JOURNAL OF DRUG DELIVERY RESEARCH

ISSN 2319-1074

RESEARCH ARTICLE

DESIGN, DEVELOPMENT AND EVALUATION OF ROSUVASTATIN BUCCOADHESIVE TABLETS

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ABSTRACT

Rosuvastatin calcium is a low bioavailable drug used for the management of hyperlipidemia. Buccoadhesive tablets of rosuvastatin calcium were prepared by direct compression method using HPMC K4M, HPMC K15M and carbopol 974P as mucoadhesive polymers and evaluated for *in vitro* drug release, *in vitro* bioadhesion, *ex vivo* residence time, swelling index, surface pH and *ex vivo* drug permeation. Fifteen formulations were developed with varying concentrations of polymers. Formulations from F1 to F5 were composed of HPMC K4M, F5 to F10 using HPMC K15M and F11 to F15 using carbopol 974. The ratio of drug and polymer were varied from 1:1 to 1:5 in F1 to F10 and 1:0.25 to 1:1.50 in F11 to F15. Formulation F3 showed maximum release of the drug (97.83 ± 0.41%), and from the same formulation maximum drug has permeated (73.14 ± 0.13%) through porcine buccal membrane with a flux of 8.35 ± 0.291µg $h^{-1}cm^{-2}$, permeation coefficient of 1.34 ± 0.05 cmh^{-1} and maximum bioadhesive force of 24.64±0.246 respectively. FTIR results showed no evidence of interaction between the drug and polymers. The results indicate that suitable bioadhesive buccal tablets with desired permeability could be prepared.

Keywords: Buccoadhesive, Carbopol, HPMC, *in vitro* bioadhesion, *in vitro* drug release, Rosuvastatin

INTRODUCTION

The oral cavity is an attractive site for the administration of drugs because of ease of administration [1], avoidance of possible drug degradation in gastro intestinal tract and first-pass hepatic metabolism [2]. In the oral cavity the delivery of drugs are classified into three categories: 1. Sublingual delivery, which is systemic delivery of drugs through the mucosal membranes lining the floor of the mouth; 2. buccal delivery, it is the drug administration through mucosal membranes lining the cheeks (buccal mucosa); and 3. Local delivery it is the drug delivery into the oral cavity. Among these routes, buccal delivery is suitable for administration of retentive dosage forms because of an excellent accessibility, an expanse of smooth muscle and immobile mucosa. So, buccal delivery of drugs is attractive alternative to the oral route of drug administration [3]. Buccal delivery involves the administration of the desired drug through the buccal mucosal membrane lining of the oral cavity [4]. In recent years delivery of therapeutic agents through buccal mucosa has gained significant attention. Drug absorption through buccal mucosa is mainly by passive diffusion into the lipoidal membrane. In the buccal

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delivery the drug directly reaches to the systemic circulation through the internal jugular vein and bypasses the drugs from the hepatic first pass metabolism and gastric irritation, which leads to high bioavailability. From the technological point of view, an ideal buccal dosage form must have three properties; it must maintains its position in the mouth for a few hours, release the drug in controlled fashion and provide drug release in a unidirectional way towards mucosa. This unidirectional drug release can be achieved using bilayer devices [5]. Moreover, buccal drug absorption can be promptly terminated in case of toxicity by removing the dosage form from the buccal cavity. It is also possible to administer therapeutic agent to patients who cannot be dosed orally to prevent accidental swallowing [6]. These buccal tablets are small, flat and are intended to be held between the cheek and teeth or in the cheek pouch [7]. A suitable buccal drug delivery system should possess good bioadhesive properties so that, it can be retained in the oral cavity for the desired time duration. Various buccal mucosal dosage forms are suggested for oral delivery which includes: buccal tablets, buccal patches and buccal gels [8, 9]. Drug delivery via the buccal route, using bioadhesive dosage forms offers such a novel route of drug administration. Rosuvastatin calcium is an antilipemic agent that competitively inhibits hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase. HMG-CoA reductase catalyzes the conversion of HMG-CoA to mevalonic acid, the rate-limiting step in cholesterol biosynthesis. Rosuvastatin belongs to a class of medications called statins and is used to reduce plasma cholesterol levels and prevent cardiovascular disease [10]. Rosuvastatin calcium undergoes first pass metabolism and efflux transport by BCRP transport protein which limits the fraction of drug absorption and as a result of that it has very low bioavailability. This molecule posses all the attributes of considerations for buccal drug delivery, hence it was selected as a drug candidate for bioadhesive buccal drug delivery.

The present study is aimed to design a mucoadhesive bilayered buccal tablets of rosuvastatin calcium to release the drug unidirectionally in buccal cavity with the objective of avoiding first pass metabolism, prolonging duration of action and to enhance the bioavailability of drug using bioadhesive polymers like HPMC K4M, HPMC K15M and carbopol 974p in different ratios with spray dried lactose as a diluent and to perform all possible evaluation parameters.

MATERIALS AND METHODS

Rosuvastatin calcium, hydroxy propyl methyl cellulose K4M, hydroxy propyl methyl cellulose K15M, spray dried lactose and carbopol 974p were obtained from Dr. Reddy's Laboratories, Hyderabad, India. Ethyl cellulose, magnesium stearate and talc were obtained from S.D. Fine chem.Ltd, Mumbai, India. All other chemicals, reagents and solvents were used are of analytical grade.

Preparation of bilayered buccal tablets

Bilayered buccal tablets were prepared by a direct compression method. Prior to direct compression, all the ingredients were screened through sieve no. 40. Rosuvastatin calcium was mixed manually with different ratios of HPMC K4M, HPMC K15M & Carbopol 974p (mucoadhesive polymers) and spray dried lactose as diluent for 10min. The blend was mixed with magnesium stearate, aspartame and talc for 3-5 min and then compressed into tablets by the direct compression method using 8mm flat faced punches on cadmach rotary tablet machine (Figure 1). The composition of the prepared bioadhesive buccal tablet formulations of rosuvastatin are given in Table1.

