

FORMULATION AND EVALUATION OF MUCOADHESIVE BUCCAL FILMS OF ATORVASTATIN USING NATURAL PROTEIN

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ABSTRACT

Objective: The objective of this study was formulation and evaluation of mucoadhesive buccal films of Atorvastatin to increase its bioavailability by using novel mucoadhesive polymer from natural source which is safe and is a biomaterial.

Methods: Atorvastatin was embedded in controlled released mucoadhesive buccal film using casein, hydroxy propyl methyl cellulose (HPMC E15) and sodium carboxy methyl cellulose (Na CMC) by solvent casting method. The films were evaluated for thickness uniformity, weight variation test, surface pH, folding endurance, drug content estimation, percentage moisture absorption, percentage moisture loss, tensile strength, *ex vivo* mucoadhesive strength and *ex vivo* drug permeation studies.

Results: Drug-polymer compatibility studies (FTIR and DSC) showed no incompatibility between the drug and the polymers. *Ex vivo* permeation studies through sheep buccal mucosa showed good controlled drug release in the range of 62.53 to 95.18 % over a period of 24 hrs. The optimized Formulation was found to be Formulation F6 showing *ex vivo* drug release of 95.18 % at the end of 24 hrs. Considering the correlation coefficient (R^2) values obtained from the kinetic equations, the drug release from all the Formulations (F1-F9) were found to follow zero order drug release mechanism.

Conclusion: It can be concluded that oral mucoadhesive buccal film of Atorvastatin, an anti hyperlipidemic agent can be formulated using casein (milk protein) as a film forming material. The study suggests that Atorvastatin can be conveniently administered orally in the form of buccal films with lesser occurrence of its side effects and improved bioavailability.

Keywords: Atorvastatin, Mucoadhesive buccal films, Casein, Hydroxy propyl methyl cellulose E15, Sodium carboxy methyl cellulose, Hyperlipidemia.

INTRODUCTION

Within the oral mucosal cavity, the buccal region offers an attractive route of administration for controlled systemic drug delivery [1,2]. Buccal route of drug delivery is a good alternative, amongst the various routes of drug delivery [3]. In buccal delivery administration of drug is via the buccal mucosa (the lining of the cheek) to the systemic circulation. The buccal mucosa lines the inner cheek and buccal formulations are placed in the mouth between the upper gingival (gums) and cheek to treat local and systemic conditions. The buccal route provides one of the potential routes for typically large, hydrophilic and unstable proteins, oligonucleotides and polysaccharides, as well as conventional small drug molecules [4]. This route is well vascularized with venous blood draining the buccal mucosa reaching the heart directly via the internal jugular vein. Moreover, buccal delivery for the transmucosal absorption of drugs into the system circulation provides a number of advantages such rapid onset of action, sustained delivery, high permeability, high blood flow, and is easily accessible for both application and removal of a drug delivery device [5,6,7,8].

Over the past few decades, the concept of use of bioadhesive polymers to prolong the contact time has gained remarkable attention in transmucosal drug delivery. Adhesion as a process is simply defined as the "fixing" of two surfaces to one another. Bioadhesion may be defined as the state in which two materials, at least one of which is biological in nature, are held together for extended periods of time by interfacial forces. In the pharmaceutical sciences, when the adhesive attachment is to mucus or a mucous membrane, the phenomenon is referred to as mucoadhesion [9,10]. Atorvastatin is an antihyperlipidemic drug and is a member of the drug class known as statins, used for lowering blood cholesterol. Like all statins, Atorvastatin works by inhibiting HMG-CoA reductase, an enzyme found in liver tissue that plays a key role in production of cholesterol in the body [11,12]. The log P (partition coefficient) value for Atorvastatin is about 5.7 and indicates that it has sufficient lipophilicity to pass through the buccal membranes. The bioavailability of the drug is 14% due to its high first-pass

