

## Original Research Article

# Formulation and characterization of caffeine biodegradable chewing gum delivery system for alertness using plasticized poly(D,L-lactic acid) as gum base

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### Abstract

**Purpose:** To formulate and evaluate biodegradable plasticized poly(D,L-lactic acid) as a base for caffeine-medicated chewing gums (MCGs) to increase alertness.

**Methods:** Biodegradable plasticized poly(D,L-lactic acid) caffeine-MCGs were formulated with a fixed concentration (15 % w/w) of different plasticizers for different formulations. Substances used as plasticizers were triacetin, stearic acid, PEG-600, tributyl citrate, soya oil, sunflower oil, glycerol, triethyl citrate, PEG-4000, and castor oil. The characteristics of the gum formulations were examined using texture profile analysis (TPA), and also evaluated for biodegradation, microstructure, in vitro drug release, and sensory features.

**Results:** The MCG-1 and MCG-7 formulations with triacetin and glycerol as plasticizers, respectively, exhibited a biodegradation score of 1 and 2, respectively, indicating considerable biodegradation. The formulation with triacetin as a plasticizer exhibited TPA values of 3750.52 g, -51.13 g·s, 1580.88, 1526.23, and 0.364 for hardness, adhesiveness, gumminess, chewiness, and cohesiveness, respectively; these values are similar to those of the Military Energy Gum. The microstructure of the gum base was characterized using scanning electron microscopy to determine surface properties. The in vitro drug release was determined as 97 % after a mean chewing time of 15 min by using a specially designed in vitro chewing machine.

**Conclusion:** Plasticized poly(D,L-lactic acid) gum formulation is suitable for the delivery of caffeine and can be used as an alternative MCG for effective management of fatigue.

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## INTRODUCTION

Chewing gums are considered as one of the popular drug delivery methods because they are easy to use, do not require water, have a good taste, and are liked by children. A medicated chewing gum (MCG) is defined by European Pharmacopeia [1] as a 'solid single dose preparation with a base mainly consisting of gum, which is intended to be chewed but not swallowed [2]'. The action of the drug delivered through chewing gums is rapid because the permeable and blood-rich oral mucosa quickly

absorbs the active substances, which subsequently pass through the jugular veins directly into the blood [3, 4]. Conventional chewing gums are formulated using synthetic or natural elastomers. The synthetic or natural elastomers in gum cuds have an adhesive-like character, which enables them to adhere to any surface if not properly discarded. To overcome the stickiness problem, biodegradable chewing gums based on poly(lactic acid-co-caprolactone) elastomers and plasticized poly(D,L-lactic acid) have been formulated in US Patent no.5672367 [5] and 6613363 [6], respectively. Such MCGs

are currently widely accepted in oral healthcare [7].

MCGs contain active drug ingredients either in a gum base or sweetened coating. However, the load of active substances and rate of release must be fine-tuned for each product; some drug ingredients have an unpleasant, bitter, or metallic taste [8]. For agents used in systemic delivery, MCG is the preferred delivery method [9].

Caffeine, a central nervous system stimulant, is an odourless white crystalline xanthine alkaloid, which inhibits the phosphodiesterase enzyme and has an antagonistic effect on the central adenosine receptor [10, 11]. Adenosine is produced in the body during energy-consuming activities and binds to the adenosine receptors, leading to restlessness and fatigue. To counter the effect of adenosine, caffeine binds to the adenosine receptor and prevents its signalling to increase alertness [10, 11]. Caffeine serves as a key component in various beverages such as tea, coffee, carbonated soft drinks, and energy drinks, which are very popular among people. Moreover, the formulation of caffeine chewing gums with synthetic ingredients and sugar-free coating and the organoleptic characterization of 20 and 50 mg caffeine gums were reported by Aslani *et al* [11]. The present study evaluated plasticized poly(D,L-lactic acid) biodegradable caffeine MCG for effectively managing fatigue.

