditions. A schematic of the apparatus and a photograph of the actual setup are shown in Figure 2 and Figure 3, respectively.

Figure 3: Photograph of the actual fabricated experimental setup

4. RESULT:

4.1 Pre-formulation Studies:

4.1.1 Organoleptic Properties:

Caffeine was observed as an odourless, white crystalline powder, while *Asphaltum punjabianum* appeared as a dark brown powder with a characteristic earthy odour both consistent with reported reference standards (Table 2).

Table 2: Organoleptic Properties of Drug Samples:

Parameter	**Caffeine**	***Asphaltum punjabianum***
Appearance	Crystalline powder	Powder
Colour	White	Dark brown
Odour	Odourless	Characteristic earthy odour

4.1.2 Preliminary Phytochemical Screening of *Asphaltum punjabianum*:

Asphaltum punjabianum tested positive for flavonoids, phenolic compounds, tannins, carbohydrates, and glycosides (Table 3), constituents associated with its antioxidant, adaptogenic, and neuroprotective activity.

Table 3: Preliminary Phytochemical Screening of Asphaltum punjabianum:

S.NO	**Phytoconstituent**	**Test Preformed**	**Observation**
1.	Alkaloids	Mayer's Test	Cream/white precipitate was observed
2.	Flavonoids	Shinoda Test	Pink colour was observed
3.	Terpenoids	Salkowski Test	Reddish-brown colour at the interface was observed
4.	Phenolic compounds	Ferric Chloride Test	Dark green colour was observed
5.	Tannins	Lead Acetate Test	White/cream-coloured precipitate was observed

4.1.3 Melting Point:

Melting point of Caffeine was observed between 235°C to 237 °C, confirming its identity and purity. *Asphaltum punjabianum* showed no definite melting point; shrinkage and particle aggregation began near 85 °C, with a compact brittle mass forming by 105 °C, consistent with its amorphous, resinous nature (Table 4, Figure 4).

Figure 4: Determination of the melting point of caffeine using a digital melting point apparatus

Table 4: Melting Point and Thermal Behavior of Drug Samples

Drug	Observation
Caffeine	Melting point observed between 235°C to 237 °C
Asphaltum punjabianum	No definite melting point observed; shrinkage and aggregation initiated around 85 °C, with formation of compact brittle mass at 105 °C

4.1.4 Partition Coefficient:

Partition coefficient: Caffeine showed a partition coefficient of 6.24, indicating moderate lipophilicity, while *Asphaltum punjabianum* showed a value of 0.200, indicating hydrophilic behaviour (Table 5).

Table 5 Partition Coefficient of Drug Samples

Drug	Solvent System	Partition Coefficient
Caffeine	Chloroform: Water	6.24 ± 0.01
Asphaltum punjabianum	Chloroform: Water	0.200 ± 0.02

Values are expressed as Mean ± SD (n = 3)

4.1.5 Calibration Curve:

The λmax of caffeine was found to be 272 nm and Caffeine exhibited linearity over 2-10 µg/mL ($y = 0.0143x + 0.0045$, $R^2 = 0.9930$).

The λmax of *Asphaltum punjabianum* was found to be 221 nm and *Asphaltum punjabianum* exhibited linearity over 20-100 µg/mL ($y = 0.0144x + 0.0279$, $R^2 = 0.9979$), confirming the reliability of both analytical methods (Tables 6-7, Figures 5-6).

Table 6: Standard Calibration Curve Data of Caffeine

S. No.	Concentration (µg/mL)	Absorbance Value 1	Absorbance Value 2	Absorbance Value 3	Mean Absorbance
1	2	0.033	0.035	0.034	0.034
2	4	0.063	0.065	0.064	0.064
3	6	0.098	0.097	0.099	0.098
4	8	0.117	0.116	0.118	0.117
5	10	0.144	0.143	0.145	0.144

