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Formulation and Assessment of Allicin Based Medicated Chewing Gum

Namrata Arya[1*], Mohd Vaseem[2], Jasdeep Kaur[3], Nutan Sharma[4]

[1]*Department of Biotechnology, Sanskriti University, Mathura, Uttar Pradesh, India*

[2]*School of Agriculture & Agri-Informatics Engineering, Shobhit Institute of Engineering & Technology, Meerut, Uttar Pradesh, India*

[3]*Department of Chemistry, RIMT University, Mandi Gobindgarh, Punjab, India*

[4]*Department of Chemistry, SGT University, Gurugram, Haryana, India*

ABSTRACT

Oral medication delivery is the most recommended administration method due to its high patient compliance, easy to handle, painless treatment and does not require any special sterile setting. However, several medications taken orally meet physical, biological, and physiological barriers that reduce the therapeutic efficiency of the medications before they reach the systemic circulation. Many researches have been conducted on uncovering alternative methods for oral drug delivery. Medicated chewing gums are an oral drug delivery system where drugs are embodied into the body via chewing gum. They have benefits of easy administration, increased bioavailability and long shelf life. In the present paper an attempt is made to fabricate a medicated chewing gum for treating inflammation and masking taste of garlic. Medicated chewing gum comprises allicin, natural gum base, sugaring agent, fillers, and plasticizers. The obtained medicated gum containing allicin was evaluated for appearance, taste, texture, consistency, elasticity and in vitro drug release activity.

Keywords: Allicin, Buccal route, Chewing gums, Drug delivery, Oral, Pharmaceutical gum

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Corresponding author: Namrata Arya
e-mail ✉: namrata.sobas@sanskriti.edu.in
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INTRODUCTION

Because of its simple administration in the body, feasible delivery, therapeutic response and improved immune activity, oral drug delivery systems have attracted the interest of many researchers [1–3]. An Oral Drug Delivery (ODD) device where the gum serves as a medium to move the drug is medicated chewing gum. These devices can be used medicinally for the treatment of oral and mucosal-related diseases. Based on factors such as chewing time, frequency and time, the drug concentration released from the gum can be determined by physical and chemical properties [4].

Garlic is native to Asia, though it is also grown in Mexico, North Africa, Europe, Egypt, and China. It is well developed in Iran, and in the traditional folk medicines of Iran and different portions of this has already been utilized in medicinal field. It is also utilized as a seasoning and food additives [5]. Garlic acts as an antioxidant that promotes the defence mechanisms of the body towards oxidative damage. It has been shown that high doses of garlic supplements improve antioxidant enzymes in individuals and dramatically reduces oxidative stress in someone having high blood pressure.

Another problem with chewing gums is that they have synthetic gum bases which are not biodegradable in nature. Although natural gum bases such as Gliadin, a protein of wheat grain also known as prolamin can be used in gum due to its good chew ability. The approach of the present study was to fabricate three layer tablets which have poor solubility in water *i.e.* chewing gum. The medicated chewing gum is fabricated from a direct compression method. The medicated chewing gum consists of calcium carbonate (filler), wheat prolamin (natural gum base), allicin (active ingredient), PVA (plasticizer), honey (sugaring agent), glycerin (softener),

cherry oil (flavor). The appearance, elasticity, drug release study and buccal adsorption was evaluated.

LITERATURE SURVEY

A review paper by Turki Al Hagbani and colleagues has discussed alternative ODD system to conventional ODD system. In this paper, the researchers have discussed different compositions of gum and methods for production of the gum. They also have discussed different characterization property of medicated chewing gum such as chewing, firmness and elasticity of chewing gum [6]. Another research paper by Mikaili, Peyman and colleagues have discussed about therapeutic properties and pharmacological uses of biological extract of garlic and shallot [7]. A medicated chewing gum containing cetirizine has been developed for treating cold by S. Chaudhary and A. Shahiwala. Medicinal chewing gums containing cetirizine has been developed for treating cold by Shivang A Chaudhary and Aliasgar F Shahiwala [8].

Thus, alternative ways of consuming oral drugs were developed which involved taste masking of compounds and increasing the bioavailability of the drug. However, the procedure for preparing the gum, on the other hand, is complicated as it consumes both the time and raw materials. Thus, in the present paper, a research was conducted on development and evaluation of allicin based chewing gum.