## EXPERIMENTAL

### Ingredients

Poly(D,L-lactic acid) powder with  $M_w$  18,000 – 28,000 was used as a bulking agent to prepare plasticized poly(D,L-lactic acid) chewing gums, and the gum former was purchased from Sigma-Aldrich (India) Private Limited. Talc, ester gum, and beeswax were purchased from C.D.H. (New Delhi, India). Photoactive titanium dioxide used as a filler was purchased as solid flakes from Smart Nanoz Private Limited (Pune, India). Distilled monoglycerides used as an emulsifier were purchased from Estelle Private Limited (Maharashtra) in liquid form; granular peppermint flavour was purchased from Glee Gum Kit (USA); Triacetin, PEG-600, tributyl citrate, soya oil, sunflower oil, glycerol, and triethyl citrate used as plasticizers were purchased from C.D.H. (New Delhi, India). Stearic acid and PEG-4000 used as plasticizers were purchased from C.D.H. (New Delhi, India) as a white powder and solid flakes, respectively. Xanthum gum used as a binder was purchased from C.D.H. (New Delhi, India) in powder form. Sugar alcohols malitol and sorbitol used as sweeteners were purchased from C.D.H.

(New Delhi, India) in solid powder form. Xylitol and neotame used as artificial sweeteners were obtained as a gift sample from J.J.D. Enterprises (Ghaziabad, UP, India). Caffeine was purchased from HiMedia Laboratories Pvt. Limited (Nasik, Maharashtra, India).

### Preparation of biodegradable plasticized poly(D,L-lactic acid) chewing gum

Biodegradable plasticized poly(D,L-lactic acid) chewing gums were prepared using a modified method recommended by Li *et al* [6]. In brief, a laboratory sigma blade mixer (1kg) with a front to rear speed ratio of 2:1 was preheated at 80 °C, and the gum base poly(D,L-lactic acid), plasticizer, and photoactive titanium dioxide were added to it. By using different types of plasticizers, different formulations of poly(D,L-lactic acid) chewing gum samples were prepared. After 15 min of mixing, talc and ester gum were slowly added by continuously mixing the polymer for 5 more min. Subsequently, beeswax and distilled monoglycerides were added and mixed using z-shaped blades of the sigma blade mixer with continuous stirring for 30 min. The ingredients were further kneaded for 15 min by using the blender. Later, the gum base was spread using a roller into a thin sheet, cut into 10-g strips, and stored at room temperature.

Poly(D,L-lactic acid) synthetic biodegradable chewing gums were prepared with (15 % w/w) of either triacetin, stearic acid, PEG-600, tributyl citrate, soya oil, sunflower oil, glycerol, triethyl citrate, PEG-4000, or castor oil as a plasticizer. Photoactive titanium dioxide (15 % w/w), talc, and ester gum (10 % w/w) were used as bulking agents. Beeswax and distilled monoglycerides (7.5 % w/w) were used as emulsifiers in the formulation.

### Coating of plasticized poly(D,L-lactic acid) chewing gum

The plasticized poly(D,L-lactic acid) chewing gum was coated with a sweetener and corn syrup, and the mixture was heated at 60 °C for 15 min and allowed to mix uniformly [12]. The sweetener blend was prepared by mixing sugar alcohols such as mannitol and sorbitol, artificial sweeteners such as neotame and xylitol, and a binder such as xanthan gum. Gum pieces were dipped in the coating solution, and a dry powder material (sweetener) was applied after 1 min ensuring that the liquid evenly covered the pieces. This process helped to dry the liquid coating and is referred to as dry charging [12,13]. A total of 10 mg of caffeine was pre-blended with the dry charge material and

peppermint flavour. The dry charge material was covered using a few liquid applications, and subsequently, the coating was dried in a hot air oven with temperatures ranging from 25 to 35 °C. To coat MCG, six coating solutions with different sweetener concentrations (1 – 6 % w/w) were used.