hepatic metabolism. Due to its rapid clearance from the body, a controlled release product is required for it to exert its pharmacological effect [12]. Casein, the major milk protein, forms an integral part of the daily diet in many parts of the world. Casein possesses a number of interesting properties that make it a good candidate for conventional and novel drug delivery systems [13]. It is inexpensive, readily available, non-toxic and highly stable. As a natural food product, this GRAS (generally recognized as safe) protein is biocompatible, biodegradable and easily digestible biodegradable [14]. It comprises of about 80% total protein content of milk, is insoluble in water, soluble in dilute alkalis and concentrated acids. Industrially it is used in sizing of textile and as an adhesive, in preparation of casein plastic and casein paints. Low toxicity and natural metabolism in physiological systems make casein extremely suitable materials for Pharmaceutical Formulations [15].

MATERIALS AND METHODS

Atorvastatin was obtained as a gift sample from MACS Bio-Pharma, Kukatpalli, Hyderabad, India. Casein and HPMC E15 were obtained from S.D. Fine-Chem Ltd., Mumbai, India. Sodium Hydroxide, Polyethylene glycol 400 and Na CMC were obtained from Merck Specialities Private Ltd., Mumbai. Propylene glycol was obtained from Merck Chemicals Pvt Ltd., India. All other chemicals and solvents used were of analytical grade and were obtained from S.D. Fine-Chem Ltd, Mumbai, India.

Fabrication of Mucoadhesive Buccal Films of Atorvastatin

Mucoadhesive buccal films of Atorvastatin were prepared by solvent casting method. Initially solution (A) was prepared by dissolving casein in sufficient amount of water by adding sodium hydroxide (5% w/v) solution drop wise, and then add plasticizer, and kept for stirring for 2 hrs. Solution (B) was prepared by dissolving drug in 1 ml of methanol as per formulation chart (Table 1) in appropriate quantities, and added to solution (A) and kept for stirring for 2 hrs. Care was taken as air bubble entrapment occurs during stirring. After uniform

mixing of two solutions, degassing was done to remove air bubbles and finally the solution was casted into pre-fabricated glass mould of size 4x4 cm size and dried over night and the

dried film was cut into appropriate sizes for further evaluation. Composition of prepared mucoadhesive buccal films of Atorvastatin was shown in Table 1.

Table 1: Formulation ingredients of Atorvastatin mucoadhesive buccal films

Ingredients	Formulation								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Atorvastatin (mg)	40	40	40	40	40	40	40	40	40
Casein (mg)	400	500	600	200	250	300	200	250	300
HPMC E15 (mg)	-	-	-	200	250	300	-	-	-
Na CMC (mg)	-	-	-	-	-	-	200	250	300
Propylene Glycol (%w/w)	11	11	11	11	11	11	11	11	11
PEG 400 (%w/w)	7	7	7	7	7	7	7	7	7
Sodium hydroxide (ml)	0.48	11	13.4	0.48	11	13.4	0.48	11	13.4
(5% w/v)	1	1	1	1	1	1	1	1	1
Methanol (ml)	9	11	13.4	9	11	13.4	9	11	13.4
Water (ml)									

*Each 4x4 cm film contains 40mg of Atorvastatin.

Evaluation of Physicochemical Parameters of Mucoadhesive Buccal Films of Atorvastatin

Fourier Transform Infrared (FTIR) Spectroscopy

The drug-polymer compatibility was confirmed by carrying out FTIR studies. Drug, polymer and physical mixture of drug-polymer were subjected to FTIR analysis using FTIR 8400S Shimadzu, Japan. Samples were prepared in Potassium Bromide disks (2 mg sample in 200 mg Potassium Bromide) with a scan range of 450-4000 cm^{-1} and the resolution of 4 cm^{-1} . FTIR studies were carried out for Atorvastatin pure drug, physical mixture of optimized formulation and optimized formulation.

Differential Scanning Calorimetry (DSC)

The drug-polymer compatibility was confirmed by carrying out DSC studies. DSC analysis using DSC Q20V24.10. Build 122, TA Instruments, USA. DSC was performed for pure drug and optimized formulation. Samples were heated between 50 and 450 $^{\circ}\text{C}$ in an inert nitrogen gas atmosphere.

