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Development of buccal tablets for curcumin using *Anacardium occidentale* gum

K. Gowthamarajan*, N. Jawahar, Prashant Wake, Kunal Jain, Sumeet Sood

Department of Pharmaceutics, JSS College of Pharmacy, Ootacamund 643001, Tamilnadu, India

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ABSTRACT

The objective of the present investigation was to develop unidirectional, bilayered, buccoadhesive tablets of curcumin using a natural buccoadhesive polymer cashew nut tree gum along with ethyl cellulose as an impermeable backing layer. A batch prepared with 20% polymer concentration, 0.1% penetration enhancer, 40 mg backing layer, compressed at 2 tons/cm^2 for 10 s was identified as an ideal batch based on its buccal residence time and optimum mucoadhesive strength of 13.99 g. The formulated tablets were stable with respect to their physicochemical and *in vitro* drug release behaviour over a period of 60 days at different temperatures and relative humidities. The kinetics of drug release was found to be non-Fickian or anomalous diffusion. The results suggest that cashewnut tree gum can be used as a polymer to produce buccoadhesive tablets of curcumin with potential to bypass the first pass metabolism and improve the bioavailability of curcumin.

1. Introduction

Buccal delivery of drug, as an alternative to the oral route of drug administration, is a subject of growing interest because of its numerous advantages such as good accessibility, robustness of epithelium, facile removal of dosage form in case of need, relatively low enzymatic activity, prevent drug degradation in gastrointestinal tract and avoid hepatic first-pass metabolism (Burgalassi, Panichi, Saettone, Jacobden, & Rassing, 1996; Harris & Robinson, 1992; Nagai & Machida, 1993). Buccal route provides potential routes for typically large, hydrophilic, unstable proteins, oligonucleotides and polysaccharides as well as small drug molecules. Among the various transmucosal sites available, mucosa of the buccal cavity was found to be the most convenient and easily available site for delivery of therapeutic agents for both local and systemic delivery as retentive dosage forms, because it has expanse of smooth muscle which is relatively immobile, abundant vascularization, rapid recovery time after exposure to stress and the near absence of Langerhans cells (Sudhakar, Kuotsu, & Bandyopadhyay, 2006). Attempts have been made to formulate various buccal mucoadhesive dosage forms, including tablets (Ali, Khar, & Ahuja, 1998), films (Kohda et al., 1997; Satishbabu & Srinivasan, 2008; Semalty, Semalty, & Kumar, 2008), patches (Nair & Chien, 1996), disks (Parodi, Russo, Caviglioli, Cafaggi, & Bignardi, 1996) and gels (Shin, Bum, & Choi, 2000). A suitable buccal drug delivery system should possess good bioadhesive properties, so that it can be retained in the oral cavity for desired duration. Bioadhesive polymers have been used extensively for use in buccal drug delivery systems. These include synthetic polymers such as polyacrylic acid, polycyanoacrylate, hydroxypropyl methyl cellulose, polymethacrylate, *etc.* (Ching, Park, Kelly, & Robinson, 1985; Gandhi & Robinson, 1992; Leung & Joseph, 1990). Since synthetic polymers pose a variety of problems when used as drug carriers, polymers from natural source have been used in past (Alur, Pather, Mitra, & Johnston, 1999; Lehr, Bouwstra, Etienne, & Hans, 1992; Sanzgiri, Topp, Benedetti, & Stella, 1994). The natural polymers offer certain specific advantages over synthetic polymers such as easy availability, bioacceptability, biocompatibility, biodegradability, non-toxicity and pollution free processing (Ifat, Karsten, & Fredmen, 2001). These polymers are hydrophilic macromolecules containing numerous hydrogen-bond forming groups (Mikos & Peppas, 1986). The development of newer excipients for potential use as buccoadhesive polymers continues to be of interest. In addition, it should release the drug in a unidirectional way towards the mucosa, in controlled and predictable manner, to elicit the required therapeutic response (Patel & Bhupender, 2007). This unidirectional drug release can be achieved by using bilayer devices (Parodi et al., 1996).

Cashew nut tree gum is obtained from the incised trunk of the tree *Anacardium occidentale* (Family: Ancardiaceae). The gum is a complex polysaccharide comprising galactose, arabinose, rhamnose, glucose, glucurine acid and other sugar residues. It is used primarily in industrial application for binding books, as adhesives for envelopes, labels, stamps and posters. It is also used as an additive in the manufacture of chewing gum because of its

* Corresponding author. Tel.: +91 423 2443393/9443089812; fax: +91 423 2442937.
E-mail address: gowthamsang@gmail.com (K. Gowthamarajan).