METHODOLOGY

Materials and methods

Cloves of *Allium sativum* was bought from the local market. It was authenticated by department of the college. Calcium carbonate, glycerin, polyvinyl acetate and honey were purchased from Sigma-Aldrich. *T. aestivum* grain was bought from the local market.

Extraction of allicin from garlic

From prior knowledge it was known that allicin cannot be extracted naturally from cloves of garlic. Alliinase is required for conversion of allin to allicin for transformation of amino acid. The formation of allicin is completed in about 6 seconds, before ingestion, once fresh garlic is smashed or mixed [9]. Acidic conditions (pH 3.5 or below) easily disrupt the function of garlic alliinase and thus eliminates the production of allicin as well as other thiosulfates. Allicin is not stable and deteriorates rapidly over time at room temperature. Allicin in chopped garlic or aqueous garlic supernatants is less soluble than it is in water as a pure substance [10]. For these purposes, garlic material was synthesized through a process that avoided the release of allinase, thus preventing the development of allicin throughout powder production and handling. Garlic cloves were cut into slices 4-5 mm thick filled into vials and lyophilized. Whenever these lyophilized slices of garlic cloves became fully desiccated, they were pulverized to acquire allicin.

Extraction of Prolamin (Gliadin) from Wheat

T. Aestivum grain was weighed and added by continuous stirring for 2 hours with 75% ethanol, and was collected using a muslin cloth. In addition, prolamin was concentrated to obtain the optimal solution. To achieve a sticky gum, this solution was combined with water and heaters at 80°C. The antibacterial and antifungal impact of the prolamin acquired can be regulated by well-diffusion assay.

Formulation of Medicated Chewing Gum

The medicated chewing gum was made using calcium carbonate (filler), wheat prolamin (natural gum base), allicin (active ingredient), polyvinyl alcohol PVA (plasticizer), honey (sugaring agent), and glycerin (softener), cherry oil (flavor). A specific selection of calcium carbonate, wheat prolamin and honey was fixed on the basis of experimenting. 450mg to 500mg and 70 to 90 mg respectively were the most convenient amounts of gum base and calcium carbonate. The gum received may become hard if the amount of gum base and calcium carbonate is raised or lowered above this range.

Using a stirrer, amounts of gum base, honey and calcium carbonate were blended evenly. PVA was soluble in small amounts of ethanol and then combined with the uniform solution previously created. In addition, they combined cherry oil and glycerin to obtain a solid mass. The mass was sliced into sticky ribbons of desired size. The concentrations of ingredients were taken as mention in Table 1.

Table 1. Composition of medicated chewing gum.

Formulation	Calcium carbonate (mg)	Wheat prolamin (mg)	Allicin (mg)	PVA (mg)	Honey (ml)	Glycerin (ml)	Cherry oil
F1	70	450	5	50	10	0.05	0.02
F2	80	450	5	50	10	0.05	0.02
F3	90	450	5	50	10	0.05	0.02
F4	70	500	5	50	10	0.05	0.02
F5	80	500	5	50	10	0.05	0.02
F6	90	500	5	50	10	0.05	0.02
F7	70	550	5	50	10	0.05	0.02
F8	80	550	5	50	10	0.05	0.02
F9	90	550	5	50	10	0.05	0.02

Evaluations of parameter

High-Pressure Liquid Chromatography (HPLC) method: 2.5g of the coarsely powdered extract was refluxed in a water bath for 15mins with 100 ml of methanol. After refluxing the mixture was cooled and filtered. The remaining residue was further refluxed with methanol until a colorless extract is obtained. Combine all the filtrates and makeup the volume to 50ml. Reference solution (allicin in methanol), chromatographic system, mobile phase (acetonitrile and water) was prepared. The spectrophotometer was set at 278nm. The results noted are represented in Table 2 & Table 3.

Table 2. Standard calibration curve of allicin by HPLC.

S. no.	Conc. ug/ml of standard solution	Peak height %
1	20	40.67
2	40	45
3	60	56.66
4	80	54.97
5	100	58.58

Table 3. Standard calibration curve of unknown solution by HPLC.