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Fig. 1: Diagram of bioadhesive buccal tablet.

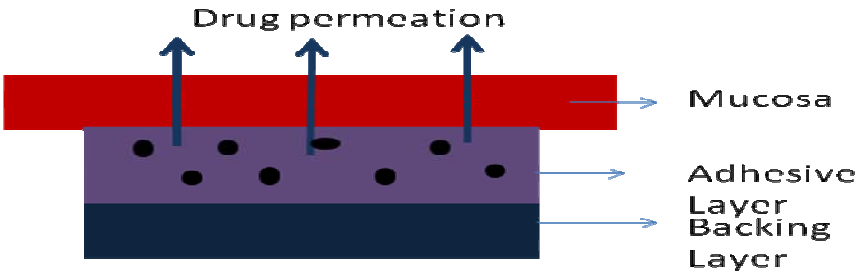

TABLE 1: COMPOSITION OF ROSUVASTATIN CALCIUM BUCCAL TABLETS

Formulation* code	Drug (mg)	HPMC K4M (mg)	HPMC K15M (mg)	Carbopol 974p (mg)	Spray dried lactose (mg)	Mg stearate (mg)	Talc (mg)	Aspartame (mg)	Ethyl cellulose (mg)
F1	5	5	-		86	1	2	1	50
F2	5	10	-		81	1	2	1	50
F3	5	15	-		76	1	2	1	50
F4	5	20			71	1	2	1	50
F5	5	25			66	1	2	1	50
F6	5	-	5		86	1	2	1	50
F7	5	-	10		81	1	2	1	50
F8	5	-	15		76	1	2	1	50
F9	5	-	20		71	1	2	1	50
F10	5	-	25		66	1	2	1	50
F11	5	-	-	1.25	89.75	1	2	1	50
F12	5	-	-	2.5	88.5	1	2	1	50
F13	5	-		3.75	87.25	1	2	1	50
F14	5	-		5	86	1	2	1	50
F15	5	-		7.5	83.5	1	2	1	50

***Total tablet weight 150 mg.**

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Evaluation of buccal tablets

Thickness

The thickness of buccal tablets was determined using digital screw gauge. Ten individual tablets from each batch were used and the results averaged.

Weight variation

Weight variation was performed for 20 tablets from each batch using an electronic balance and average values were calculated [11].

Hardness

Tablets require certain amount of strength or hardness to withstand mechanical shocks of handling in manufacture, packaging and shipping [12]. The hardness of the tablets was conducted for 3 tablets from each batch using Pfizer hardness tester and average values were calculated.

Assay

Ten tablets were weighed and grounded in a mortar with pestle to get fine powder; powder equivalent to the mass of one tablet was dissolved in methanol by sonication for 30 mins and filtered through Whatman filter paper. The drug content was analyzed spectrophotometrically at 250 nm using an UV spectrophotometer.

Swelling studies

Buccal tablets were weighed individually (designated as W_1) and placed separately in petri dishes containing 15ml of phosphate buffer (pH 6.6) solution. At regular intervals (0.5, 1, 2, 3, 4, 5 and 6 hrs), the buccal tablets were removed from the petridishes and excess surface water was removed carefully using the filter paper. The swollen tablets were then reweighed (W_2)**.** This experiment was performed in triplicate. The swelling index (water uptake) calculated according to the following equation [13, 14].

Swelling index = $(W_2\text{-}W_1)/W_1 \times 100$

Surface pH study

The bioadhesive tablet was allowed to swell by keeping it in contact with 1ml of distilled water for 2 hrs at room temperature. The pH was measured by bringing the pH-meter electrode, in contact with the surface of the tablet and allowing it to equilibrate for 1 min. The surface pH of the mucoadhesive tablets was determined to find out the possibility of any side effects when swallowed. An acidic or alkaline pH may cause irritation to the mucosa [15, 16].

Measurement of bioadhesion strength

Bioadhesive strength of the tablets was measured on a modified physical balance [17]. The apparatus consisted of a modified double beam physical balance in which a lighter pan had replaced the right pan and the left pan had been replaced by a glass slide (4 cm length and 2.5 cm width) with plastic hang suspended by Teflon rings and copper wire. The left-hand side of the balance was exactly 5 gm heavier than the right side. The height of the total set up was adjusted to accommodate a glass container of 6.6cm height. In order to find out the bioadhesion strength first buccal tablet (n=3) was stacked to the glass slide with the help of knob, which was situated at the base of physical balance. Now five grams of weight from the right pan was then removed. This lowered the glass slide along with the tablet over the membrane with a weight of 5.0 gm. This was kept undisturbed for 5 min. Then the weights on the right-hand side were slowly added in increments of 0.1 gm till the tablet just separated from the membrane surface. The excess weight on the right pan, i.e. total weight minus 5gm was taken as a measure of the bioadhesive strength.

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In vitro dissolution studies

The United States Pharmacopeia (USP) XXIII rotating paddle method was used to study the drug release from the buccal tablets. The dissolution medium consisted of 500ml of phosphate buffer, pH 6.6. The release was performed at 37°C ± 0.5°C, with a rotation speed of 50 rpm [18]. The backing layer of buccal tablet was attached to the glass slide with instant adhesive (cyanoacrylate adhesive). The slide was placed into the bottom of the dissolution vessel. Samples (5ml) were withdrawn at predetermined time intervals and replaced with fresh medium. The samples were filtered through filter paper and analyzed by UV spectrophotometer at 248 nm.