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thickening power. It is used as a jellying agent in canned food and jellies for fruits jam (Azeez, 2005; de Paula, Heatley, & Budd, 1998; de Paula & Rodrigues, 1995). Literature survey reveals that cashew nut tree gum had been studied as binder (Okoye, Onyekweli, Ohwoavworhua, & Kunle, 2009; Onunkwo & Okoye, 1997). Gelling property of cashew gum in aceclofenac gel also had been studied (Kumar, Patil, Patil, & Paschapur, 2009). In our previously published work, we have investigated utility of cashewnut tree gum as a binder in the formulation of paracetamol tablets (Gowthamarajan, Kumar, Gaikwad, & Suresh, 2011).

Curcumin is a phenolic phytochemical obtained from turmeric (*Curcuma longa* L.). It has antioxidant, anti-inflammatory, antispasmodic, anticoagulant, anticarcinogenic, immunomodulatory activities. It has been found that the therapeutic effectiveness of curcumin is often limited due to its poor absorption from the gastrointestinal tract. When taken orally, only traces appear in blood whereas most of the dose is excreted through the faeces (38–75%). The physicochemical properties of curcumin, its half-life of 1.39 h, and its low molecular weight of 368.39 makes it a suitable candidate for administration by buccal route (Sharma, Gescher, & Steward, 2005). The overall goal associated with the present study was to demonstrate utility of *A. occidentale* gum to serve as sustained release and mucoadhesive tablet excipient.

2. Materials and methods

2.1. Materials

Curcumin was a kind gift from Sanjivani Pharmaceutical Ltd. (Pune, India). Cashewnut tree gum was collected from various places of Andhra Pradesh (India). Ethyl cellulose was purchased from Pioma Chemicals (Mumbai, India). Avicel PH 101 was purchased from Signet Chemicals (Mumbai, India). Sodium lauryl sulphate was purchased from Alkem Pharma (Mumbai, India). Hydroxy propyl methyl cellulose (HPMC K4M) and menthol were purchased from S.D. Fine Chemical Ltd. (Mumbai, India). All other reagents and chemicals used were of analytical reagent grade.

2.2. Isolation of water-soluble fraction of cashew nut tree gum

The water-soluble fraction of cashew nut tree gum was collected as described previously (Gowthamarajan et al., 2011). The collected crude cashew nut tree gum (100 g) was ground by using mortar and pestle. The ground gum was dissolved in water (300 ml). The solution was filtered through several folds of muslin cloth and the filtrate was collected. To the filtrate, alcohol (90%, v/v) was added in 1:1 ratio and precipitate was obtained. The precipitate was filtered and dried in a hot air oven at 45 °C. 100 g of powder obtained was dissolved in 100 ml of water, filtered through several folds of muslin cloth. Then the filtrate was centrifuged at 3000 rpm for 10 min and the supernatant fluid was collected, evaporated and dried to obtain solid mass, which was ground. This mass was passed through sieve no. 80 and stored in an airtight container for further studies.

2.3. Characterization of gum

The gum was characterized for surface analysis, purity, pH, surface tension and porosity. The surface analysis was determined by scanning electron microscope (SEM, Hitachi S-2400, Japan). The gum was evaporated with carbon and then sputtered with gold to make the sample electrically connected. Carbon was layered to a thickness of approximately 10 nm and gold was layered to approximately 25 nm. The pH of the gum solution (1%, w/v) was determined using digital pH meter (pH system 361, Systronics, Mumbai). The surface tension of the gum solution (0.1%, w/v solution) was determined by drop count method, using stalagmometer. The bulk density of the sample was calculated by mass of sample/bulk volume of sample. A given quantity of sample was transferred to a measuring cylinder and was tapped mechanically, using a bulk density apparatus (Electrolab, Mumbai, India) until a constant volume was obtained, which was referred a bulk volume. True density of sample was determined by using the liquid displacement method and acetone was used as the liquid for displacement. The percentage porosity of the gum was calculated as, porosity = (bulk density − true density)/bulk density. All the experiments were made in triplicate.

2.4. Determination of water absorption

Water absorption characteristics of the gum were carried out on 1% agar gel plates. The gum was compressed into discs of 100 mg weight using hydraulic press. The prepared discs were placed on the surface of agar gel plates and incubated at 37 °C until constant weight was obtained. The initial and final weights of discs were noted and the mean of three determinations was taken to represent the uptake volume (Ahuja, Dogra, & Agarwal, 1995).