The gum pieces were rolled on the coating solution containing the sweetener and then dipped in the coating solution to make the coating even. Subsequently, the gum pieces were placed on a glass dish covered with a plastic wrap in a refrigerator.

### **Coating firmness determination**

To determine the firmness of the coating solution, a TA.XT Express Enhanced Texture Analyser (Stable Micro Systems, Godalming, Surrey, UK) was used. To record and analyse the results, the Exponent Light Express software (version 5.1.1.1, Stable Micro Systems), was used. Macros were used in the software to calculate the variables and parameters, and the data was further analysed in MS Excel.

### **Characterization of plasticized poly(D,L-lactic acid) chewing gum**

#### **Texture profile analysis**

Texture profile analysis (TPA) is a test for analysing the textural properties of food, in which the samples are double-compressed using a texture analyser [14]. This method was first developed by General Foods Corporation in 1963 [15,16]. In this test, food samples are compressed twice in a motion that mimics biting and chewing to calculate many primary and secondary textural parameters, such as hardness, fracturability, springiness, cohesiveness, adhesiveness, gumminess, chewiness, and resilience [17]. The probe used for TPA was a 35-mm diameter (P/35) compression platen.

#### **Biodegradation studies**

To test the degradability of chewing gum bases, they were rolled into 2 mm thick slabs and placed on metal plates with dimensions 5 cm × 25 cm. The weathering was examined using the methods described in US Patent no. 7479293B2 [16,18], which is similar to that in ISO 4892, in which a wetting cycle is run for 2 h at 40 °C, alternating with 6 h of illumination with a UV bulb at 45 °C. The cycle was run until an illumination period of 2500 h was achieved. The degradation of the chewing gum base is associated with the

increase in chalking on the surface. The chalking on the surface of test slabs was visually assessed in each case before and after weathering and qualitatively assessed on a scale from 1 to 6, where 1 denoted severe chalking and 6 denoted no chalking.

### **Microstructure characterization**

To further investigate the morphological surface properties of the gum base, the microstructure of the gum base was examined using scanning electron microscopy (SEM) [19]. The MCGs with or without a plasticizer, sweetener coating, and drying were fixed on aluminium stubs and examined at a magnification of 120x through a Philips scanning electron microscope, model 30 at an accelerating voltage of 5 kV [20].