S. no.	Conc. ug/ml of test solution	Peak height %
1	Unknown	40.06

General appearance: The prepared batches were evaluated for general appearance, color, texture, aroma and taste. The texture of gum was estimated by pressing the gum between thumb and finger. The texture was differentiated into sticky, good and solid mass.

Elasticity study: Elasticity is one of the most significant characteristics of chewing gum. A suitable elasticity of medicated chewing gum makes efficient patient compliance as well as lead to proper drug release. The elasticity was calculated using texture analyzer. The gum of size 1x1mm3 was kept in between two clamps that pressed the gum and started pulling apart till the chewing gum broke. The force needed was recorded. Data collection and calculations were performed.

Buccal absorption test: Beckett et al. have developed a method of estimating permeability of drugs via buccal cavities at different pH. The test was performed using human subjects by swirling 20 ml of solution at pH of 6.0, 6.5, and 7.0 and expelled it after 15 minutes. The subjects then rinsed their mouth with distilled water. The expelled solution and distilled water were mixed together. The concentration of drug present in the expelled was then used to determine the concentration of drug absorbed.

Chewing study of gum formulation: The good taste in the mouth should retain while chewing gum. These performances of six subjects were observed. They were differentiated between good, bad and sticky.

Study of drug release: The *in vitro* study of drug release using phosphate buffer was relatively different from traditional dosage form. Mechanical force is applied to extract drugs from gum. The drug release was affected by chewing ability of the subject. Thus, drug release of allicin medicated chewing gum was performed by creating human saliva like atmosphere. The stimulated saliva contained potassium chloride, calcium carbonate dihydrate, citric acid, potassium bicarbonate, sodium phosphate, potassium phosphate monobasic, and sodium chloride dissolved in water.

RESULTS AND DISCUSSION

Purity determination of allicin

Using HPLC analysis method, purity of extract was performed depending upon retention time. HPLC graph is given in Figure 1.

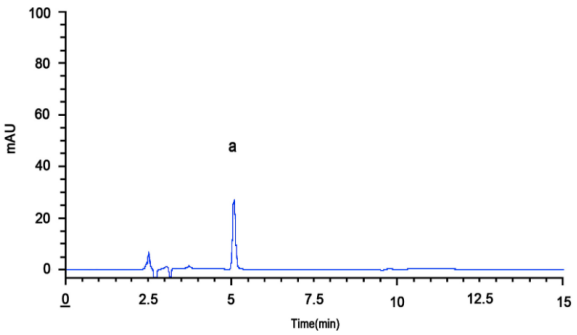

Figure 1. HPLC chromatogram of allicin.

General appearance

Different results were obtained for different formulations as given in the Table 4. Formulations F1, F2, and F8 had demonstrated good texture. Formulations F4 and F7 were sticky, while F3, F6, and F9 were hard. Formulation F5 had a good texture with suitable softness and hardness.

Table 4. Formulation of medicated chewing gum.

Formulation	Color	Texture and Consistency	Total weight	Drug content (%)	Elasticity study (mm)
F1	Dark yellow	Good	605.32 ± 0.13	97.1	11.4
F2	Dark yellow	Good	615.34 ± 0.24	96.6	9.2
F3	Dark yellow	Solid mass	625.7 ± 0.15	95.4	9.4
F4	Dark yellow	Sticky	648 ± 0.10	93.2	10.45
F5	Dark yellow	Very good	667.40 ± 0.23	98.0	10.31
F6	Dark yellow	Solid mass	688.21 ± 0.12	97.1	6.7
F7	Dark yellow	Sticky	701.32 ± 0.05	95.2	10.59
F8	Dark yellow	Good	712.34 ± 0.038	95.2	8.29
F9	Dark yellow	Solid mass	724.14 ± 0.9	95.1	3.7

Elasticity study

The elasticity result obtained by CT3 analyzer was graphically present in Figure 2. Formulations F4, F5, and F7 were highly elastic. Formulations F1, F4, and F7 having increase in amount of gum base at same amount of calcium carbonate (low level) demonstrated elevated elasticity. Formulation F3, F6, and F9 having increased in amount of gum base at same amount of calcium carbonate (high level) demonstrated decrease in property of elasticity.

