FORMULATION AND EVALUATION OF MEDICATED CHEWING GUM OF TERBUTALINE SULFATE FOR THE ASTHAMATIC MANAGEMENT

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ABSTRACT

Objective: This experiment aimed to improve the bioavailability of terbutaline sulfate by formulating it as medicated chewing gum.

Methods: By employing zein as the gum foundation and the melting process, chewing gum was created with the desired outcome.

Results: All formulations had thicknesses ranging from 3.61 to 3.68 mm in the lateral direction and from 5.22 to 5.41 mm in the longitudinal direction. All formulations had hardness values between 3.1 and 3.4 kg/cm². All formulations had weight variations between 1.6% and 2.1%. All of the formulations had the same quantity of medication, which varied between 95.2 and 96.9%. Drug release from terbutaline sulfate chewing gum (TCGs) in simulated saliva (pH 6.8 buffer solution) was investigated by examining the samples up to a half-hour later. It was discovered that the drug release from the formulations ranged from 64.28 to 89.56% in 30 min.

Conclusion: The release of the medication was reduced when the gum basis (zein) content in the formulations was increased. It was discovered that, after 30 min, TCG1 emitted the most proportion of terbutaline sulfate. As a result, it may be regarded as the finest formulation available.

Keywords: Chewing gum, Oral delivery, Terbutaline sulfate, Zein, Anti-asthmatic.

INTRODUCTION

Because oral medication distribution is easier to use than other dose forms, it is the most widely accepted method of drug administration. Chewing gum has a confectionery purpose, but nowadays, because it absorbs substances quickly through the mouth canal, it also demonstrates the greatest and most convenient medication delivery technology [1]. Chewing gum with medication is a local or systemic delivery method. Drugs may be quickly absorbed by the oral mucosa for systemic disorders, resulting in a fast beginning of action and bioavailability, or they may be released locally for oral therapy [2-6]. By doing this, first-pass metabolism and gastrointestinal tract metabolism are avoided. For the distribution of medications meant to have a rapid beginning of action, this delivery strategy is therefore greatly appreciated [7-10].

A beta-2 adrenergic receptor agonist called terbutaline sulfate is prescribed to asthmatic patients who have bronchitis and emphysema to treat reversibly occurring bronchospasm. The inhaled version can be taken up to 3 times a day; therefore, its duration is brief, and its therapeutic window is broad. Since the medication is inhaled and asthmatic episodes require a rapid beginning for spasm treatment, it is not suitable for usage in youngsters in particular [11].

Therefore, the idea was to create a medicated chewing gum delivery system that would release and absorb terbutaline sulfate quickly, enhancing patient compliance and speeding up the drug's beginning of action.

METHODS

Preformulation study

The procured sample of terbutaline sulfate was investigated for its physical characteristics, color, and smell. The characters that were seen were contrasted with those described in books [12].

Calibration curve of terbutaline sulfate by ultraviolet (UV) spectrophotometry [13]

10 mg of terbutaline sulfate was carefully weighed before being put into a 10 mL volumetric flask. After adding 5 mL of distilled water, the liquid was sonicated for 15 min. After adding distilled water to get the final amount to 10 mL, it was well mixed (1 mg/mL). The resultant solution was further diluted to yield concentrations ranging from 10 to 100 μg/mL using distilled water as blank.

Fourier-transform infrared spectroscopy (FT-IR) spectral study

To determine if the medicine and the polymer are compatible, the FT-IR spectra of terbutaline sulfate and a physical combination of zein and terbutaline sulfate were collected and examined for the vibrational peaks of the functional groups present.

Formulation of terbutaline sulfate chewing gum (TCG)

The TCG was made using the standard melting technique. Briefly, the gum base (zein) was warmed over a hot water bath to generate a molten mass and to the molten mass was added the plasticizer (glycerine) and combined completely while slowly heating in a porcelain dish. The dish was kept in a water bath with the temperature regulated between 35°C and 45°C. To the aforesaid bulk, a precisely determined amount of the medication terbulatine sulfate was added. The aforementioned mixture was continuously stirred for up to 30 min while the necessary amounts of mannitol and sucrose were added. Eventually, the concoction was combined with just the right quantity of flavor – peppermint oil. After pouring the bulk into the mold, it was let to cool at ambient temperature. The gum pieces were removed [14].