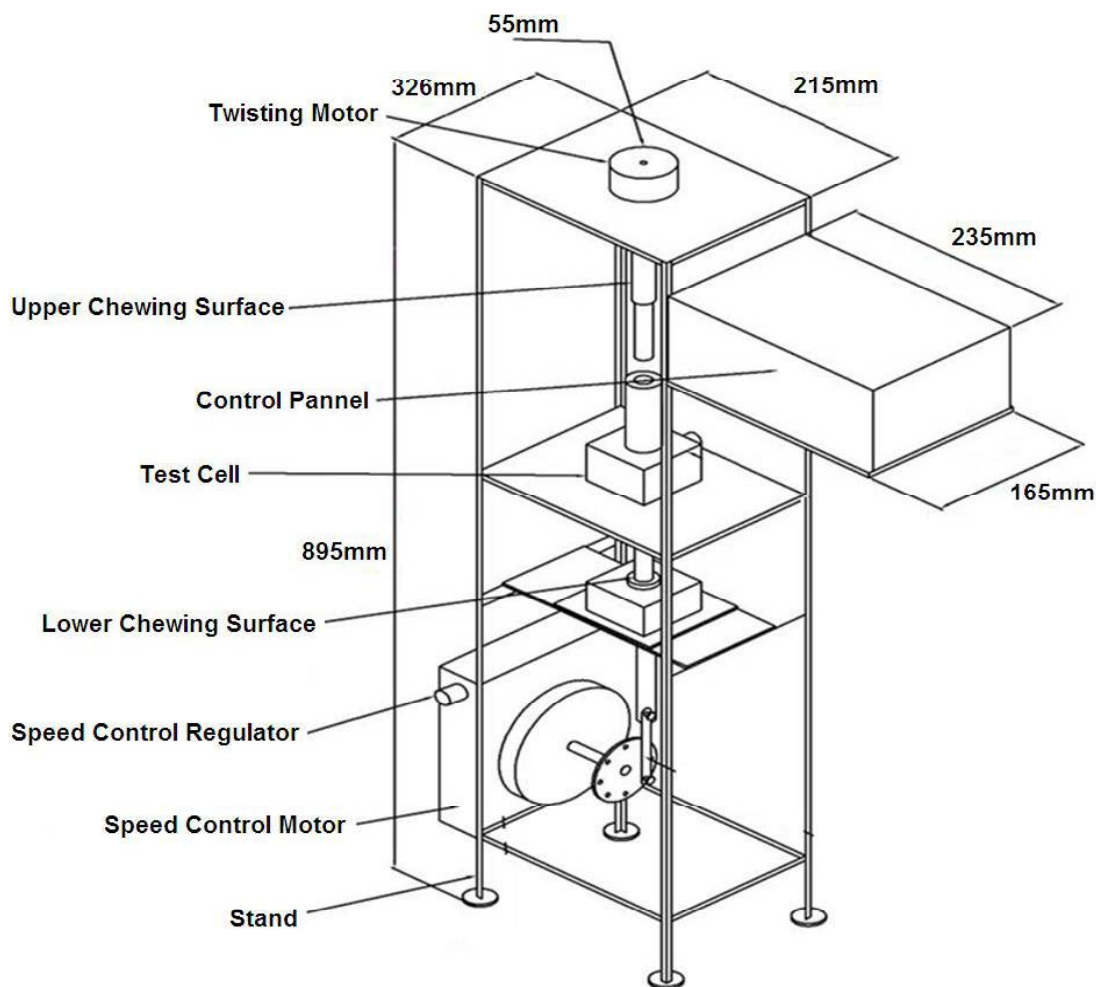
### **In vitro drug release**

To examine the drug release *in vitro*, a modified chewing apparatus was fabricated to mimic human chewing. The device is registered as application/design number: 260364, journal number 34/2015, under the Controller General of Patents, Designs and Trademarks, Department of Industry Policy and Promotion, Ministry of Commerce, Government of India [21]. A schematic of the modified *in vitro* chewing machine is presented in Figure 1. It has functions similar to those of the chewing apparatus developed by Kvist *et al* [22], which has a single chewing module comprising a stainless steel test cell on which two vertically oriented pistons are mounted, serving as upper and lower chewing surfaces, respectively [16]. The cell is filled with 25–50 mL of aqueous medium, and the chewing gum is loaded onto the lower chewing surface. The lower surface moves up and down, and the upper surface has a motor that twists to masticate the chewing gum and to agitate the test medium.

The distance between chewing surfaces, frequency of the strokes, and the angle of twisting can be adjusted as required [22]. A chamber in thermal contact with the lower surface provides thermostat.

### **Sensory evaluation**

The future commercialization of plasticized poly(D,L-lactic acid) caffeine chewing gums depends on consumers' response. Sensory evaluation methods were adopted in this study to investigate the attributions of the poly(D,L-lactic acid) caffeine chewing gum.



**Figure 1:** *In vitro* chewing apparatus

The sensory evaluation helps to identify critical attributes that must be considered during product and process development. The sensory evaluation of the poly(D,L-lactic acid) caffeine chewing gum with a low-calorie sweetener was performed to detect any variation in the sensory attributes of the chewing gum resulting from the incorporation of the sweetener coating solution (1– 6 % w/w) containing artificial sweeteners [23]. The evaluation was performed in a well-lit room, which was free from any odour. For the evaluation of appearance and colour, panel booths were uniformly illuminated with special specific daylight bulbs. A team of three men and three women was selected based on their sensitivity to sweetness and trained to identify and quantify the sensory characteristic [16] of the plasticized poly(D,L-lactic acid) caffeine chewing gum. Informed written consent was obtained from all participants. The sensory evaluation was conducted on the basis of the 9-point hedonic scale, in which 9 denoted 'like extremely' and 1 denoted 'dislike extremely' [16]. The plasticized poly(D,L-lactic acid) caffeine chewing gum was graded with a low-calorie sweetener against a

control with 6 % w/w sucrose [23] for taste and sweetness, consistency, softness, and overall acceptability.