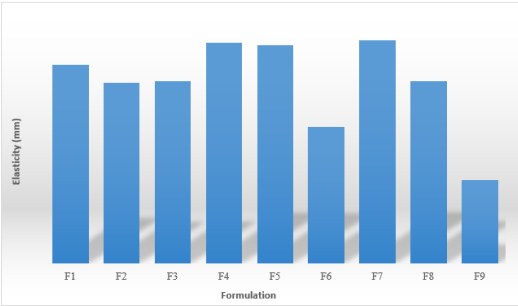

Figure 2. Elasticity of different formulation. It can be concluded that the formulation having high amount of gum base showed high elasticity.

Buccal absorption test

The buccal study concluded that more than 95% of drug was absorbed in 5 min at ph=6.0. The buccal absorption of drug at different pH is represented in Figure 3.

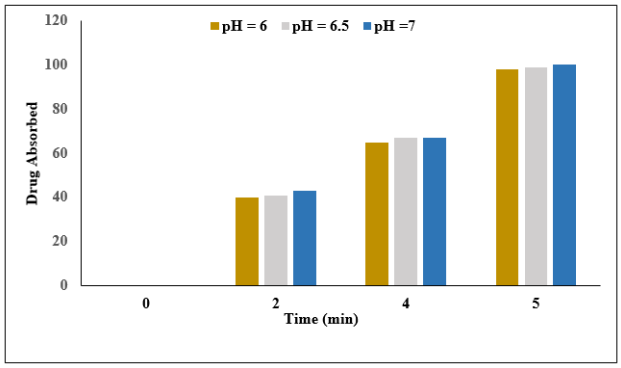

Figure 3. Buccal absorption test. It can be concluded that more than 95% of drug was absorbed at pH - 6.0.

Study of drug release

In vitro study of drug release is made in laboratory prepared saliva. Formulations F2 to F6 demonstrated faster release of the drug (more than 85%) within 16 min. F1, F6, F7, and F8 demonstrated more than 82% to 87% drug release within 16 min. F9 demonstrated incomplete release of drug (78%) within 16 min. F5 demonstrated the highest drug release (97%) within 17 min. *In vitro* dissolution study performed for F5 in simulated saliva released more than 96.23% of drug within 18 min as given in Figure 4.

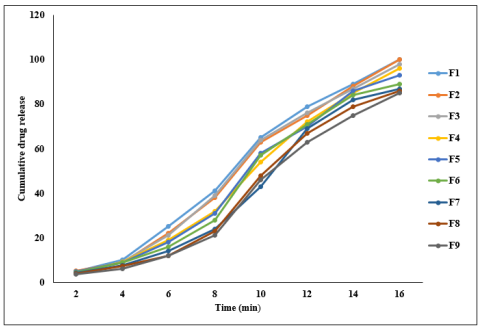

Figure 4. Dissolution study of medicated chewing gum. It can be concluded that formulation F5 demonstrated the highest drug release (97%) within 17 minutes.

Chewing study of gum formulation

The chewing study of gum formulation by all the six subjects was outlined in Table 5.

All six subjects considered F5 formulation have good texture, consistency and can be chewed easily.

Table 5. Chewing study performed by subjects where++ symbolizes very good, + symbolizes good, -symbolizes sticky.

Formulation	Number of human subjects					
	A	B	C	D	E	F
F1	+	-	+	+	-	+
F2	+	+	+	+	+	+
F3	+	+	+	+	+	+
F4	-	-	-	-	-	-
F5	++	++	++	++	++	++
F6	+	+	+	+	+	+
F7	-	-	-	-	-	-
F8	+	+	+	+	+	+
F9	+	+	+	+	+	+

CONCLUSION

The present research aimed to fabricate a medicated chewing gum for treating inflammation. This chewing gum possesses allicin which has the ability to act as antioxidant and reduce inflammation. The gum developed herein proved to be better than conventional dosage form of allicin. Another plus point of preparing this gum is that the base used in the gum is naturally obtained. There was increased bioavailability of drugs. The natural base has antifungal and antibacterial activity. Calcium carbonate and natural base showed elevated elasticity, chew ability and satisfactory dissolution study. Thus, buccal drug delivery system of medicated chewing gum can be considered as good alternative for traditional ODD system.

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