2.5. Determination of swelling index of gum

A specified quantity of the gum (1 g), previously reduced to the required fineness, was introduced into a 50 ml glass stoppered measuring cylinder. Water (25 ml) was added and the mixture was shaken thoroughly every 10 min for 1 h. It was allowed to stand for 3 h at room temperature. The volume in ml occupied by the gum, including any sticky hydrogel, was measured. The experiment was carried out in triplicate and the mean value was calculated (Desai & Kumar, 2004).

2.6. In vitro disintegration of the gum

Pellets of the gum (100 mg) were prepared in a hydraulic press and its disintegration pattern was observed by immersing the pellets in glass Petri dish, containing 25 ml phosphate buffer of pH 6.8 at room temperature. The morphological changes of each pellet were observed over a period of 4 h (Mahmood & Hung, 1995).

2.7. Evaluation of buccal residence time and buccal acceptance

The placebo tablets prepared were stuck to the buccal cavity (behind the upper lip) of nine healthy human volunteers and observations were made every hour until the device lost its integrity. During the study, the volunteers were allowed to perform normal activities and their response to the presence of buccal tablets, such as discomfort, taste, salivation, dryness, irritation, redness, and disintegration, were evaluated up to 14 days using placebo tablets containing 10%, 15%, 20%, and 25% (w/w) of gum (Desai & Kumar, 2004). All the volunteers gave written consent and the study protocol was approved by ethical committee of the institution.

2.8. Formulation of unidirectional, bilayered, buccoadhesive tablet of curcumin

Unidirectional, bilayered, buccoadhesive tablets of curcumin, using cashew nut tree gum as mucoadhesive polymer were prepared by double compression technique in a hydraulic press (Table 1). Initially, a backing layer was made using ethyl cellulose, onto which, the drug containing granules were placed and recompressed to get bilayer tablets. The granules were prepared by wet granulation method using warm water as granulating agent. The desired quantities of curcumin, cashew nut tree gum, sodium lauryl sulphate and microcrystalline cellulose PH 101 were dry mixed

Table 1
Formulation of different batches of curcumin buccal tablets using cashew nut tree gum.

	Batch code			
	F1	F2	F3	F4
Drug	100	100	100	100
Cashewnut tree gum	20	30	40	50
Sodium lauryl sulphate	0.2	0.2	0.2	0.2
Avicel pH 101	77.8	67.8	57.8	47.8
Menthol	1	1	1	1
Magnesium stearate	1	1	1	1
Total (mg/tablet) (Drug containing layer)	200	200	200	200
Ethyl cellulose (mg/tablet)(Backing layer)	40	40	40	40

for 5 min using mortar and pestle and then moistened with appropriate amount of warm water and mixed thoroughly. Massing was continued for 5 min and the wet mass was granulated by passing it manually through a mesh 16 sieve and dried in a hot air oven for 30 min at 60 °C. Dried granules were sieved through a mesh 16/22 sieve and granules were collected which were passed through 22 sieve. Menthol and magnesium stearate were added to dried granules. Finally, the required quantity of the drug containing granules were placed on the precompressed backing layer in a hydraulic hand press and recompressed into tablets of 10 mm diameter. The hardness of the tablets was determined using a Monsanto hardness tester (Cadmach, Ahmedabad, India). The percentage of friability of the tablets was determined using Roche tablet friabilator (Indian Equipment Corporation, Mumbai, India) operated at 25 rpm for 4 min. The weight variation test of the tablets was performed by following the official method given in USP (United States Pharmacopeia-24, 2000).

2.9. Effect of concentration of gum

Four different batches (F1 to F4) of curcumin buccoadhesive tablets corresponding to different (10%, 15%, 20% and 25%, w/w) concentration of gum were prepared, keeping compressional time (10 s), compressional force (2 tons/cm^2), concentration of backing layer (40 mg ethyl cellulose) and concentration of penetration enhancer (0.1%, w/w, SLS) as constant. The effect of concentration of gum on weight and thickness of tablet, hardness, friability, mucoadhesive strength, swelling index and drug content was investigated.