### Statistical analysis

Data were analysed using one-way analysis of variance followed by a least significant difference test for multiple sample comparison by using Sigma Stat (version 3.5, Systat Software Inc., Chicago, IL, USA). Statistical significance was set at  $p < 0.05$ .

## RESULTS

### Coating firmness

Table 1 summarizes the coating firmness data for plasticized poly(D,L-lactic acid) chewing gum formulations (MCG-1 to MCG-10). Coating firmness was determined with a cylindrical aluminium probe (P/3) with a diameter of 3 mm. The results are shown in Table 1.

**Texture profile**

Table 2 presents TPA parameters [16] of plasticized poly(D,L-lactic acid) chewing gum formulations (MCG-1 to MCG-10). The reference standard for determining TPA values was the Military Energy Gum (Marketrigh Inc., IL, USA). The control standard was a branded chewing gum named Chicza manufactured by Mayan Rainforest Company, Suffolk, UK [16].

**Biodegradation**

Biodegradation results of MCG-1 to MCG-10 formulations are presented in Table 3. MCG-1 and MCG-7, which were plasticized using triacetin and glycerol, exhibited significant biodegradation with a chalking score of 1 and 2, respectively.

**Table 1:** Coating firmness (kg) for plasticized poly(D,L-lactic acid) chewing gum

Formulation code	Coating-1	Coating-2	Coating-3	Coating-4	Coating-5	Coating-6
MCG-1	0.755	0.916	0.937	1.470	1.464	1.871
MCG-2	0.898	0.910	1.176	1.140	1.493	1.887
MCG-3	0.868	1.051	1.086	1.095	1.060	1.664
MCG-4	0.896	0.912	1.284	1.288	1.404	1.482
MCG-5	0.588	0.658	0.965	0.779	0.941	1.061
MCG-6	0.791	0.859	0.746	1.039	1.419	1.378
MCG-7	0.797	0.836	0.877	0.957	0.979	1.384
MCG-8	0.822	1.010	1.043	1.177	1.255	1.350
MCG-9	0.799	0.882	1.028	1.289	1.116	1.269
MCG-10	0.740	0.800	0.860	0.769	1.362	1.501
Avg.	0.795	0.883	1.002	1.100	1.249	1.484
SD	0.090	0.109	0.158	0.224	0.208	0.260

**Table 2:** TPA values of various plasticized poly(D,L-lactic acid) chewing gum formulations

Test ID	Hardness (g)	Adhesiveness (g-s)	Springiness*	Cohesiveness*	Gumminess <sup>#</sup>	Chewiness (g)	Resilience*
TPA,MCG-1	3750.523	-51.13	0.966	0.364	1580.88	1526.23	0.249
TPA,MCG-2	4143.839	-	0.316	0.215	1021.71	332.887	0.203
TPA,MCG-3	4347.27	-	0.321	0.213	844.839	301.691	0.177
TPA,MCG-4	4091.319	-	0.304	0.211	910.349	312.215	0.162
TPA,MCG-5	4019.025	-	0.308	0.214	915.739	316.362	0.165
TPA,MCG-6	4244.023	-	0.326	0.211	929.163	302.513	0.167
TPA,MCG-7	3963.121	-21.12	0.314	0.210	926.170	268.425	0.165
TPA,MCG-8	4567.104	-	0.341	0.215	1070.635	314.450	0.199
TPA,MCG-9	4116.321	-	0.326	0.217	995.414	340.061	0.182
TPA,MCG-10	4054.287	-	0.345	0.225	903.169	301.122	0.166
Coef.var	0.065	-42.13	0.031	0.034	0.070	0.065	1.597
SD	221.870	21.220	0.203	0.047	211.78	385.11	0.027
Avg.	4141.971	-36.125	0.386	0.229	1009.800	431.59	0.183