A glycerin and sweetener solution was used to coat the TCG. After 15 min of heating at 60°C, this mixture was given time to thoroughly

combine. To enable the liquid to cover the gum pieces uniformly, they were dipped in the solution for duration of 1 min.

Evaluation of TCGs [15-17]

Weight variation test

Ten chewing gums were weighed in a batch, and the average weight was determined. After that, each gum was weighed separately, and the formula was used to determine the percentage of weight difference from the average weight.

$$\%weight\ variation = \frac{\left(Individual\ weight - average\ weight\right) \times 100}{Average\ weight}$$

Hardness

The Monsanto hardness tester was used to measure the TCG's hardness. To crush the ZCG, the gum was positioned in between the plunger and tightened. The force needed was plainly observed on the scale.

Stickiness

After placing the medicated chewing gum on a flat surface, it was struck for 10 min by a 250 g Teflon hammer. Thirty hammerings/min were used. The mass that adhered to the hammer was measured and recorded after the allotted length of time.

Thickness

Using a Vernier caliper, the TCGs' longitudinal and lateral thicknesses were measured.

Uniformity of content

The chewing gum was broken up by hand and put into a flask with 10 mL of ethyl acetate. The suspension was centrifuged at 10,000 rpm for 15 min using a benchtop centrifuge (Remi, Mumbai) after the flask had been vortexed for 15 min. The supernatant was collected and subjected for UV examination for estimating the terbutaline concentration as specified in the calibration curve technique. The quantity of terbutaline was determined using the equation of the calibration curve.

In vitro release

A TCG was submerged in a pH solution (buccal cavity) kept at a constant pH of 6.8. It was then put on a magnetic stirrer and stirred. Every 5 min, 2 mL of the solution were removed and replaced with a new buffer solution. At regular intervals of 5, 10, 15, 20, 25, and 30 min, the sample was removed. After the procedure was finished, the release profile and the quantity of terbutaline sulfate in each sample were calculated using UV analysis.

RESULTS AND DISCUSSION

Preformulation studies

The terbutaline sulfate produced from the source was found to have the following physical characteristics (Table 2). The results were in consonance with reported data [18].

The calibration curve of terbutaline sulfate was constructed by analyzing the absorbance obtained in the spectrum of various dilutions of known concentration and plotting the concentration against the absorbance value. The UV spectrum of terbutaline sulfate is shown in Figs. 1 and 2 displays the results from the calibration curve. The absorption maxima of terbutaline sulfate in distilled water were found to be 277.1 nm.

The FT-IR spectrum of terbutaline sulfate revealed the expanding peaks of vibrations of C-N, C-O, O-H, N-H, C-C, and C-H. All these peaks were also present in the physical mixture of the drug and zein suggesting a physical compatibility among them (Fig. 3a and b).

Table 1: Composition of TCG

S. No.	Ingredient	TCG1	TCG2	TCG3	TCG4
1	Zein (%w/w)	25	35	45	55
2	Terbutaline sulfate (%w/w)	1	1	1	1
3	Mannitol (%w/w)	14.6	14.6	14.6	14.6
4	Sucrose (%w/w)	56	46	36	26
5	Peppermint oil (%w/w)	0.6	0.6	0.6	0.6

TCG: Terbutaline sulfate chewing gum

Table 2: Physical characteristics of terbutaline sulfate

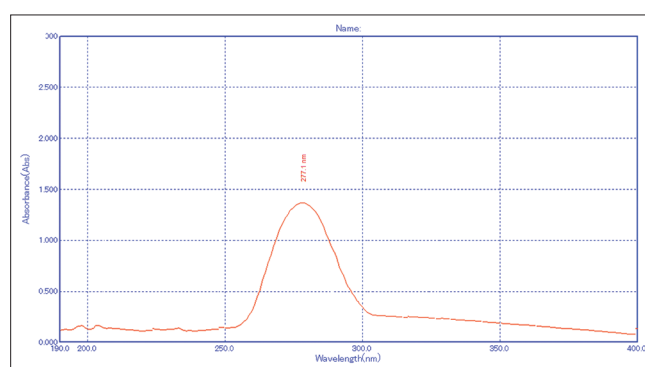| S. No.	Test parameter	Observation
1	Color	Greyish-white
2	Odor	Odorless
3	Taste	Bitter
4	Appearance	Crystalline
5	Melting point	249–251°C
6	Solubility	Soluble in water and insoluble in organic solvents