2.10. Evaluation of mucoadhesive strength

Mucoadhesive strength was determined by using a modified physical balance (Desai & Kumar, 2004; Gupta, Garg, & Khar, 1992; Khanna, Agarwal, & Ahuja, 1996). The left pan of the physical balance was removed and a weight hanger of 2 cm length with a bottom platform having 1.4 cm diameter, was hanged with copper rings. A stainless steel block of 3.8 cm diameter and 2 cm height was fabricated with an upward protrusion of 2 cm height and 1.5 cm diameter on one of its face. This was kept inside the glass container, which was then placed below the left hand set up of the balance. On the right pan, 150 ml plastic beaker was placed to collect water from the burette. The total set up was then balanced so that the left hand side was exactly 3 g heavier than the right. The two sides of the balance were first balanced with a 3 g weight on the right hand side. Goat intestinal membrane, excised and washed, was tied tightly with the mucosal side upwards, over the protrusion in the stainless steel block. The block was then lowered into the glass container, which was then filled with phosphate buffer of pH 6.8 and kept at 37 ± 1 °C such that the buffer reaches the surface of the mucosal membrane and keeps it moist. This was then kept below the left hand side of the balance. The backing layer was stuck to the lower surface of the hanging platform on the left hand side and the balance beam was raised such that the left side was exactly 3 g heavier than the right, as an initial applied force. This lowered the hanging platform along with the tablet over the mucosa. The balance was kept in this position for 3 min and then the nozzle of the burette was opened to produce as slow and constant rate of water flow. After the tablet was separated from the mucosal surface, the water flow was stopped and the bioadhesive strength of the tablet was calculated, using the formula, bioadhesive strength (g) = weight of water collected in the beaker − 3 g.

After each measurement, the tissue was gently washed with phosphate buffer of pH 6.8 and left for 5 min before the next measurement. One membrane was used for 3 such measurements. The average mucoadhesive strength and standard deviation were then calculated.

2.11. Swelling studies of the buccal tablets

Buccal tablets were weighed individually (W_1) and placed in Petri dish containing 4 ml of phosphate buffer (pH 6.8). At the end of 2 h, the tablets were removed from the Petri dish and excess surface water was removed carefully using filter paper and swollen tablets were reweighed (W_2). The swelling index (SI) was calculated according to formula:

$$SI = \frac{W_2 - W_1}{W_1} \times 100$$

The experiment was carried out in triplicate and mean value was calculated (Desai & Kumar, 2004).

2.12. Drug content and in vitro drug release studies

The drug content of the prepared buccoadhesive tablets was determined by UV spectrophotometry. Five tablets from the batch were taken and powdered and a quantity equivalent to 100 mg of the drug was dissolved in a mixture of phosphate buffer (pH 6.8) and 3% Tween 80 and analysed at 426 nm against a blank.

USP dissolution apparatus with paddle was used for the *in vitro* dissolution studies of buccoadhesive tablets with a simple modification. A two-end open glass cylinder of 3 cm diameter and 10 cm length was taken. The prepared buccoadhesive tablet was placed by applying a moderate pressure onto a moistened membrane having a thickness of ~500 μm and this was then tied to one end of the cylinder, taking care to place the tablet inside the cylinder. This cylinder was then placed on the surface of dissolution medium (900 ml of phosphate buffer pH 6.8 containing 3% Tween 80) maintained at 37 ± 0.5 °C at 100 rpm for 8 h. At specified time intervals, 5 ml samples were withdrawn and immediately replaced with an equal quantity of fresh buffer. The samples were filtered and analysed after appropriate dilution by UV spectrophotometry at 426 nm.

2.13. Comparative study

To evaluate the efficacy of the cashew nut tree gum, comparative study was carried out with a batch prepared with HPMC as standard mucoadhesive polymer. Two batches of the buccal tablets were prepared using 20% cashew nut tree gum and 20% HPMC keeping other parameters constant. These batches were then evaluated for *in vitro* release studies.

2.14. Stability studies

Stability of a formulation can be defined as the time from date on manufacture of the formulation until its chemical or biological activity is not less than a predetermined level of labelled potency and its physical characteristics have not changed appreciably or

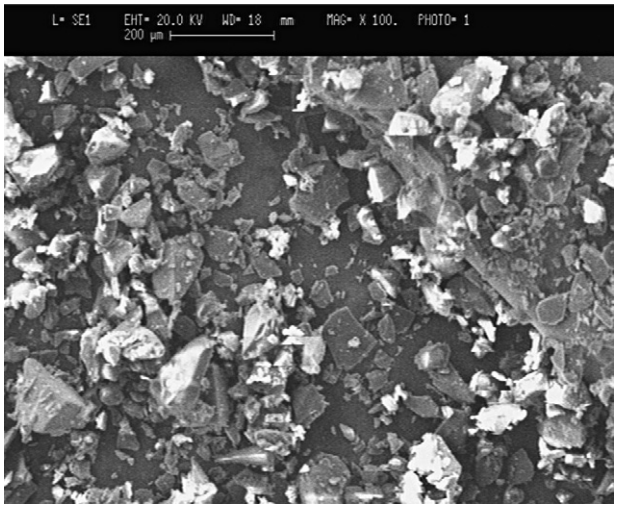

Fig. 1. Microphotograph depicting SEM cashew nut tree gum.