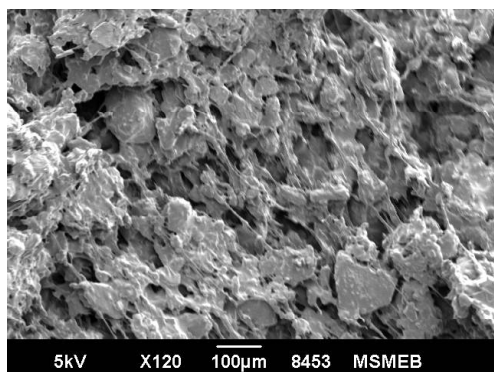
\*Springiness, cohesiveness, and resilience are ratios and are therefore presented without units. <sup>#</sup>Gumminess is a result of hardness and cohesiveness [16]

**Table 3:** Biodegradation results

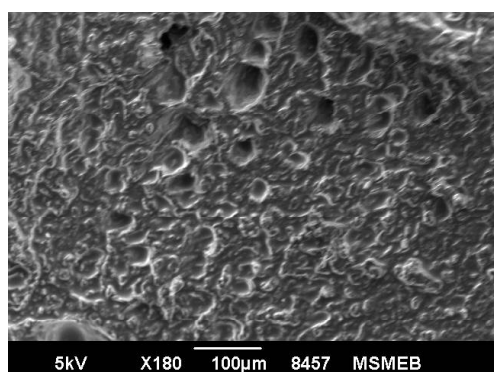
Formulation code	Chalking before weathering	Chalking after weathering (mean± SD, n=6)
MCG-1	6	1 ± 0.10
MCG-2	6	5 ± 0.18
MCG-3	6	6 ± 0.12
MCG-4	6	3 ± 0.17
MCG-5	6	5 ± 0.12
MCG-6	6	6 ± 0.11
MCG-7	6	2 ± 0.12
MCG-8	6	5 ± 0.13
MCG-9	6	4 ± 0.04
MCG-10	6	3 ± 0.12

**Microstructure characteristics**

The SEM images in Figures 2 and 3 reveal that formulations with a plasticizer, sweetener coating, and drying had smoother surfaces compared with those without a plasticizer, sweetener coating, and drying. Overall, the SEM results demonstrated that the addition of plasticizers, coating with sweetener, and drying can increase the acceptance of MCGs among patients because of the aesthetic appearance of these MCGs.



**Figure 2:** SEM image of MCG-1 formulation before coating and drying



**Figure 3:** SEM image of MCG-1 formulation after coating and drying

### **In vitro drug release**

Table 4 presents the drug release profiles of MCG-1 to MCG-10 formulations. With a mean chewing time of 15 min, the highest drug releases of 87 % and 80 % were observed in the MCG-1 and MCG-9 formulations, which were plasticized using triacetin and triethyl citrate, respectively. MCG-5 formulation, in which soya oil was used as a plasticizer, exhibited the lowest drug release of 57 % among various formulations.

### **Sensory properties**

The sensory evaluation results in Table 5 suggest the feasibility of creating commercial plasticized poly(D,L-lactic acid) caffeine chewing gum formulations. Coating three solution used for coating MCG was similar to control and possessed the same required taste, consistency, and softness. However, the overall acceptability score of the plasticized poly(D,L-lactic acid) caffeine chewing gum was lower ( $p < 0.05$ ) than that of sucrose, which was used as a control.