Thickness Uniformity

Three films of each formulation were taken and cut into 2x2 cm size by using sharp blade. The films thickness was measured using digital screw gauge at six different places and the mean thickness value was calculated [16].

Weight Variation Test

Mucoadhesive buccal films of size 4x4 cm were cut into 2x2 cm with the help of a sharp blade. Three films of same size were randomly selected for the weight variation test. Each film was calibrated individually on digital balance and average weight was calculated [17].

Surface pH

The surface pH of the mucoadhesive buccal films was measured by using combined glass electrode. The films (2x2 cm) were allowed to swell by keeping it in contact with 1 ml of distilled water for 2 hrs at room temperature. The pH was measured by bringing the electrode in contact with the surface of the patch and allowing it to equilibrate for 1 minute and the pH was determined [17,18,19,20].

Folding Endurance

Three films of each formulation of size (2x2 cm) were cut by using sharp blade. Folding endurance of the buccal films was determined by repeatedly folding a small strip of film at the same place till it broke. The number of times, the film could be folded at the same place without breaking which gave the value of folding endurance of film. This study was performed in triplicate and the average of three readings was calculated [17,20,21].

Drug Content Estimation

A film was cut into three pieces of size 2x2 cm were taken in separate 100 ml of pH 6.8 phosphate buffer was added and continuously stirred for 24 h. The solutions were filtered, suitably diluted and analyzed at 245 nm in a UV Spectrometer. The average of drug content of three films was taken as final reading [16].

$$\text{Drug Content} = \frac{\text{Concentration} \times \text{Dilution factor} \times \text{Dissolution medium}}{1000}$$

Percentage Moisture Absorption

The percentage moisture absorption (PMA) test was carried out to check the physical stability of the buccal films at high humid conditions. In the present study the moisture absorption capacity of the films were determined as follows. Three 2x2 cm films were cut out and weighed accurately and were placed in desiccator containing saturated solution of aluminium chloride, keeping the humidity inside the desiccator at 79.5 %. After 3 days the films were removed, weighed and percentage moisture absorption was calculated. Average percentage moisture absorption of three films was found [16,22].

$$\text{Percentage moisture absorption} = \frac{W_t - W_0}{W_0} \times 100$$

Where,

W_t = Weight of film at time 't'

W_0 = Weight of film at 'zero' time.

Percentage Moisture Loss

Percentage moisture loss (PML) was carried to check the integrity of films at dry condition. Three films 2x2 cm were cut out and weighed accurately and kept in desiccator containing fused anhydrous calcium chloride. After 72 hours the films were removed, weighed. Average percentage moisture loss of three films was found out [16,23,24].

$$\text{Percentage moisture loss} = \frac{W_0 - W_t}{W_0} \times 100$$

Where,

W_0 = Initial weight

W_t = Final weight.

Tensile Strength

The Tensile strength value of the films directly characterizes the flexibility of films. Tensile Strength of films was performed using tensile tester (Instron 1121, Japan). One end of film strip of dimension 2x2 cm was fixed between the two iron screens to give support to the film and another end was connected to the paper

holder in which hook was inserted. A thread was tied to this hook, passed over the pulley and a small pan attached to the other end to hold the weight. A small pointer was attached to the thread, which travels over the scale affixed on the base plate. To determine tensile strength, the patch was pulled by means of a pulley system. Weights were gradually added to the pan to increase the pulling force till the patch was broken. The weights required to break the patch was considered as a tensile strength and it was calculated as kg/cm² using following formula [25].

$$\text{Tensile strength (kg/mm}^2\text{)} = \frac{\text{Force at break}}{\text{Initial crosssectional area of the film (mm}^2\text{)}} \times 100$$