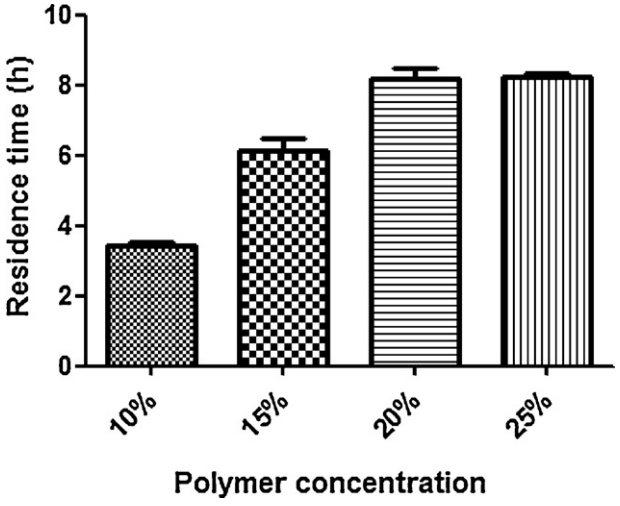

Fig. 2. Buccal residence time of different batches of buccal tablets.

deleteriously. The ideal batches of the formulated buccoadhesive tablets containing 100 mg curcumin were packed in polyethylene bags and then kept in stability chamber at 25 °C/60% RH, 40 °C/75% RH and room temperature. Samples were withdrawn at 15, 30 and 60 days and evaluated for their physical appearance, drug content and *in vitro* drug release at specified intervals of time. T_{50} was also calculated by using dissolution studies (Kulkarni, Gowthamarajan, & Suresh, 2004).

3. Results and discussion

The gum was purified using water as solvent and alcohol 90% (v/v) as non-solvent. The yield was 70% (w/w). Water-soluble portion was separated from the purified gum. The water-soluble gum was used as mucoadhesive polymer for developing buccoadhesive tablets. The water-soluble gum was characterized for surface characters by SEM, purity, pH, porosity, surface tension to assess the gum as excipient for developing buccal tablets. The SEM microphotograph showed that the gum was smooth and crystalline in nature as shown in Fig. 1. The test for purity revealed the presence of carbohydrates and glycosidic sugars indicating the presence of the polysaccharide. The pH of gum solution (1%, w/v) was 4.39, this falls within natural pH of *Acacia senegal* with a range of 3.8–4.9 (Azeez, 2005), which indicates that it would not cause irritation to the epithelium and mucous membrane of the buccal cavity. The porosity and surface tension of the gum were 69.5% and 12.652 dyn/cm, respectively. The high porosity and lower surface tension probably enabled good wetting and swelling of polymer and entanglement of polymer and mucin chains. The water absorption of gum was found to be 72.35 ± 3.54%, over 4 h periods. It is known that the adhesive and cohesive property of any mucoadhesive polymer is generally influenced by its swelling nature. The higher water uptake may help in establishing a quicker and stronger interpenetration of polymer chains into the mucous and improves its contact time. The swelling index of the gum was found to be 11.5 ± 0.36 ml, indicating good water absorbing capacity of the polysaccharide and hence its capability to form hydrated three dimensional networks from which drug release might follow by diffusion. The polymer pellets did not show any disintegration in the *in vitro* disintegration test in phosphate buffer of pH 6.8 over a period of 4 h and retained its integrity. The non-disintegrating behaviour is helpful in maintaining the compactness of the buccal tablets during its stay in the oral cavity and would lead to improved patient acceptance and comfort. The characterized gum was selected as an excipient for preparing buccoadhesive tablets to find out its mucoadhesive characteristic. The gum was selected from natural sources as mucoadhesive polymer due to its distinguished characters such as low cost, abundant availability, ease if isolation, mucoadhesion, surface tension and porosity.