Release kinetics and mechanism

To know the release mechanism and kinetics of formulations (F1-F15), the data was subjected to fit into mathematical models and n, r^2 values for zero order, first order, higuchi and peppas models were calculated. The Peppas model is widely used, when the release mechanism is not well known or more than one type of release could be involved [19]. The semi-empirical equation shown as

$$\mathbf{Mt/M\infty = kt^n}$$

Where, Mt/M∞ is fraction of drug released at time't', k represents a constant, and n is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process. For non-fickian release, the value of n falls between 0.5 and 1.0; while in case of Fickian diffusion, n = 0.5; for zero-order release (case II transport), n = 1; and for supercase II transport, n > 1.

Determination of ex vivo residence time

The *ex vivo* residence time was determined using a locally modified USP disintegration apparatus [20], the disintegration medium was composed of 800 ml phosphate buffer, pH 6.6 maintained at 37±2°C. The porcine buccal tissue was glued to the surface of a glass slab, vertically attached to the apparatus. The buccal tablet was hydrated from one surface using 0.5 ml of phosphate buffer, pH 6.6 and then the hydrated surface was brought into contact with the mucosal membrane. The glass slab was vertically fixed to the apparatus and allowed to run in such a way that the tablet was completely immersed in the buffer solution at the lowest point and was out at the highest point. The time necessary for complete erosion or detachment of the tablet from the mucosal surface was recorded. The experiments were performed in triplicate (n=3) and mean of triplicate was determined.

Ex vivo permeation of drug solution through porcine buccal mucosa

The aim of this study was to investigate the permeability of buccal mucosa to rosuvastatin calcium. It is based on the generally accepted hypothesis that the epithelium is the rate-limiting barrier in buccal absorption.

Tissue preparation

Buccal tissue was taken from pigs at slaughter-house. It was collected within 10 minutes after slaughter of the pig and tissue was kept in Kreb's buffer solution. It was transported immediately to the laboratory and was mounted within 2 hours of isolation of buccal tissue. The tissue was rinsed thoroughly using phosphate buffer saline to remove any adherent material. The buccal membrane from the tissue was isolated using surgical procedure. Buccal membrane was isolated and buccal epithelium was carefully separated from the underlying connective tissue. Sufficient care was taken to prevent any damage to the buccal epithelium.

Procedure

The buccal epithelium was carefully mounted in between the two compartments of a Franz diffusion cell with an internal

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diameter (ID) of 2.4cm (4.52 cm^2 area) and with a receptor compartment. 14 ml of phosphate buffer pH (6.6) was placed in the receptor compartment. The drug solution (5 ml) was placed gently in the donor compartment. The entire setup was placed over magnetic stirrer and temperature was maintained at about 37 °C. The samples (1ml) were collected at predetermined time intervals and stored under refrigerated conditions till the analysis was carried out. All the experiments were performed in triplicate (n = 3) and mean values were used to calculate flux (J) and permeability coefficient (P).

$$J = \frac{dQ/dt}{A}$$

$$P = \frac{dQ/dt}{\Delta C A}$$

Where J, Flux ($mg.hrs^{-1}cm^{-2}$); P, permeability coefficient (cm/h); dQ/dt, slope obtained from the steady state portion of the curve; ΔC, the concentration difference across the mucosa and A, area of diffusion (cm^2).

Ex vivo permeation of buccal tablet

Ex vivo permeation study of buccal tablets through the porcine buccal mucosa was performed using Franz-type diffusion cell at 37 °C ± 0.2 °C and 50 rpm. This temperature and rpm was maintained by using magnetic stirrer. Porcine buccal mucosa was obtained from a local slaughter house and used within 2 hrs of slaughter. The tissue was stored in Krebs' buffer at 4 °C upon collection. The epithelium was separated from underlying connective tissues with surgical scissors and clamped between donor and receiver chambers of the Franz-type diffusion cell. After the buccal membrane was equilibrated for 30 mins with Krebs' buffer solution between both the chambers, the receiver chamber was filled with fresh pH 6.6 buffer solution. The buccal tablet was placed in donor chamber and 1ml of buffer solution (pH 6.6) was added. Aliquots (1ml) were collected at predetermined time intervals and filtered through a filter paper, and the amount of drug permeated through the buccal mucosa was then determined by measuring the absorbance at 250 nm using a UV spectrophotometer. The medium of the same volume (1ml), which was prewarmed at 37°C, was then replaced into the receiver chamber. The experiments were performed in triplicate (n = 3) and mean value was used to calculate the flux and permeability coefficient.

Enhancement ratio$_{flux}$ = Q_{enh}/Q_{con}

Fourier Transform Infrared (FTIR) Spectroscopic studies:

FTIR spectroscopic studies were conducted for optimized formulation and pure drug (Rosuvastatin calcium). The samples were analyzed between wave numbers 4000 and 400 cm^{-1}.

RESULTS AND DISCUSSION

Tablets were evaluated for weight variation, hardness, friability, thickness and drug content. The results for these parameters are given in Table 2. The hardness of the tablets ranged from 4.8 to 7.7 kg/cm^2 and the friability values were less than 0.49% indicating that the tablets were compact and hard. The thickness of the tablets ranged from 2.26 to 2.71 mm. The assay values were also within the limits 97.17 to 99.87 % with good uniformity.