Ex Vivo Mucoadhesive Strength

Mucoadhesive strength of the film was measured on a modified physical balance. The fresh sheep buccal mucosa was cut into pieces and washed with phosphate buffer pH 6.8. A piece of buccal mucosa was tied to the open mouth of a glass vial, which was filled completely with phosphate buffer pH 6.8. The glass vial was placed and tightly fitted in the centre of glass beaker. The phosphate buffer (pH 6.8, 37±10 °C) was filled in the glass beaker just touches the mucosal surface. The film was stuck to the lower side of rubber stopper with cyanoacrylate adhesive. Two pans of the balance were balanced with 5gm weight on the right hand side pan. A weight of 5 gm was removed from the right hand side pan, which lowered the pan along with the film over the mucosa. The balance was kept in this position for five minutes contact time. The water (equivalent to weight) was added slowly with infusion set (100 drops/min.) to the right-hand side pan until the film detached from the mucosal surface. The weight in grams required to detach the film from the mucosal surfaces gave the measure of mucoadhesive strength [26,27,28].

Surface Morphology

Surface morphology of Atorvastatin loaded buccal film was performed using scanning electron microscopy (Hitachi S-3700N, Japan) to study the surface texture of films and to determine the uniform distribution of active pharmaceutical ingredient. Samples were mounted on round brass sample holder using double-backed adhesive tapes and then placed in the equipment. Pictures were taken at an excitation voltage of 15 kV.

Ex Vivo Drug Permeation Studies

The *ex vivo* drug permeation studies of the mucoadhesive buccal films was performed by using Franz diffusion cell. Sheep buccal mucosa was used as a barrier membrane. The buccal mucosa of freshly sacrificed sheep was procured from the local slaughter house. The buccal mucosa washed in isotonic phosphate buffer of pH 6.8 and used immediately. The permeability across the sheep buccal membrane was determined in order to evaluate diffusion studies by using Franz diffusion cell. Films of 2x2 cm area were used for each formulation. The buccal mucosa was mounted between the donor and receptor compartments. The receptor compartment was filled with 20 ml of phosphate buffer of pH 6.8 which was maintained at 37 ± 0.2 °C and stirred with a magnetic bead at 100 rpm. Aliquots of 5ml was withdrawn at predetermined time intervals and replaced with fresh medium. Absorbance was analyzed using an UV-VIS spectrophotometer (UV-1800 Shimadzu corporation, Japan) at 245 nm [29,30].

Kinetics and Release Mechanism

The *ex vivo* release profiles were tested for their kinetic behavior in order to establish the order of mechanism of drug release. Data was fitted into Zero order, First order, Higuchi, Hixson Crowell and Korsmeyer-Peppas equations and analyzed. From the Korsmeyer-Peppas equation, if the release exponent value (n) is less than 0.5, then the system follows fickian diffusion mechanism, if "n" value is more than 0.5 and less than 1, then the drug transport mechanism follows non-fickian diffusion or anomalous diffusion. If the release exponent is more than 1, then the system follows case II transport mechanism [31].

Stability Studies

Stability studies were carried out as per ICH guidelines at 40±2 °C and 75±5% RH. The films were found to be stable at the end of 90 days study period and their physical characteristics remained unchanged. The drug content was found to be 98.78% at the end of the study indicating that the drug was stable in the mucoadhesive buccal films [18,32].

RESULTS AND DISCUSSION

Fourier Transform Infrared (FTIR) Spectroscopy

FTIR spectra of Atorvastatin and formulation F6 were shown in Fig. 1 and Fig. 2 respectively. The IR spectrum peaks of Atorvastatin was observed at the region of 3412.08 cm⁻¹ due to the O-H stretching (alcohols, phenols), a peak at 3277.06 cm⁻¹ due to the N-H stretching (1°, 2° amines, amides), 2960.73 cm⁻¹ due to the O-H stretch (carboxylic acids) and a peak at 1651.07 cm⁻¹ was observed due to the -C=C- stretch (alkenes). At the lower frequencies 1315.45 cm⁻¹ for C-N stretching (aromatic amines), 1220.94 cm⁻¹ for C-F stretching (alkyl halides) was observed. The IR spectrum of the physical mixture was observed similar to that of peaks of pure drug and polymers peaks. The results indicated that there was no interaction between drug and polymers and the drug in the formulation was stable.