The residence time of any buccal formulation is an important criterion for its acceptance or rejection. An ideal buccoadhesive device should not cause any local irritation, salivation, redness, unpleasant taste, *etc.*, and should stay in buccal cavity without interfering with normal buccal activities. The results of buccal residence time of the different batches of placebo buccal tablets, prepared using different concentrations of polysaccharide, revealed that the mean residence time increases as the polymer concentration increases (Fig. 2). This may be due to the higher mucoadhesive strength obtained at higher concentrations of the polymer. As the polymer content of the formulation increases the degree of swelling increases, which in turn allows the formation of a greater number of interpenetrating chains between the polymer and the mucous. This physical interaction results in a linear increase of adhesion with polymer concentration and increase in the residence time. Thus above 20% (w/w) of the polymer content, the residence time did not increase significantly ($p > 0.05$) and hence, 20% (w/w) of polymer concentration was considered optimal for the buccal acceptance evaluation. The result of buccal acceptance study of the placebo tablets (containing 20%, w/w, polymer) showed that 7 out of 9 volunteers favoured the buccal administration and only two felt slight irritation (Fig. 3). Based on the above evaluation, it can be safely concluded that the formulated buccal tablets are suitable for buccal administration of the drugs and the polymer has sufficient *in vivo* mucoadhesive property, required for the development of buccoadhesive dosage forms. The effect of polymer concentration on the physicochemical properties of the formulated buccal tablets is given in Table 2. There was no significant ($p > 0.05$) effect on the average weight, thickness and drug content. The hardness of batch F2 was not significant ($p > 0.05$) in comparison to F1. However, the hardness of F3 and F4 was highly significant ($p < 0.01$) and extremely significant ($p < 0.001$) in comparison to F1, respectively. The friability of the formulated tablets was within limits. The swelling index of F1 was found to be 68.615 ± 2.050%. There was no significant variation ($p > 0.05$) in swelling index of F2, but at higher concentration of polymer (20% and 25%, w/w) the increase in swelling index was found to be extremely significant ($p < 0.001$). The swelling behaviour of a buccal adhesive system is an important property for uniform and prolonged release of drug and effective bioadhesiveness (Peppas & Bury, 1985). The swelling index study indicated that rate of swelling was directly proportional to polymer content.

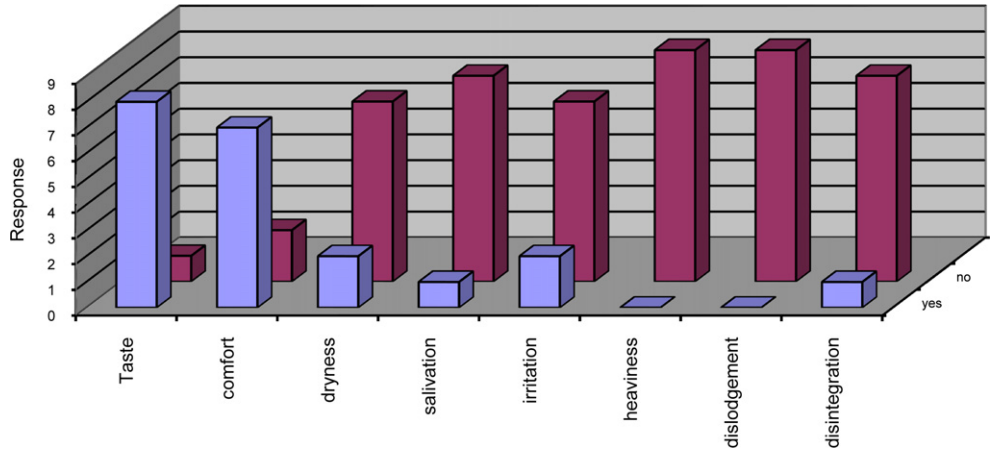

Fig. 3. Comparative results of buccoadhesive tablet acceptance.

Bilayered tablets containing 25% of polymer exhibited the highest swelling index (81.728 ± 1.8355). The agar plate model used in this study simulates the secreting fluid around the buccal mucosa which is required for adhesion, swelling and release of the drug from tablets (Emami, Varshosaz, & Saljoughian, 2008). Mucoadhesion may be defined as the adhesion between a polymer and mucus. In general, mucoadhesion is considered to occur in 3 major stages: wetting, interpenetration, and mechanical interlocking between mucus and polymer. The strength of mucoadhesion is affected by various factors such as molecular weight of polymers, contact time with mucus, swelling rate of the polymer, and biological membrane used in the study (Park & Robinson, 1987). In this study, goat intestinal membrane was used as biological membrane for mucoadhesion. It was observed that mucoadhesive strength of the buccal tablets increased with increase in concentration of the polymer and was extremely significant ($p < 0.001$) in comparison to F1. The maximum mucoadhesive strength was noted with F4 (15.409 ± 0.187 g) whereas it was minimum with F1 (7.758 ± 0.538 g). The reason for higher mucoadhesion with higher cashew nut tree gum content may be due to formation of secondary bioadhesion bonds with mucin and its capability to undergo extensive interpenetration with mucus layer (Ilango, Kavimani, Mullaicharam, & Jayakar, 1997). The *in vitro* drug release studies of various batches with different concentration of polymer showed that an increase in polymer concentration reduced the drug release throughout (Fig. 4). However, there was no significant difference ($p > 0.05$) in release profile of batches prepared with 10% (w/w) polymer (F1) in comparison to 15% (F2) and 20% (w/w) (F3) polymer. The amount of drug released at the end of 8 h was 97.20 ± 0.24%, 96.35 ± 0.31% and 95.89 ± 0.30% for batch F1, F2 and F3, respectively. The release of drug from batch prepared with 25% (w/w) polymer concentration was extremely significant ($p < 0.001$) in comparison to other batches. This might be attributed to higher concentration of the polymer which upon swelling reduces the diffusion of the drug