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TABLE 2: POST COMPRESSION EVALUATION OF ALL FORMULATIONS

Formulation Code	Thickness (mm)	Weight variation(mg)	Friability (%)	Hardness (Kg/cm^2)	%Drug content
F1	2.69±0.020	150.0±0.35	0.08	6.4±0.12	99.66
F2	2.63±0.060	148.1±0.70	0.42	5.2±0.24	98.10
F3	2.51±0.024	152.8±0.25	0.06	7.7±0.10	97.62
F4	2.69±0.015	149.2±0.55	0.28	5.1±10.12	99.63
F5	2.26±0.020	146.0±0.24	0.17	4.8±0.33	99.17
F6	2.64±0.010	155.2±0.70	0.07	6.6±0.10	99.04
F7	2.71±0.030	156.3±0.20	0.31	5.1±0.05	98.39
F8	2.64±0.030	157.3±0.60	0.08	6.7±0.05	99.07
F9	2.49±0.045	150.0±0.55	0.12	7.6±0.08	97.17
F10	2.38±0.057	152.9±0.48	0.42	4.9±0.15	99.37
F11	2.63±0.060	148.1±0.70	0.42	5.2±0.24	98.10
F12	2.61±0.030	157.2±0.50	0.23	4.5±0.05	99.03
F13	2.50±0.035	153.5±0.15	0.04	6.1±0.05	98.43
F14	2.56±0.039	156.5±0.41	0.06	6.1±0.08	99.12
F15	2.63±0.056	149.5±0.54	0.05	5.8±0.25	99.87

***In vitro* dissolution studies**

The results indicate that the release of rosuvastatin calcium from different formulations varied according to the type and ratios of the matrix forming polymers. For all formulations (F1-F15), the cumulative drug release at the end of 6th hour was calculated. From formulations F1-F5, drug release was good for F3 (97.83%), from formulations F6-F10, drug release was good for F7 (89.68%), from formulations F11-F15, drug release was good for F12 (82.63%). HPMC is a hydrophilic swellable polymer, which is able to form a viscous gel layer which controls the drug release via diffusion through the gel and erosion of gel barrier. Carbopol has excellent mucoadhesive, gelling properties and also helps in sustaining effect. The results indicate that the rate of drug release was higher for F3 formulation. The rate of drug release decreased by increase in the concentration of HPMC K4M which may be due to the increase in viscosity produced by the gelling of the hydrophilic polymer HPMC K4M. The data of the *in vitro* release was fit in different equations and kinetic models to explain the release kinetics of rosuvastatin calcium from buccal tablets. Formulations (F1-F15) exerted Fickian diffusion mechanism with *n* value which varied from 0.434-0.497. For optimized formulation (F3) showing highest release, r^2

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(0.9863) value was found to follow higuchi release and since 'n' value is 0.445, it follows Fickian diffusion. The comparison of cumulative percent drug release of all formulations is shown in Figure 2, 3, 4 and 5.

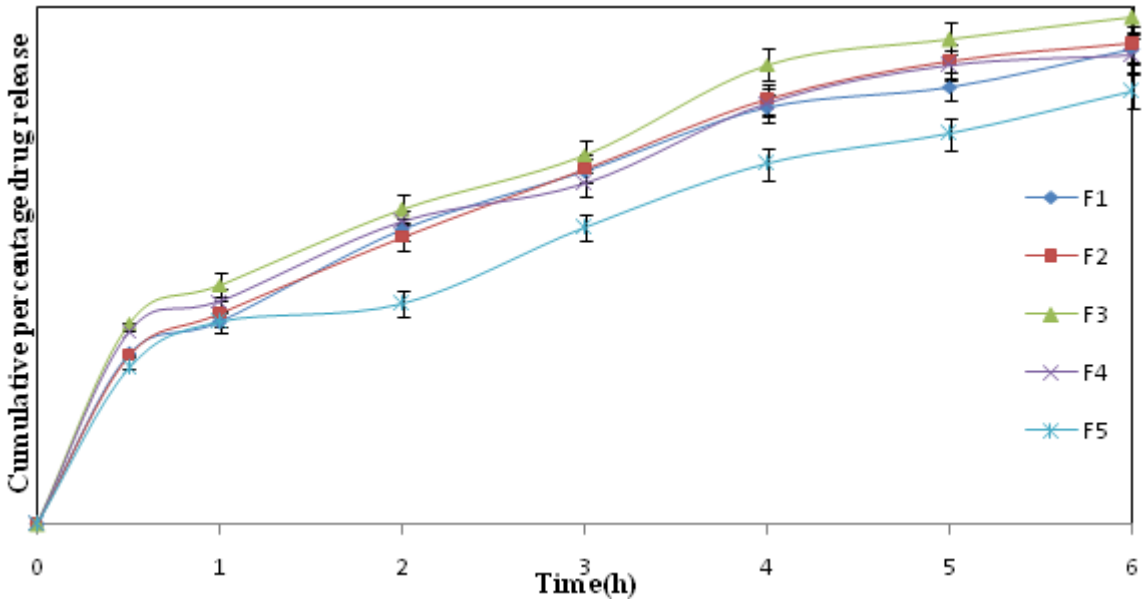

Fig 2: *in vitro* cumulative percentage drug release profile of formulations with HPMC K4M