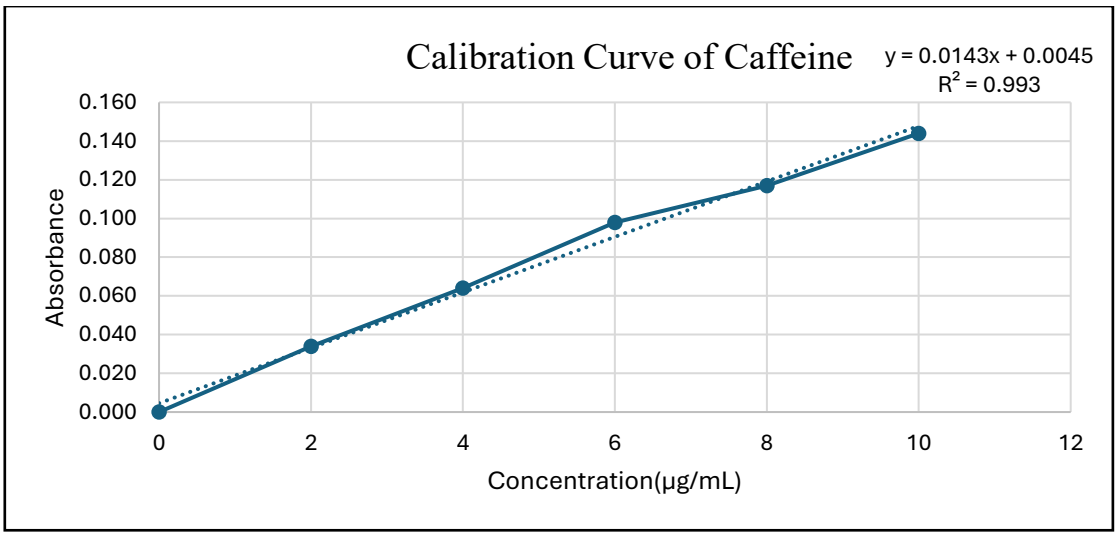

Figure 5: Calibration curve of caffeine

Table 7: Standard Calibration Curve Data of *Asphaltum punjabianum*

S. No.	Concentration (µg/mL)	Absorbance Value 1	Absorbance Value 2	Absorbance Value 3	Mean Absorbance
1	20	0.323	0.325	0.324	0.324
2	40	0.624	0.626	0.625	0.625
3	60	0.904	0.905	0.906	0.905
4	80	1.201	1.203	1.202	1.202
5	100	1.434	1.435	1.436	1.435