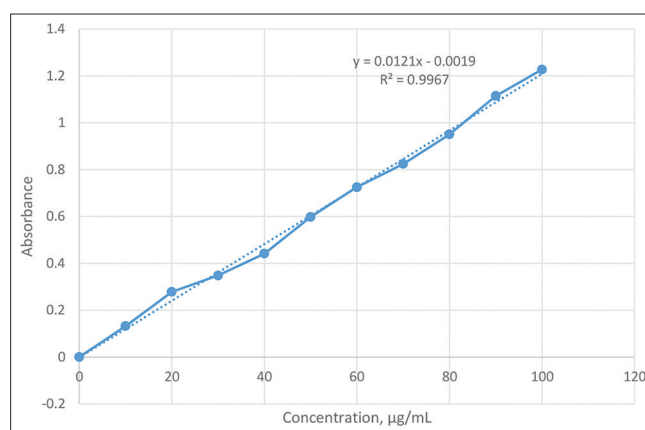**Fig. 1: Ultraviolet spectrum of terbutaline sulfate**

Fig. 2: Calibration curve of terbutaline sulfate

Formulation of TCGs

The melting technique was used to create TCGs. The gum base was zein, the plasticizer was glycerine, the sweeteners were sucrose and mannitol, and the flavoring was peppermint oil. The chewing gum includes of a water-insoluble component, the gum base which needs to remain in the oral cavity, and a water-soluble portion, the medication, which is dissolved in the gum base during the production process. The medication is released during the chewing process from the base and absorbed through the extensive capillary network found in the buccal cavity.

Table 3: Quality parameters of TCGs

Formulation code	Thickness (mm)		Hardness (Kg/cm^2)	Weight variation (%)	Stickiness	Drug content (%)
	Longitudinal	Lateral				
TCG1	5.22	3.61	3.1	1.6	Non-sticky	95.2
TCG2	5.41	3.67	3.2	1.9	Non-sticky	95.4
TCG3	5.33	3.65	3.4	1.8	Non-sticky	96.7
TCG4	5.35	3.68	3.3	2.1	Non-sticky	96.9

TCG: Terbutaline sulfate chewing gum

Table 4: *In vitro* release of terbutaline from TCGs

Formulation	5 min	10 min	15 min	20 min	25 min	30 min
TCG1	28.63	44.28	59.56	71.39	77.54	89.66
TCG2	22.62	34.58	44.28	50.24	64.48	72.29
TCG3	19.22	28.15	37.11	48.26	59.59	68.63
TCG4	16.41	24.29	30.18	41.03	53.44	64.28

TCG: Terbutaline sulfate chewing gum

Evaluation of TCGs

Weight variation, hardness, thickness, weight homogeneity, and drug release were assessed for the TCGs (Table 3).

All formulations had thicknesses ranging from 3.61 to 3.68 mm in the lateral direction and from 5.22 to 5.41 mm in the longitudinal direction. The formulation's consistent thickness facilitates simple and beautiful packaging. It also aids in guaranteeing individual compliance.

Every formulation's tablet hardness fell between 3.1 and 3.4 kg/cm^2. Due to the combination of formulations, the hardness of each formulation varied. The low hardness of the formulations makes it simple to chew the formulation and illustrates the correct distribution of the plasticizer throughout the formulation.

All formulations had weight variations between 1.6% and 2.1%. Each gum may hold the same quantity of medication if there is less variance in the weight of the gums.

All of the formulations had the same quantity of medication, which varied between 95.2% and 96.9%. Every formulation is safe to eat due to its consistency in thickness, hardness, weight fluctuation, and medication concentration.

By striking the gums against the formulations and watching the hammer's bells and surface for any trapped material, the stickiness of the formulations was assessed. In the test, it was discovered that none of the formulations were sticky.