**Table 4:** *In vitro* drug release with the following adjustments: twisting angle, 20°; RPM 60 strokes/min; distance, 1.5 mm; and temperature, 37.5 °C

Time interval (min)	% Drug release <sup>#</sup>									
	MCG-1	MCG-2	MCG-3	MCG-4	MCG-5	MCG-6	MCG-7	MCG-8	MCG-9	MCG-10
5	74±0.12	45± 0.10	48±0.16	69±0.4	43± 0.13	44±0.12	72±0.14	47±0.13	71±0.17	44±0.12
10	80± 0.15	54± 0.11	59±0.10	74± 0.16	51± 0.11	55± 0.19	77±0.12	55±0.11	75±0.11	53±0.16
15	87± 0.18	59± 0.09	65±0.14	77±0.18	57± 0.15	60± 0.11	82±0.13	62±0.11	80±0.13	59±0.19
20	93± 0.11	67± 0.13	73±0.17	81± 0.17	64± 0.13	68± 0.10	89±0.19	71±0.10	85±0.17	66±0.14
25	97± 0.09	73± 0.11	79±0.19	86± 0.15	70± 0.13	75± 0.11	94±0.11	76±0.11	92±0.10	71±0.13

<sup>#</sup>Data are expressed as mean ± SD (n = 6)

**Table 5:** Sensory evaluation of plasticized poly(D,L-lactic acid) chewing gum

Characteristic	Control	Coating 1	Coating 2	Coating 3	Coating 4	Coating 5	Coating 6
Taste and sweetness	09 ± 0.1 <sup>a</sup>	06 ± 0.1 <sup>b</sup>	06.5± 0.3 <sup>b</sup>	08 ± 0.5 <sup>a</sup>	07± 0.5 <sup>b</sup>	07 ± 0.5 <sup>b</sup>	07.5± 0.5 <sup>b</sup>
Consistency	09 ± 0.2 <sup>a</sup>	06 ± 0.2 <sup>b</sup>	06.5± 0.8 <sup>b</sup>	07 ± 0.5 <sup>b</sup>	07 ± 0.7 <sup>b</sup>	07 ± 0.6 <sup>b</sup>	07.0± 0.4 <sup>b</sup>
Softness	09 ± 0.6 <sup>a</sup>	07 ± 0.6 <sup>b</sup>	07 ± 0.5 <sup>b</sup>	07.5± 0.4 <sup>b</sup>	07.5± 0.2 <sup>b</sup>	07.5± 0.1 <sup>b</sup>	07.5± 0.8 <sup>b</sup>
Overall acceptability	09 ± 0.7 <sup>a</sup>	07 ± 0.5 <sup>b</sup>	07 ± 0.3 <sup>b</sup>	09 ± 0.6 <sup>a</sup>	07.5± 0.2 <sup>b</sup>	07.5± 0.1 <sup>b</sup>	07.5± 0.1 <sup>b</sup>

Means in each row with different superscripts (a, b) are significantly different (least significant difference test,  $p < 0.05$ ) from each other. Data are presented as mean ± standard error mean (n=6)

## **DISCUSSION**

MCGs are made of water-insoluble and non-biodegradable synthetic rubber. The stickiness and adhesive texture [14] of a gum makes it impossible to be removed from the site of

adherence. The high cleaning cost of environmental pollution caused by synthetic gums results in demands for the development of biodegradable chewing gums, which are palatable and have an appropriate texture, reasonable shelf life, and long-lasting flavour.

Wakefulness is necessary for individuals who work late at night such as those in the emergency services. Through a caffeine chewing gum, rapid doses of caffeine can be delivered within few minutes of chewing.

Aslani *et al* [11] prepared 22 formulations of the caffeine chewing gum by using four synthetic gum bases and evaluated their organoleptic properties at different stages of formulations. Henry *et al* [24] demonstrated that the caffeine gum has a slow drug release rate after 40 min of chewing, a condition in which 97 % of drug has been already released. In previous studies, encapsulating the caffeine particles with zein, shellac, and hydroxypropylmethyl cellulose [25] caused changes in the physical properties of caffeine.