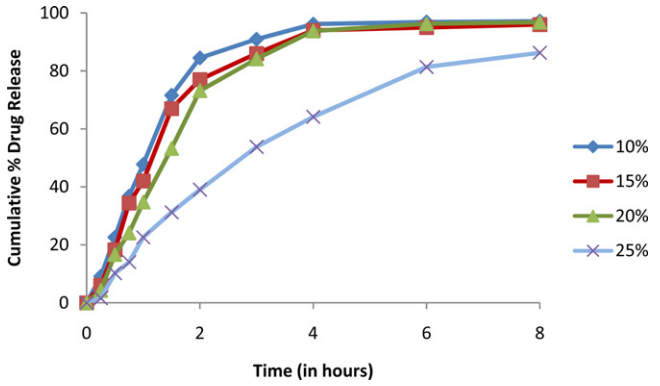

Fig. 4. *In vitro* dissolution profile of curcumin buccal tablets prepared with different concentration of cashew nut tree gum (10%, 15%, 20% and 25%, w/w).

from the matrix of buccal tablets. A batch prepared with 20% polymer concentration, 0.1% penetration enhancer, 40 mg backing layer, compressed at 2 tons/cm^2 for 10 s was identified as an ideal batch based on its buccal residence time and optimum mucoadhesive strength of 13.99 g. Comparative *in vitro* dissolution profile of curcumin using 20% (w/w) cashew nut tree gum (20% CTG) and 20% (w/w) hydroxy propyl methylcellulose (20% HPMC) is shown in Fig. 5. The results indicate that buccal tablets prepared with cashew nut tree gum showed faster release (96.8%) compared to HPMC (86.18%) at the end of 8 h. The dissolution data of the optimized batches of buccal tablets, prepared using the polysaccharide, were subjected to data fitting according to Korsmeyer–Peppas equation that deals with drug release from polymeric system (Costa & Lobo, 2001). The value of release exponent (n) was found to be 0.847. This indicates an anomalous release pattern ($n > 0.5$). Stability studies of formulated curcumin buccal tablets with 20% polymer were

Table 2
Effect of concentration of polymer on different physicochemical parameters (mean ± S.D., $n = 3$).

S. No.	Evaluation	Batch code (Polymer concentration %w/w)			
		F1 (10%)	F2 (15%)	F3 (20%)	F4 (25%)
1	Average weight (mg)	240.527 ± 0.501	240.710 ± 0.397	240.849 ± 0.454	240.821 ± 0.565
2	Average thickness (mm)	1.999 ± 0.035	2.021 ± 0.012	2.031 ± 0.028	2.056 ± 0.036
3	Hardness (Kg/cm^2)	3.149 ± 0.098	3.339 ± 0.159	3.615 ± 0.014	3.787 ± 0.067
4	Friability (%)	0.159 ± 0.012	0.155 ± 0.012	0.115 ± 0.003	0.119 ± 0.003
5	Mucoadhesive strength (g)	7.758 ± 0.538	11.292 ± 0.256	13.996 ± 0.238	15.409 ± 0.187
6	Drug content (%)	95.845 ± 0.468	96.983 ± 0.662	97.628 ± 0.641	96.265 ± 0.988
7	Swelling index (%)	68.615 ± 2.050	70.642 ± 0.630	76.672 ± 1.265	81.728 ± 1.835

Table 3
Stability evaluation of curcumin buccal tablets stored at different temperatures and relative humidities conditions (mean ± S.D., $n = 3$).