***In vitro* release**

When compared to traditional oral medication delivery systems, the drug release mechanism of medicated chewing gums is significantly different. The medication administration in medicated chewing gums may be impacted by the patient's chewing behavior in addition to the dose type. To provide the medication to the teeth without involving dissolution, mechanical therapy is necessary. Drug release from TCGs in simulated saliva (pH 6.8 buffer solution) was investigated by examining the samples up to a half-hour later. It was discovered that the drug release from the formulations ranged from 64.28 to 89.56% in 30 min (Table 4).

The formulations made it easy for the medicine to be released. The data in Fig. 4 demonstrate that a reduction in the drug's release occurred when the gum base (zein) content in the formulations was increased. It could be because the gum base is insoluble in water, which limits the drug's ability to travel through it. The results showed that after 30 min, TCG1 emitted the most proportion of terbutaline
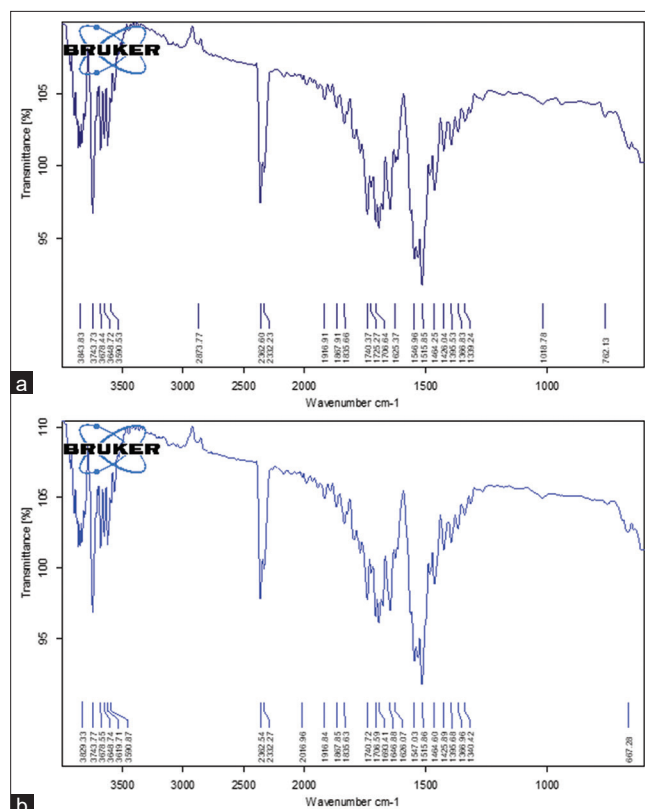

Fig. 3: (a) Fourier-transform infrared spectroscopy spectrum of terbutaline sulfate and (b) Fourier-transform infrared spectroscopy spectrum of terbutaline sulfate and zein (physical mixture)
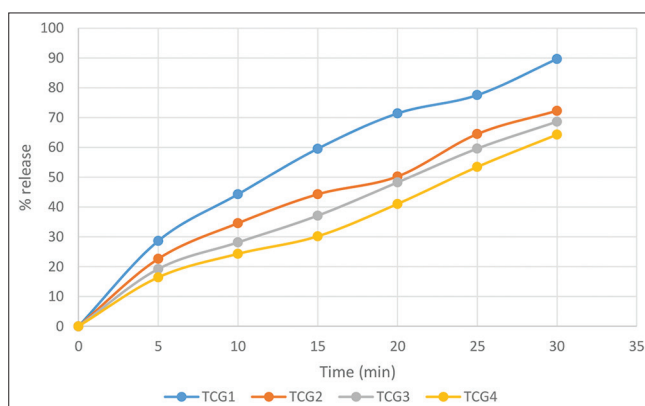

Fig. 4: Percent release of terbutaline sulfate from terbutaline sulfate chewing gums

sulfate. As a result, it may be regarded as the finest formulation available.

CONCLUSION

Zein offers a superior gum foundation for melting-method chewing gum manufacturing. With the exception of TCG1, every formulation had the required qualities, although the release was lower. In the future, more research will be required to improve the parameter for the formation of TCGs with the most desired qualities.

ACKNOWLEDGMENTS

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHOR FUNDINGS

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