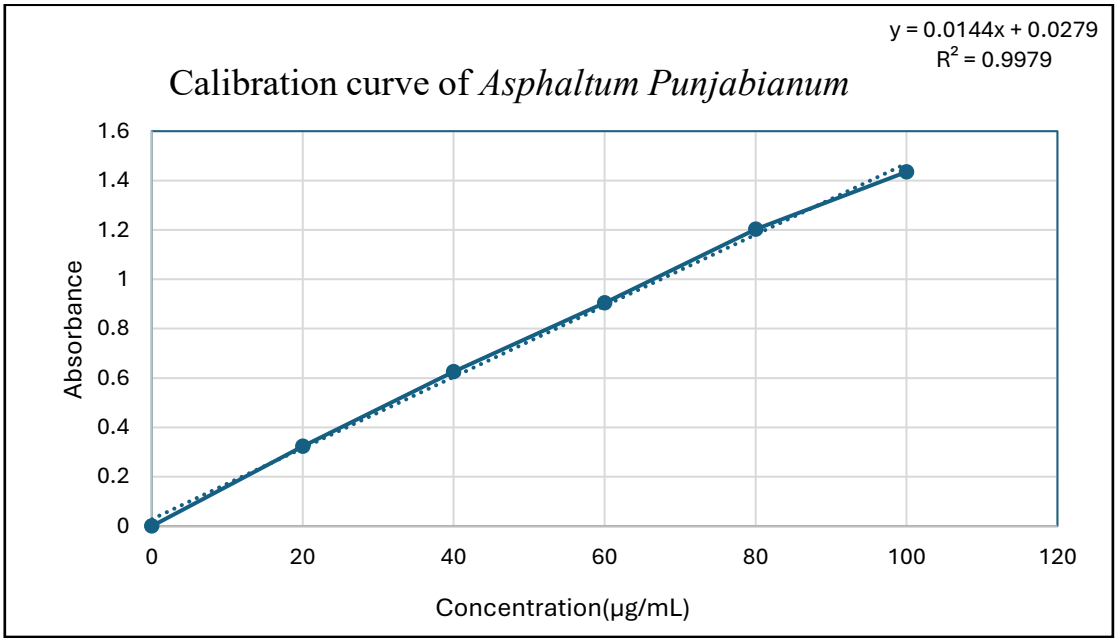

Figure 6: Calibration Curve of *Asphaltum punjabianum*

4.1.6 Fourier Transform Infrared Spectroscopy (FTIR):

The FTIR spectrum of the physical mixture demonstrated retention of all major characteristic absorption bands of the individual components without significant wavenumber shifts or the emergence of new functional group bands, confirming full retention of functional groups and drug-excipient compatibility (Figure 7). These findings confirm the absence of chemical interactions among caffeine, *Asphaltum punjabianum*, and mastic gum, establishing their compatibility for medicated chewing gum formulation.