	Day 0	25 °C/60% RH			40 °C/75% RH		
		Days			Days		
		15	30	60	15	30	60
Physical Appearance	White colour	No significant change	No significant change	No significant change	No significant change	No significant change	No significant change
Average weight (mg)	240.849 ± 0.454	240.849 ± 0.454	240.718 ± 0.111	239.906 ± 0.481	240.514 ± 0.233	240.455 ± 0.175	240.447 ± 0.867
Average thickness (mm)	2.031 ± 0.028	2.031 ± 0.028	2.024 ± 0.010	2.034 ± 0.021	2.036 ± 0.011	1.999 ± 0.011	1.983 ± 0.017
Hardness (kg/cm^2)	3.615 ± 0.014	3.615 ± 0.014	3.576 ± 0.104	3.644 ± 0.065	3.734 ± 0.047	3.690 ± 0.208	3.833 ± 0.037
Friability (%)	0.115 ± 0.003	0.132 ± 0.003	0.133 ± 0.023	0.142 ± 0.006	0.126 ± 0.005	0.115 ± 0.005	0.123 ± 0.003
Mucoadhesive strength (g)	13.996 ± 0.238	13.996 ± 0.238	13.497 ± 0.216	13.755 ± 0.574	13.597 ± 0.340	13.487 ± 0.233	13.368 ± 0.246
Drug content (%)	97.628 ± 0.641	97.628 ± 0.641	96.030 ± 0.202	96.026 ± 0.204	95.662 ± 0.602	95.710 ± 0.672	95.654 ± 0.713
Swelling index (%)	76.672 ± 1.265	76.672 ± 1.265	74.561 ± 0.494	75.275 ± 0.363	76.580 ± 1.509	73.168 ± 0.522	72.629 ± 1.526
T50 dissolution (h)	1.408	1.413	1.419	1.475	1.411	1.416	1.426

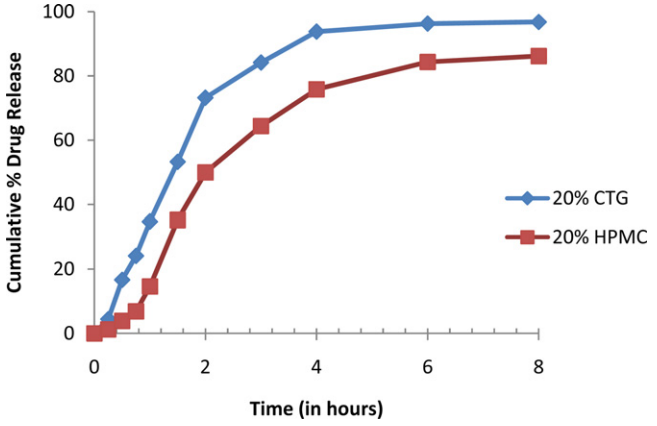

Fig. 5. Comparative *in vitro* dissolution profile of curcumin buccal tablets using 20% (w/w) cashew nut tree gum (20% CTG) and 20% (w/w) hydroxypropyl methylcellulose (20% HPMC).

carried out at 25 °C/60% RH and 40 °C/75% RH. All tablet formulations were subjected to various evaluation parameters and the results obtained were within the range. The results are given in Table 3. The weight variation test indicates that all the tablets were uniform weight. The tablet thickness values ranged from 1.983 to 2.093 mm, hardness of all the tablets was within the range of 3.482–3.833 kg/cm^2. The loss in total weight in friability test was in the range of 0.11–0.14%. The percentage drug content for different formulation varied from 95.654 to 97.928%. There was no significant change in release characteristics and physicochemical properties of the tablets used in the release study. Based on the results it can be concluded that the formulated buccoadhesive tablets were stable over a period of 60 days.

4. Conclusion

These results demonstrate that the novel, natural gum, *A. occidentale*, may not only be used to sustain the release of curcumin from a unidirectional-release buccal tablet, but also demonstrate that the tablets are sufficiently mucoadhesive for clinical application. The mucoadhesive buccal tablets evaluated represent an improved transbuccal delivery system for conventional drug substances. The mechanism of bioadhesion may potentially result from chain interpenetration and physical entanglement of gum with the mucus layer. The rate of release of the drug substance as well as the bioadhesive bond strength of the formulation can be modulated by varying the amount of gum included in the tablet. The mucoadhesive buccal tablets evaluated in the present study were easy to formulate, inexpensive, provide easy application and convenient removal from the mucosal surface. Therefore, such tablet formulations containing a polysaccharide bioadhesive gum, *A. occidentale*, may represent an improved buccal delivery system for a variety of low molecular weight drug substances.

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