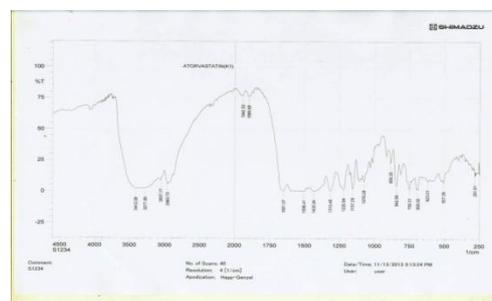


Fig. 1: FTIR spectra of pure drug Atorvastatin

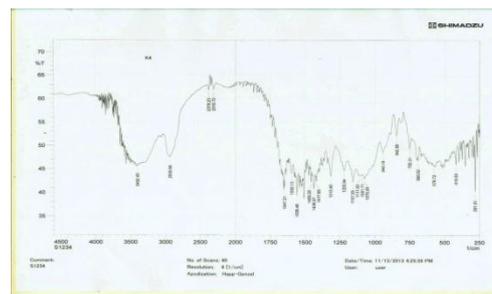


Fig. 2: FTIR spectra of Formulation F6

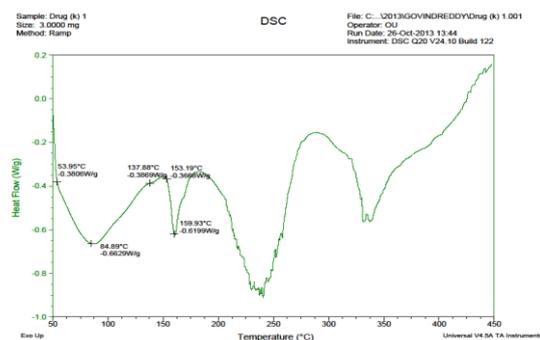


Fig. 3: DSC thermogram of pure drug Atorvastatin

Differential Scanning Calorimetry (DSC)

DSC thermogram of Atorvastatin showed two endothermic peaks one of which at 159.93°C corresponding to the melting point of the Atorvastatin and another at 84.89°C as shown in Fig. 3. Physical

mixture of formulation F6 showed endothermic peaks at 136.65 °C and 73.86 °C as shown in Fig. 4. This indicated that the characteristic peaks of Atorvastatin appeared in the physical mixture of Formulation F6 indicating that there was no possible interaction between the drug and the excipients in the mucoadhesive buccal film formulation.

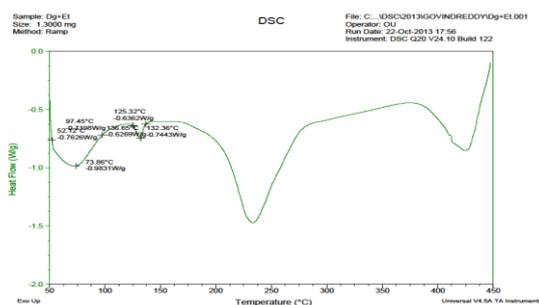


Fig. 4: DSC thermogram of Formulation F6

Evaluation of Physicochemical Parameters of Mucoadhesive Buccal Films of Atorvastatin

Physical appearance was examined with visual inspection of films and texture by touching it. The prepared films are having visually smooth surface and the drug/polymer distribution was uniform.

Thickness Uniformity

Thickness of each film was measured using Screw gauge at 6 different locations. The thickness of the mucoadhesive buccal films varied between 0.21 ± 1.06 to 0.42 ± 1.82 mm. According to the obtained results it was observed that increase in polymer concentration increases thickness of the film. All the films prepared

showed uniform thickness (Table 2) as it is important factor to consider which ascertains the accuracy and uniform distribution of dose in the strip.

Weight Variation Test

The weight of all the films was found to be uniform. It was found to be in a range of 59.12 ± 0.34 to 152.3 ± 0.65 mg. According to the obtained results it was observed that increase in polymer concentration increases weight of the film. Weight variation is an important parameter to consider as any variation in the weight of film leads to under medication or over medication. Average weight results were shown in Table 2.