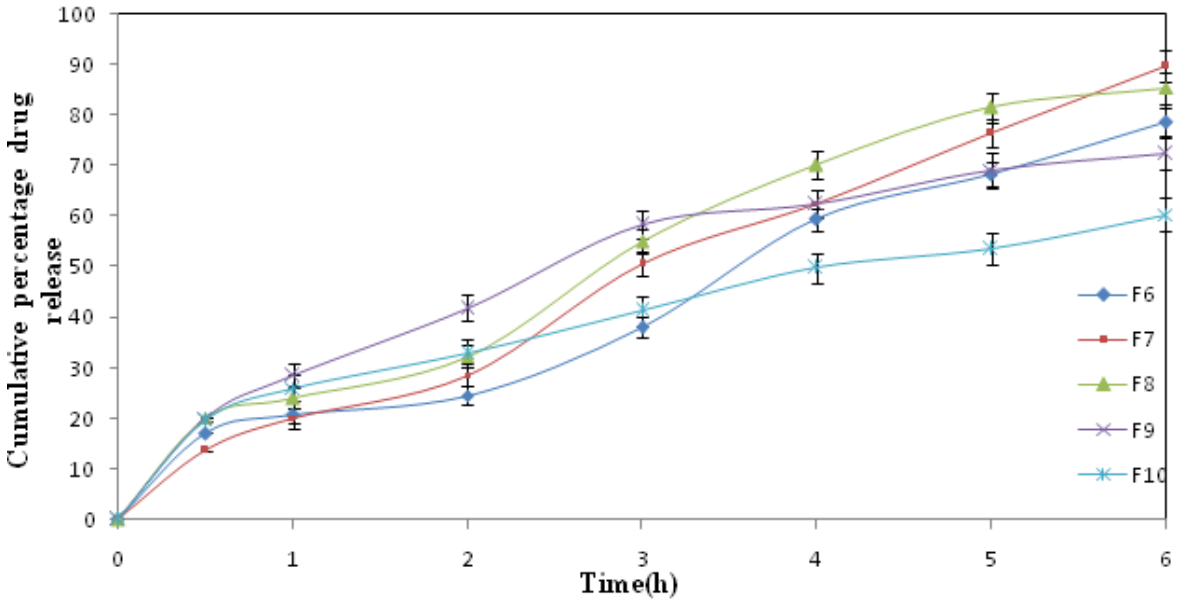

Fig. 3: *in vitro* cumulative percentage drug release profile of formulations with HPMC K15M

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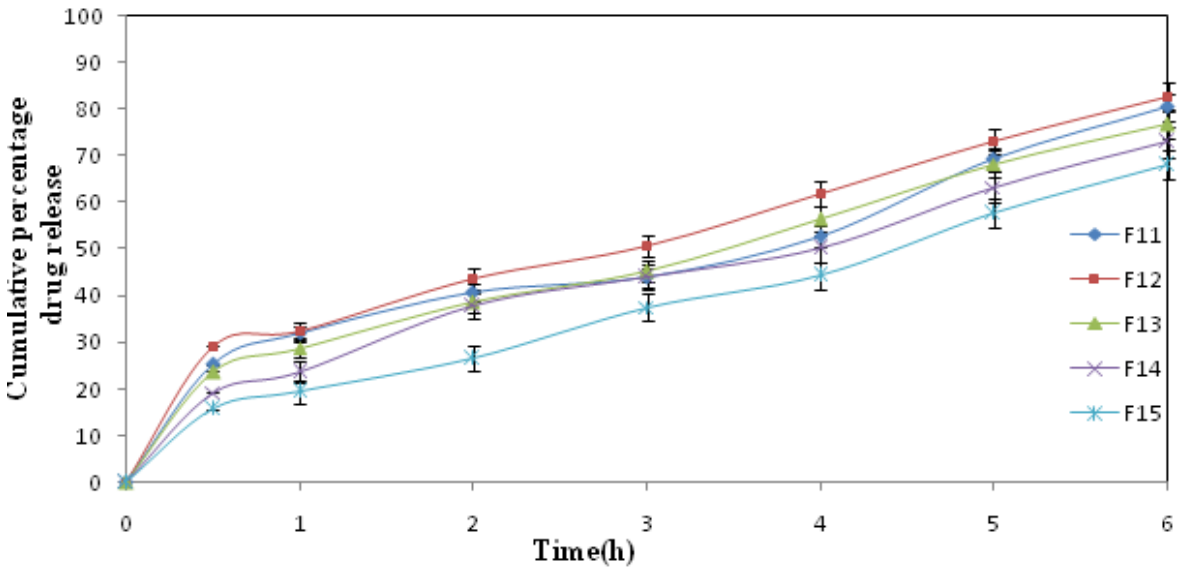

Fig. 4: *in vitro* cumulative percentage drug release profile of formulations with carbopol 974p

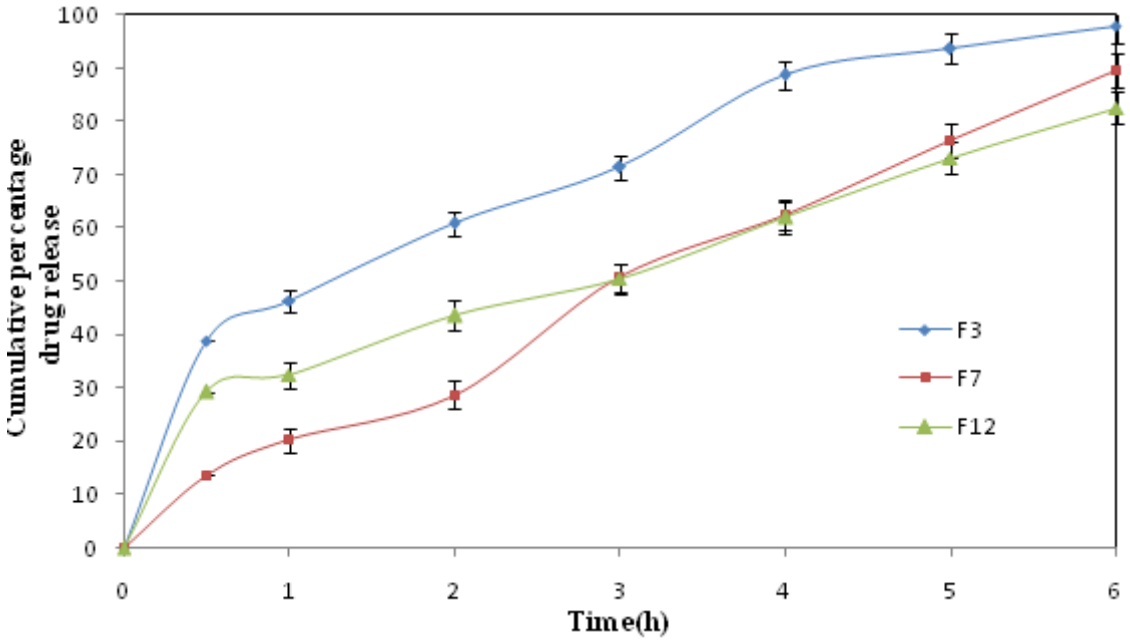

Fig. 5: Cumulative percentage drug release profile of selected formulations

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Swelling studies of buccal tablets:

In formulations containing HPMC K4M, F3 (selected optimized formulation) showed swelling index of 102.8; the formulations containing HPMC K15M and carbopol 974p showed maximum swelling index i.e. 123 and 138.6 respectively. The formulation containing carbopol showed higher swelling index values than HPMC containing formulations. The bioadhesion and drug release profile are dependent upon swelling behavior of the buccal tablets. As the proportion of these polymers in the matrix increased, there was an increase in the amount of water uptake and proportionally greater swelling leading to a thicker gel layer. An increase in polymer concentration causes an increase in the viscosity of the gel as well as formation of a gel layer with a longer diffusional path. This could cause a decrease in the effective diffusion coefficient of the drug and therefore a reduction in the drug release rate [21]. The values of all formulations (F1-F15) were found in the range of 34.3 to 142.6 respectively and swelling behavior of buccal tablets as a function of time are represented in Figure 6, 7 and 8.

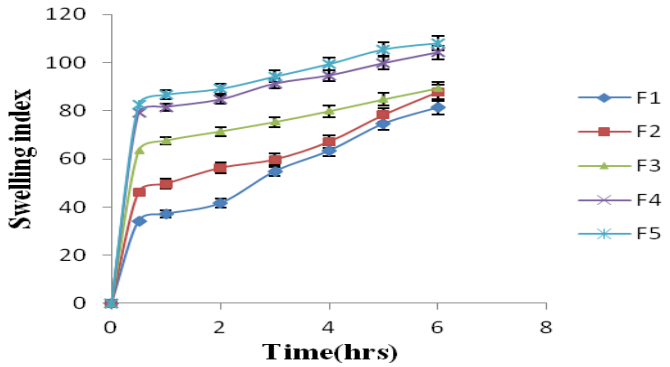

Fig. 6: Swelling index profile of formulations containing HPMC K4M

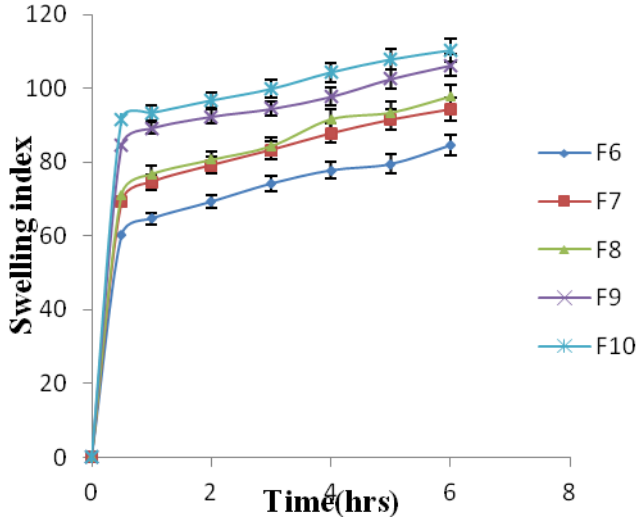

Fig. 7: Swelling index profile of formulations containing HPMC K15M

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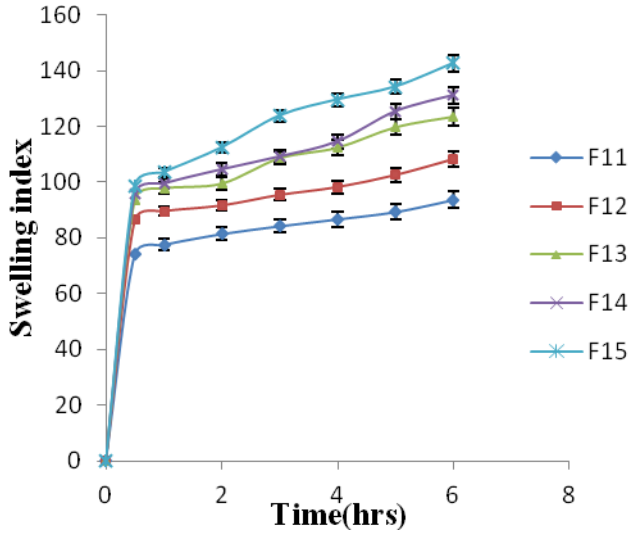

Fig. 8: Swelling index profile of formulations containing Carbopol 974

Measurement of bioadhesion strength

The maximum bioadhesion strength for formulations containing HPMC K4M (F5), HPMC K15M (F10) and carbopol 974p (F15) were found to be 28.5 ± 0.06 g, 32.3± 0.21g, 42.4±0.12 g respectively. The force of adhesion gradually decreased with the increase in HPMC K4M, HPMC K15M and carbopol 974p percentage in the formulations. Comparatively weak bioadhesion force of the non ionic polymer HPMC may be attributed to the absence of a proton-donating carboxyl group which reduce its ability for the formation of hydrogen bonds where as carbopol 974p exhibits stronger bioadhesion force as it contains branched molecules with more or less cross-linked segments of comparable length. The difference observed in adhesion force reflect their structural difference as carbopol 974p is a polyacrylic acid cross-linked with allyl sucrose. In all the formulations (F1-F15) as the polymer concentration increased, the bioadhesive strength also increased. The order of bioadhesion was <HPMCK4M< HPMC K15M < carbopol 974p. Buccal tablets formulated with carbopol 974p showed stronger mucoadhesion than HPMCK4M and HPMC K15M. Very strong bioadhesion could damage the epithelial lining of the buccal mucosa. Optimized tablet (F3) showed 24.1±0.04 g of bioadhesion strength. Bioadhesion strength values of all the formulations (F1-F15) are represented in Figure 9.