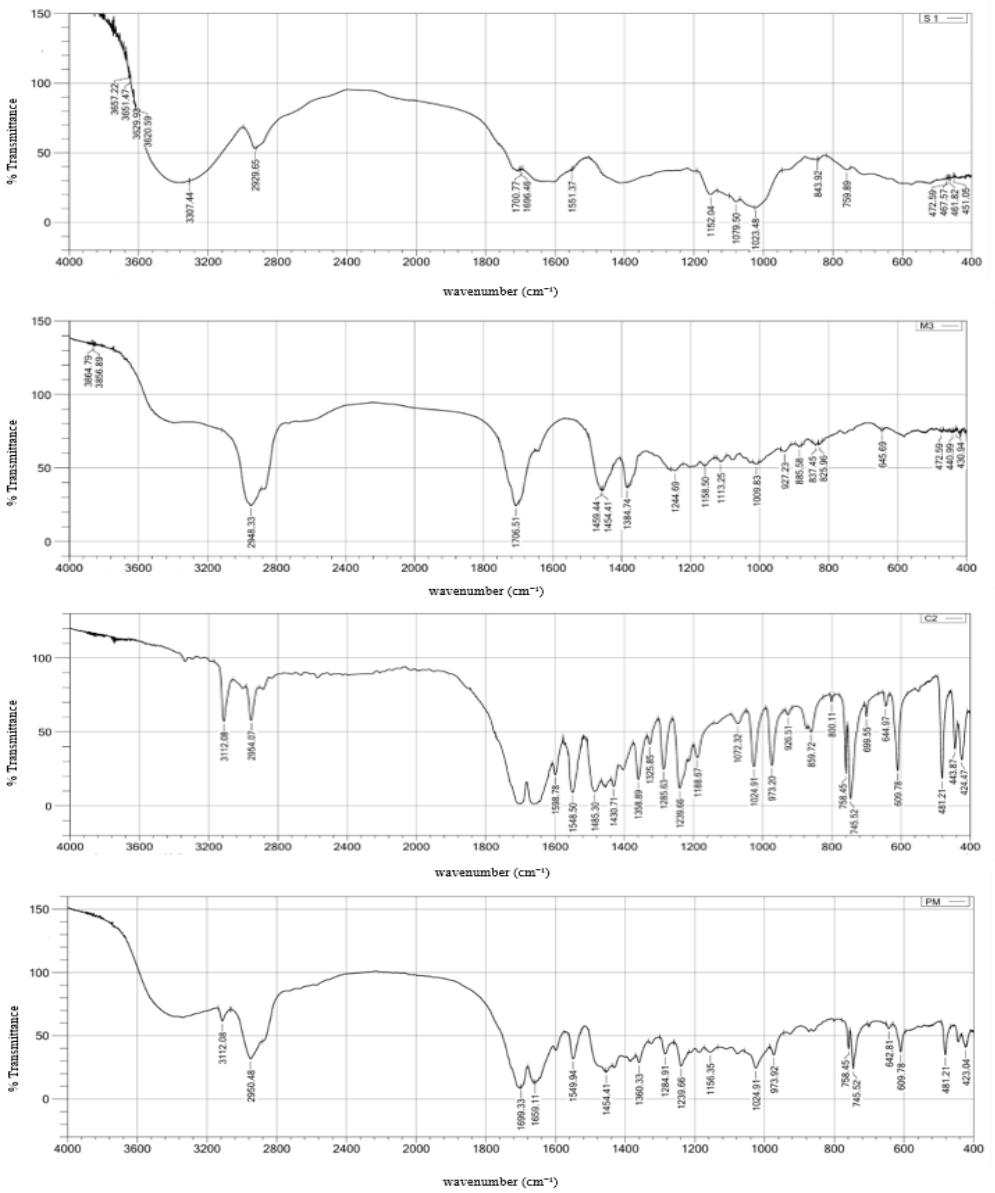

Figure 7: FTIR spectra of *Asphaltum punjabianum* (S1), Mastic Gum (M3), Caffeine (C2), and their Physical Mixture (PM) showing characteristic functional group peaks and compatibility of formulation components

4.2 Formulation Evaluation:

4.2.1 Organoleptic Evaluation:

All formulations (MCGF1-MCGF5) displayed a uniform dark brown colour with characteristic odour, attributable to *Asphaltum punjabianum*, and showed satisfactory chewability and cohesive structure (Table 8).

Table 8: Organoleptic Evaluation of Medicated Chewing Gum Formulations

Formulation	Color	Odour	Texture
MCGF1	Dark brown	Characteristic	Soft, slightly sticky
MCGF2	Dark brown	Characteristic	Smooth, slightly sticky
MCGF3	Dark brown	Characteristic	Smooth, cohesive
MCGF4	Dark brown	Characteristic	Firm, cohesive
MCGF5	Dark brown	Characteristic	Firm, less sticky

4.2.2 Evaluation of Physical Properties:

4.2.2.1 Elasticity and Stickiness:

Elasticity is among the most important mechanical parameters for medicated chewing gum, since it governs chewability, structural cohesion, and drug release behaviour during mastication. All five formulations showed satisfactory elasticity, reflecting their capacity to withstand repeated deformation while retaining structural integrity. Elasticity and stickiness data for the prepared formulations are summarized in Table 9.

As the concentration of mastic gum increased, the resulting matrix became structurally more rigid and mechanically more stable. Stickiness evaluation of the formulations is depicted in Figure 8, while manual elasticity testing performed by stretching the gum matrix between two fingers shown in Figure 9.

Figure 8: Evaluation of stickiness of medicated chewing gum

Figure 9: Manual evaluation of elasticity of medicated chewing gum by stretching the gum matrix between two fingers

Table 9: Elasticity and Stickiness of Medicated Chewing Gum Formulations

Formulation	Elasticity	Stickiness
MCGF1	Moderate	Sticky
MCGF2	Good	Sticky
MCGF3	Excellent	Moderate
MCGF4	Very Good	Moderate
MCGF5	Very Good	Minimal

4.2.2.2 Softening Point:

The softening point serves as a key indicator of a medicated chewing gum's thermal stability, storage behaviour, and its ability to resist deformation under physiological and environmental temperature conditions. Softening points for all five formulations were measured using an infrared thermometer, with the results summarized in Table 10. The experimental setup employed for this determination is shown in Figure 10.

Table 10: Softening point of Medicated Chewing Gum Formulations

Formulation	Softening Point(°C)
MCGF1	51.3
MCGF2	52.4
MCGF3	53.0
MCGF4	53.2
MCGF5	53.8

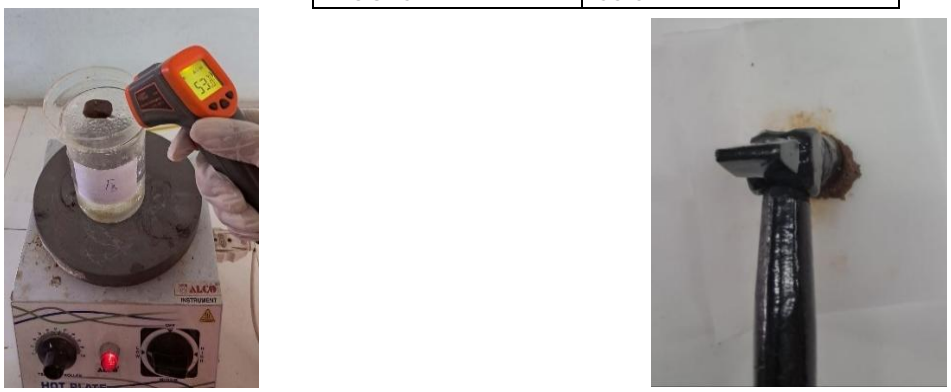

Figure 10: Determination of the softening point of medicated chewing gum using a hot plate and infrared thermometer