Military Energy Gum (Marketright Inc.) was used as the reference standard. The firmness of the third coating solution was 1.002 kg, which is similar to that of the reference chewing gum. Moreover, the coating firmness increased from 0.795 to 1.484 kg with the increase in sweetener concentration. The coating operation should be performed immediately after formulation to prevent the migration of water from the core of the gum to the surface during storage.

The results of TPA by using a 35-mm probe indicated that the peak load required to deform MCGs (MCG-1 to MCG-10) was 4141.97 g. The MCGs deformed and then aggregated together to form a chewable gum mass during the test. MCG-1 and MCG-7 with triacetin and glycerol as plasticizers exhibited adhesiveness values of -51.13 and -21.12 g-s, respectively. During storage, the plasticizer of the chewing gum gets evaporated, and the chewing mass gets entrapped in a sponge, which presents the textural characteristic to the chewing gum. MCG-3 and MCG-6 with PEG-600 and sunflower oil as plasticizers, respectively, had a biodegradation score of 6, which represents no chalking and no biodegradation. Moreover, the biodegradation data were consistent with TPA data. The high biodegradation values of 1 and 2 in MCG-1 and MCG-7 formulations, respectively, could be because of their low hardness values of 3750.523 and 3963.121 g, respectively, indicating severe chalking on the gum surface.

SEM images captured the plasticized poly(D,L-lactic acid) gum base before and after coating and drying for 1 h at 50 °C. The images revealed a spongy material with a highly porous surface and large ridge-like areas that might be created because of the shearing and drying of the samples. Moreover, MCG-1 formulation exhibited

a smoother surface compared with the formulations without coating. Thus, MCG-1 formulation may receive a higher patient acceptance because of its aesthetic surface property.

A modified *in vitro* chewing apparatus was used to determine *in vitro* drug release. Among all plasticized poly(D,L-lactic acid) caffeine MCG formulations, MCG-1 with triacetin as the plasticizer, exhibited the highest drug release of 97 % after 25 min of chewing, which indicates that the drug was uniformly distributed in the gum matrix. A study by Aslani and Jalilian demonstrated that 20 and 50 mg [11] of caffeine MCGs released 88 % and 89 % of their drug after 30 min, respectively. The drug release from the MCG depends on the chewing speed, chewing intensity, and the amount of saliva produced during chewing [11]. We observed a drug release pattern of 43 – 74 % after 5 min, 57 – 87 % after 15 min, and 70 – 97 % after 25 min of kneading by a modified *in vitro* chewing apparatus for various plasticized poly(D,L-lactic acid) caffeine MCG formulations. A study conducted by Henry *et al* [24] on the drug release of caffeine chewing gums demonstrated a drug release of 88 % after 20 min and 97 % after 40 min.

For MCGs containing different blends of sweeteners (1–6 % w/w), neotame was used as an artificial sweetener, which completely masked the bitter taste of caffeine. The high score for taste, consistency, and softness of the control could be because of its sucrose content. Sucrose is responsible for the binding effect in MCGs and helps to form a network of microfibrils, which creates a binding effect in the product. Sensory evaluation results revealed that the low-calorie sweetener neotame can be beneficial to consumers because it provides few empty sugar calories.

## CONCLUSION

The study findings indicate the feasibility of formulating MCG with plasticized poly(D,L-lactic acid) as the gum base and a combination of sweeteners as the taste enhancer. Plasticized poly(D,L-lactic acid) caffeine chewing gums possess the advantages of synthetic chewing gums as well as additional advantages such as effective and efficient caffeine delivery to control fatigue. Furthermore, triacetin and glycerol used as plasticizers are functional and edible, producing a desirable gum texture, and are biodegradable.

## DECLARATIONS

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### Conflict of Interest

No conflict of interest associated with this work.

### Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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