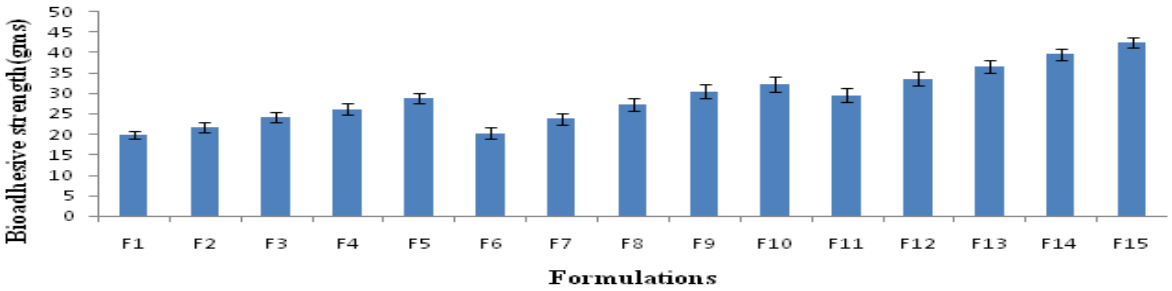

Fig. 9: Bioadhesion strength of formulations

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***Ex vivo* residence time**

The *ex vivo* residence time for selected formulations varied from 5-7 hrs. The maximum residence time (5.53±0.15 h, 6.50±0.20 h, 6.96.±0.23 h) was found for formulations F3, F7, F12 are represented in Table 3 and low residence time was found for optimized formulation F3 (5.53±0.15 h). Bilayered tablets containing higher proportion of carbopol 974p, the mucoadhesion time was found to be increased. This is because of the high mucoadhesive nature of the polymer and interpenetration of polymeric chains into the mucus membrane.

TABLE 3: *EX VIVO* RESIDENCE TIME OF SELECTED FORMULATIONS

Formulation	*Ex vivo* residence time (hr)
F3	5.53±0.15
F7	6.50±0.20
F12	7.12.±0.23

Surface pH study of buccal tablets

The surface pH of the buccal tablets was determined in order to investigate the possibility of any side effects *in vivo*. As an acidic or alkaline pH may cause irritation to the buccal mucosa, it was determined to keep the surface pH as close to neutral as possible. Surface pH of the optimized formulation F3 was found to be 7.18±0.085. This pH is near to the neutral, so the formulation does not cause any irritation on the mucosa. Surface pH values for all the formulations (F1-F15) are represented in Table 4.

TABLE 4. SURFACE pH VALUES OF FORMULATIONS

Formulation	Surface pH
F1	7.05±0.070
F2	5.91±0.010
F3	7.18±0.085
F4	6.21±0.015
F5	6.81±0.035
F6	6.85±0.015
F7	6.75±0.010
F8	6.92±0.015
F9	6.85±0.030
F10	6.13±0.010
F11	6.91±0.040
F12	6.85±0.005
F13	6.63±0.050
F14	7.7±0.09
F15	6.26±0.45

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***Ex vivo* permeation of buccal tablets**

The results of drug permeation from buccal tablet of rosuvastatin calcium through the porcine buccal mucosa reveal that drug was released from the formulation and permeated through the porcine buccal membrane and hence can possibly permeate through the human buccal membrane [22]. Figure 10 represent comparison of cumulative percent drug permeated from drug selected formulations. The results indicated that the cumulative percentage drug permeation was more in F3 among the selected formulations and about 73.14% of rosuvastatin calcium was be permeated through the buccal membrane in 6 hrs, flux and permeation coefficient were found to be 8.35 ± 0.291 µg $h^{-1}cm^{-2}$, 1.34 ± 0.05 cm h^{-1} respectively.

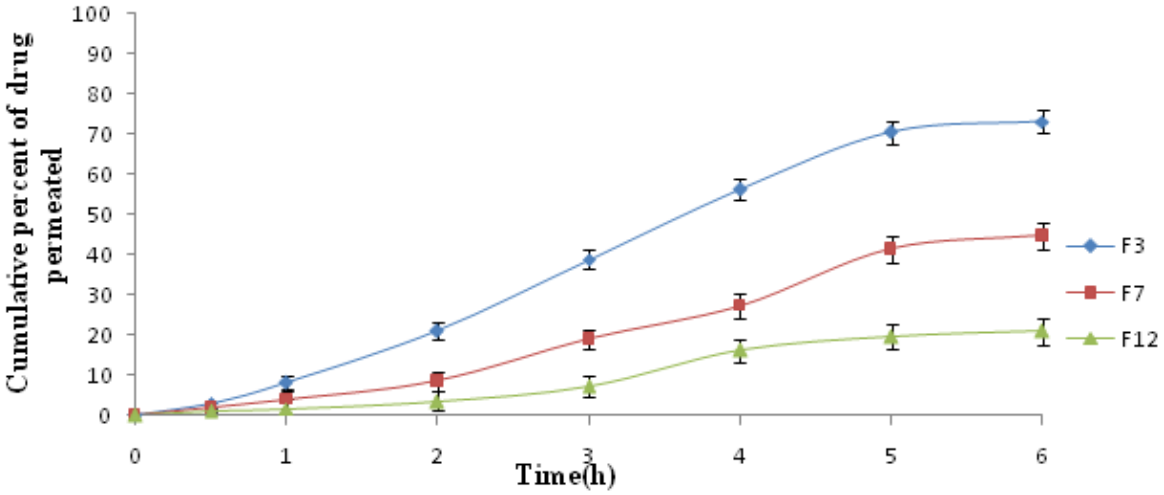

Fig. 10: Cumulative percent drug permeation of selected formulations

Fourier transform infrared (FTIR) spectroscopic studies

To investigate the possibility of chemical interaction between drug and polymer FTIR spectra of pure rosuvastatin calcium and optimized formulation were analyzed over the range 400–4000 cm−1. The IR spectrum of pure rosuvastatin calcium (Figure 11) showed strong absorption bands at wave numbers of 3324.87cm-1, 3326.65 cm-1 and 1435.67cm-1 corresponding to cyclic amines, C-H stretching, C=O stretching, O-H bending and chlorine respectively. FTIR spectra of the optimized formulations displayed all the characteristic bands of both drug and excipients, without any significant spectral shift. This suggested that there was no potential chemical interaction between the components of the formulations.