4.2.2.3 Thickness:

Ranged from 3.81 to 4.01 mm across batches, indicating satisfactory dimensional uniformity (Table 11).

Table 11: Thickness of Medicated Chewing Gum Formulations

Formulation	Thickness (mm)
MCGF1	3.81 ± 0.05

MCGF2	3.88 ± 0.04
MCGF3	3.92 ± 0.03
MCGF4	3.95 ± 0.04
MCGF5	4.01 ± 0.05

Values are expressed as Mean ± SD (n = 3)

4.2.2.4 Weight Variation

Average weights ranged from 3.18 to 3.23 g, reflecting consistent manufacturing (Table 12).

Table 12: Weight Variation of Medicated Chewing Gum Formulations

Formulation	Average Weight (g)
MCGF1	3.18 ± 0.04
MCGF2	3.19 ± 0.03
MCGF3	3.21 ± 0.03
MCGF4	3.22 ± 0.04
MCGF5	3.23 ± 0.05

Values are expressed as Mean ± SD (n = 3)

4.2.2.5 Content Uniformity:

Caffeine content ranged from 98.42-99.11%, and Shilajit content from 98.15–99.02%, both within acceptable pharmacopoeial limits (Table 13).

Table 13: Content uniformity data for Caffeine and *Asphaltum punjabianum* in different formulations

Formulation	Caffeine (%)	Shilajit (%)
MCGF1	98.42 ± 0.81	98.15 ± 0.92
MCGF2	99.11 ± 0.74	98.96 ± 0.68
MCGF3	98.86 ± 0.69	99.02 ± 0.73
MCGF4	98.67 ± 0.77	98.58 ± 0.80
MCGF5	99.05 ± 0.71	98.88 ± 0.76

Values are expressed as Mean ± SD (n = 10)

4.3 *In-vitro* Drug Release Study:

In-vitro dissolution testing in pH 6.8 phosphate buffer, simulating the salivary environment, showed rapid and efficient release of both actives across all formulations within 20 minutes.

- Caffeine release ranged from 87.67% to 95.00% (Table 14, Figure 11).
- *Asphaltum punjabianum* release ranged from 79.07% to 89.47% (Table 15, Figure 12).

Release rate showed an inverse relationship with mastic gum concentration: formulations with higher mastic gum content exhibited greater mechanical strength but comparatively slower release, while those with lower mastic gum content released the actives faster but showed reduced structural integrity. MCGF3 offered the most balanced profile among mechanical strength, dosage uniformity, and dissolution efficiency, and was identified as the optimised formulation.

Table 14: *In-vitro* Release Profile of Caffeine

Time (min)	MCGF1	MCGF2	MCGF3	MCGF4	MCGF5
0	0	0	0	0	0
2	33.31%	37.26%	38.45%	32.18%	29.73%
4	50.24%	51.35%	51.74%	48.41%	45.81%
6	53.68%	54.92%	58.77%	52.64%	48.76%
8	61.91%	62.74%	65.12%	56.66%	54.06%
10	76.38%	76.77%	77.30%	72.39%	65.43%
12	78.40%	82.93%	83.34%	76.87%	67.27%
14	81.81%	85.76%	87.05%	80.39%	74.45%
16	84.87%	87.36%	88.47%	83.25%	80.13%
18	87.14%	89.41%	91.72%	85.63%	83.29%
20	91.37%	92.34%	95.00%	89.28%	87.67%