Surface pH

The surface pH of all the films exhibited uniformity in their values and were found to be between 6.81 ± 0.09 to 6.99 ± 0.04 indicating its compatibility with buccal pH (Table 2). Hence no mucosal irritation was expected and ultimately achieved patient compliance. Drug content of all the films was found to be uniform which indicated that the drug was distributed uniformly in all the films.

Folding Endurance

The folding endurance gives an idea over the flexibility of films as brittle films gives less value of folding endurance and films with good flexibility gives high value of folding endurance.

Buccal films which shows folding endurance more than 300 times represents good mechanical characteristics. According to the obtained results all the films did not show any crack or cut after 300 times folding and all were having satisfactory flexibility. Also, it was observed that increase in thickness of polymer concentration decreases folding endurance value (Table 2). The folding endurance was found to be highest for formulation F1 which contained 400 mg casein.

Table 2: Physicochemical parameters of mucoadhesive buccal films of Atorvastatin

Formulation	Thickness (mm)*	Mean Weight (mg)*	Surface pH*	Folding Endurance*
F1	0.21 ± 1.06	71.02 ± 0.91	6.93 ± 0.09	548 ± 0.08
F2	0.32 ± 2.01	114.6 ± 0.06	6.97 ± 0.16	522 ± 0.14
F3	0.42 ± 1.82	152.3 ± 0.65	6.99 ± 0.04	496 ± 0.03
F4	0.21 ± 0.06	59.12 ± 0.34	6.81 ± 0.09	432 ± 0.12
F5	0.31 ± 1.23	85.76 ± 0.29	6.83 ± 0.14	395 ± 0.06
F6	0.41 ± 2.14	102.2 ± 0.12	6.86 ± 0.12	382 ± 0.12
F7	0.21 ± 0.09	67.26 ± 0.69	6.83 ± 0.04	361 ± 0.01
F8	0.30 ± 0.03	79.65 ± 1.45	6.89 ± 0.11	322 ± 0.06
F9	0.38 ± 0.12	94.91 ± 2.10	6.93 ± 0.06	302 ± 0.13

* Mean \pm SD, n = 3

Drug Content Estimation

The drug content estimation was performed to ensure the accurate distribution of drug. The test was performed for all the formulations in triplicate and results were tabulated in Table 3. The results of content uniformity indicated that the drug was uniformly dispersed. The drug content or percentage of drug content varied in between 98.00 ± 0.12 to $99.11 \pm 0.15\%$.

Percentage Moisture Absorption

Percentage moisture absorption (PMA) test was conducted on mucoadhesive buccal films of Atorvastatin to determine its physical stability of the film at high humid conditions. Optimum moisture content in the formulations helps the film to remain stable, non brittle and free from complete drying. Optimum values of moisture absorption in F6 formulation indicate less chance of microbial contamination and maintain integrity through the films shelf life. The obtained values were in a range of 3.72 ± 0.06 to $6.71 \pm 0.04\%$ (Table 3).

Percentage Moisture Loss

Percentage moisture loss (PML) was conducted on mucoadhesive

buccal films of Atorvastatin to determine the integrity of the film at dry conditions. The observed results were in Table 3. The obtained values were in a range of 1.02 ± 0.09 to $2.94 \pm 0.16\%$.

Tensile Strength

Tensile strength gives an indication of the strength and elasticity of the film. Results revealed that all the formulations showed good tensile strength. Tensile strength of all formulations was found to be in a range of 4.92 ± 0.12 to 6.98 ± 0.05 kg/mm² (Table 3). It has been observed that with increase in thickness of the film, there was a decrease in tensile strength of the film. Tensile strength was found to be highest for formulation F1 which contained only casein as film former.

Ex Vivo Mucoadhesive Strength

Mucoadhesive strength was found to be highest for formulation F6 which contained both Casein as film former and HPMC E15 as mucoadhesive polymer. The films composed of casein and higher amounts of the HPMC E15 showed the greatest mucoadhesive strength (Table 3).