ISSN 2319-1074

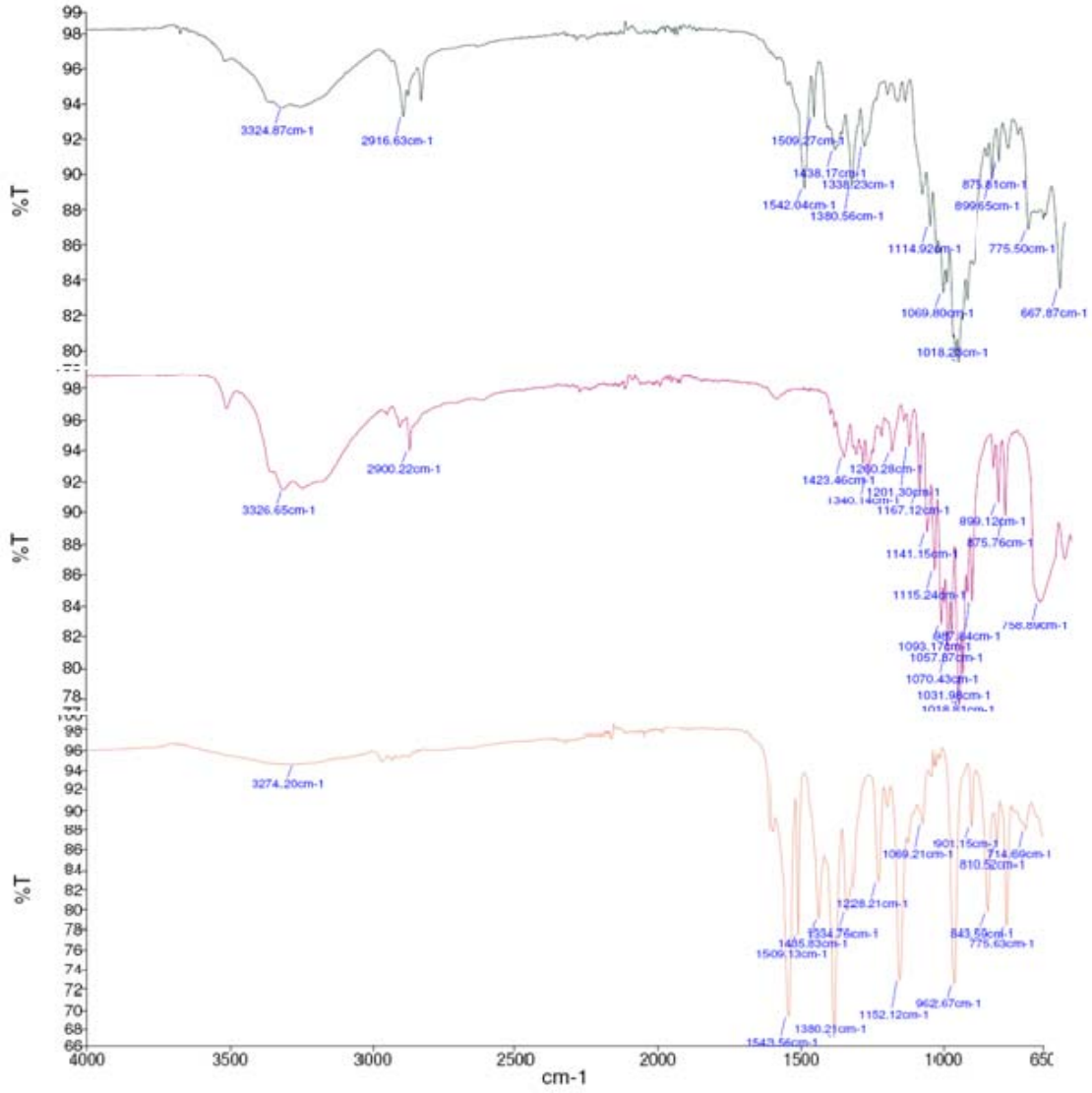

Fig. 11: FTIR spectra of a) Drug (rosuvastatin calcium) b) Optimised formulation c) Spray dried lactose

CONCLUSION

Development of bioadhesive buccal drug delivery of rosuvastatin calcium tablets is one of the alternative routes of administration of to avoid first pass effect, efflux transport and overcome the poor oral bioavailability, provide prolonged release and enhance patient compliance. From the results, it was concluded that the *in vitro* drug release, bioadhesion strength, swelling index, *ex vivo* residence time, *ex vivo* drug permeation of the optimized formulation is

ISSN 2319-1074

suitable for buccal delivery. The results strongly suggest that the increase in cumulative drug permeated was due to effect of HPMC K4M on paracellular and transcellular pathways. FTIR studies concluded that there was no interaction between drug and excipients. In addition, these formulations reduce the need of frequent administration, dose dependent side effects and enhance patient compliance.

ACKNOWLEDGEMENTS

The authors wish to thanks Dr. Reddy's Laboratories, Hyderabad, India providing Rosuvastatin calcium gift sample.

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