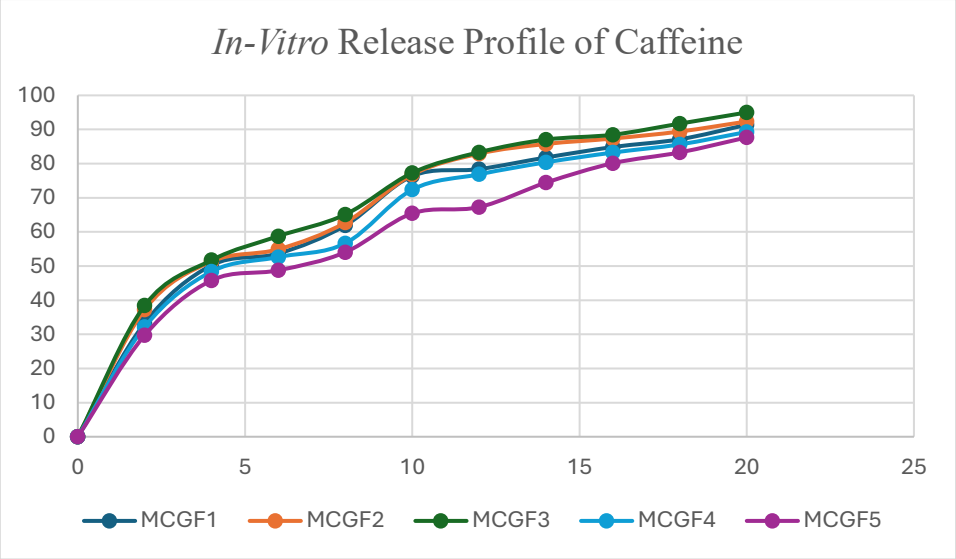

Figure 11: *In-vitro* release profile of caffeine from medicated chewing gum formulations (MCGF1-MCGF5)

Table 15: *In-vitro* Release Profile of *Asphaltum punjabianum*:

Time (min)	MCGF1	MCGF2	MCGF3	MCGF4	MCGF5
0	0	0	0	0	0
2	29.38%	30.17%	30.96%	28.09%	27.25%
4	34.37%	34.96%	35.93%	32.32%	30.85%
6	37.13%	40.31%	41.12%	33.46%	32.94%
8	41.24%	45.16%	46.11%	39.70%	33.71%
10	46.14%	57.61%	53.82%	42.92%	41.58%
12	58.35%	67.23%	61.73%	55.97%	54.86%
14	67.64%	76.00%	72.14%	64.86%	63.65%
16	76.44%	78.14%	79.66%	72.68%	70.75%
18	79.84%	81.84%	83.79%	76.12%	73.75%
20	85.39%	87.24%	89.47%	81.33%	79.07%

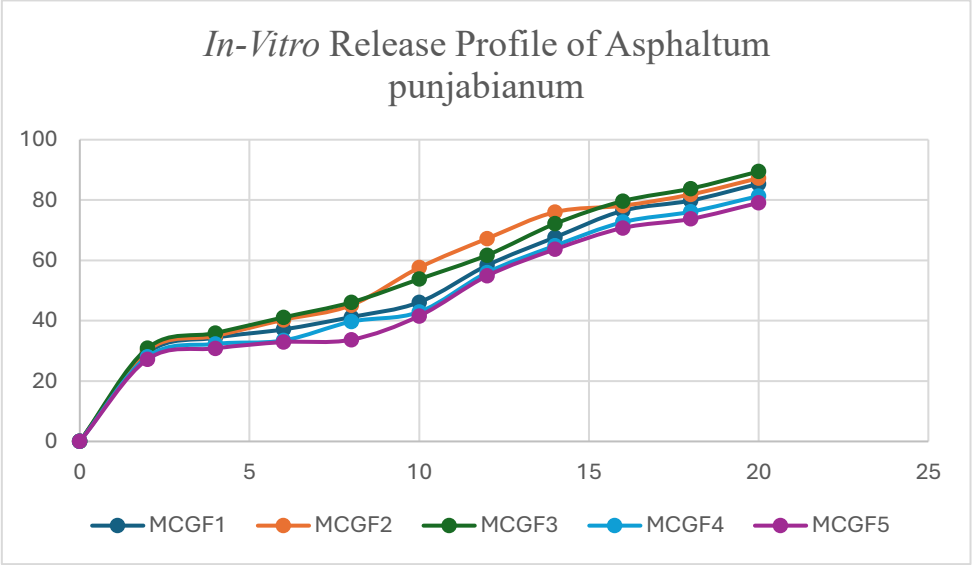

Figure 12: *In-vitro* release profile of *Asphaltum punjabianum* from medicated chewing gum formulations (MCGF1-MCGF5)