Table 3: Physicochemical parameters of mucoadhesive buccal films of Atorvastatin

Formulation	%Drug Content*	%Moisture Loss* (kg/mm ²)	%Moisture Mucoadhesive	Tensile Strength* Ex vivo		
F1	98.88±0.06	6.71±0.04	1.22±0.06	6.98±0.05	10.88±0.06	
F2	98.66±0.12	6.69±0.16	1.06±0.14	6.52±0.17	12.06±0.12	
F3	98.88±0.02	6.65±0.06	1.02±0.09	5.35±0.19	12.88±0.02	
F4	99.11±0.15	4.22±0.21	2.94±0.16	5.32±0.04	13.61±0.15	
F5	99.02±0.08	4.28±0.09	2.62±0.24	5.26±0.08	15.42±0.08	
F6	99.04±0.06	4.25±0.03	2.74±0.08	5.19±0.11	18.84±0.04	
F7	98.00±0.12	3.88±0.16	1.62±0.26	5.29±0.25	9.82±0.03	
F8	98.22±0.06	3.79±0.04	1.68±0.09	5.16±0.09	9.16±0.16	
F9	98.04±0.08	3.72±0.06	1.71±0.17	4.92±0.12	8.26±0.09	

* Mean ± SD, n = 3

Table 4: Estimated values of Atorvastatin release exponent (n) and correlation coefficient (R²) from mucoadhesive buccal films for all the formulations

Formulation code	Zero order First order Higuchi Hixson Crowell				Korsmeyer-Peppas		
	R ²	R ²	R ²	R ²	R ²	R ²	n (Value)
F1	0.8974	0.8580	0.7199	0.8919	0.9912	0.9912	0.6861
F2	0.9129	0.8802	0.7398	0.8882	0.9892	0.9892	0.7055
F3	0.9443	0.9257	0.7871	0.8698	0.9898	0.9898	0.6973
F4	0.9639	0.9428	0.8094	0.8862	0.9422	0.9422	0.8240
F5	0.9717	0.9534	0.8258	0.8790	0.8884	0.8884	0.9040
F6	0.9753	0.9572	0.8329	0.8729	0.8765	0.8765	0.9376
F7	0.9407	0.9153	0.8042	0.8154	0.9830	0.9830	0.6556
F8	0.9241	0.8982	0.7713	0.8387	0.9930	0.9930	0.5924
F9	0.9607	0.9423	0.8161	0.8462	0.8462	0.8462	0.6015

Stability Studies

Optimized Formulation (F6) did not show any physical changes during the study period and also exhibit excellent drug content over

the storage period, as shown in Table 5. Folding endurance remained unchanged and the drug content was 98.78±0.12 at the end of 90 days study period.

Table 5: Stability studies of the optimized Formulation (F6)

Time (days)	0	15	30	45	60	90
Surface pH	6.86±0.12	6.87±0.18	6.86±0.09	6.85±0.26	6.83±0.12	6.81±0.21
Folding endurance	382±0.12	382±0.02	382±0.16	382±0.06	383±0.19	383±0.62
% Drug Content	99.04±0.06	99.02±0.12	99.01±0.12	98.97±0.12	98.89±0.12	98.78±0.12

CONCLUSION

It can be concluded that oral mucoadhesive buccal film of Atorvastatin, an anti hyperlipidemic agent can be formulated using casein (milk protein) as a film forming material. The Atorvastatin buccal films were prepared by the method of solvent casting technique. pH of Formulation F6 was 6.86±0.12 i.e. in between the salivary pH range, which maintains the drug in non-ionized form, resulted in the proper release of drug from the formulation. Highest drug release was obtained with the films containing casein and HPMC E15 in combination in Formulation F6 which showed a drug release of 95.18 % at the end of 24 hrs. From the result of *ex vivo* drug permeation studies it was found that the release kinetics follows zero order drug release. Therefore, Atorvastatin can be conveniently administered orally in the form of buccal films with lesser occurrence of its side effects and improved bioavailability.

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