5. DISCUSSION:

The present study established the technical feasibility of formulating a natural medicated chewing gum (MCG) system incorporating caffeine alongside *Asphaltum punjabianum* within an organic mastic gum matrix. Choice of active agents was guided by established literature classifying caffeine as a central nervous system stimulant and *Asphaltum punjabianum* as a protective adaptogenic substance; nevertheless, this research was restricted to laboratory characterizations, meaning biological claims remain hypothetical pending experimental validation.

Fourier transform infrared spectroscopy confirmed chemical compatibility among formulation components, evidenced by the preservation of principal diagnostic bands across all constituents and additives. Formulation mechanical characteristics depended closely on the ratio of gum base to plasticizing agent. Elevating the proportion of mastic gum enhanced structural integrity and elasticity while minimizing surface stickiness, whereas higher concentrations of olive oil yielded softer, tackier matrices. Recorded thermal softening values (51.3°C-53.8 °C) demonstrated suitable physical stability across anticipated storage conditions.

In-vitro release profile evaluation via mechanical mastication apparatus showed rapid dual-agent liberation within 20 minutes (87.67%-95.00% caffeine; 79.07%-89.47% *Asphaltum punjabianum*). Release rates demonstrated an inverse relationship with mastic base concentration, driven by matrix viscosity effects. Formulation MCGF3 offered the most favorable balance among structural cohesion, minimal tackiness, and dissolution performance. Subsequent *in-vivo* pharmacokinetic and clinical evaluations remain essential to determine transmucosal permeation efficiency and bioequivalence.

7. CONCLUSION:

This investigation was successful in proving the feasibility of the formulation of a dual action medicated chewing gum containing caffeine and *Asphaltum punjabianum* into a sustainable mastic gum core. The fusion manufacturing methodology was proven to be a highly reproducible, cost-effective and simple processing technique to produce matrices of natural gums with satisfactory physicochemical and mechanical properties. All the preformulation diagnostics were performed to confirm identity, purity, and chemical stability of the starting materials, and the results of the spectroscopic data confirmed that there were no undesirable interactions between the drug and excipients, which indicated good formulation stability for further development. Evaluation studies showed that each batch prepared met fully the acceptable pharmaceutical quality standards for the important parameters such as appearance, weight variation, thickness uniformity, drug content distribution, elasticity, adhesion behavior, and thermal softening points. Moreover, the physiological chewing condition was successfully reproduced by the custom made in-house mastication simulator, which can be used as a reliable biomimetic tool to characterize the mechanical release profiles of the formulations. The *in-vitro* dissolution profiles showed that this delivery system helps in releasing the caffeine and *Asphaltum punjabianum* quickly which strongly supports the suitability of the medicated chewing gum as a fast-acting buccal drug delivery system.

Among all the developed candidates, MCGF3 was identified as the optimized formulation, exhibiting excellent elasticity, moderate stickiness, a softening point of 53.0 °C, uniform thickness (3.92 ± 0.03 mm), consistent weight (3.21 ± 0.03 g), and high drug content uniformity (98.86% for caffeine and 99.02% for *Asphaltum punjabianum*), along with the most balanced *in-vitro* drug release profile (95.00% caffeine and 89.47% *Asphaltum punjabianum* within 20 minutes). This formulation demonstrated the best structural performance and optimal mass transfer kinetics and was therefore considered for further study.

Overall, the formulated medicated chewing gum is a novel and patient-friendly delivery system that could effectively deliver caffeine and *Asphaltum punjabianum to* aid in neurocognitive and anxiolytic therapy. This formulation has different clinical benefits over the traditional oral formulations such as easy administration without water, increased patient compliance, rapid drug release and the most beneficial one of direct transmucosal absorption through the buccal cavity.

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