

Design and Development of Pravastatin Sodium Fast Dissolving Films from Natural Mucilage of Ocimum Bacilicum Seeds

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ABSTRACT

The present research work, aims to prepare and evaluate the fast dissolving oral films containing Pravastatin sodium, an anti hyperlipidemic drug using different ratios of polymers, Hydroxypropyl methylcellulose E3,E5,E6, Polyvinyl alcohol and Ocimum bacilicum mucilage powder. The film was prepared by solvent casting technique using Glycerine and Propylene Glycol, PEG 400 as plasticizers, Aspartame as sweetner, Eugenol as flavouring agent and Xylitol, Mannitol, Sorbitol and as Film modifiers. The study examines the influence of polymers ratio on physicochemical properties and drug release potential of films. Pravastatin sodium, a HMGCoA- Reductase inhibitor with the absorption rate of 34% but the bioavailability is 45% due to its first pass effect, the half life of the drug was around 1.5-2 hours. The present study investigated the possibility of developing Pravastatin sodium fast dissolving films allowing fast, reproducible drug dissolution in the oral cavity, thus bypassing first pass metabolism to provide rapid onset of action of the drug. The films were thin, smooth, flexible, and uniform in drug content, weight and thickness as observed from low SD values. The film formulation, (F14) consisting of polyvinyl alcohol and ocimum bacilicum mucilage powder in the ratio of (1.5%: 0.5%) was found to be suitable in the form of fast dissolving oral film. The optimized formulation, F14 showed less disintegration time and faster drug release. All the systems were found to be stable with respect to drug content as well as physical changes at $40 \pm 2^\circ\text{C}$; Relative Humidity (RH) Maintained at $75\% \pm 5\% \text{RH}$.

Keywords: Anti hyperlipidemic, fast dissolving films, HMGCoA- Reductase inhibitor, ocimum bacilicum mucilage powder, Pravastatin sodium

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INTRODUCTION

There are many different forms into which a medicinal agent can be placed for the convenient and efficacious treatment of a disease. Amongst all the routes of administration oral route is most preferred route receiving more attention in the pharmaceutical field because of flexibility in the designing of dosage form than drug delivery design of other routes. The peroral application is an effective and inexpensive way for drugs that can be absorbed in the gastrointestinal tract [1, 2]. Mouth dissolving product (tablets and films) may show greater patient acceptability and convenience [3]. They can be taken with ease at any time by the patient without

water [4, 5]. Rapidly dissolving dosage forms have acquired great importance in the pharmaceutical industry because of their unique properties [6, 7]. Rapidly dissolving dosage forms are also called as quick dissolving delivery systems, quick disintegrating, mouth dissolve dosage forms or melt-in-mouth dosage forms [8, 9]. These dosage forms disintegrate or dissolve in the salivary fluids of the oral cavity with in 1 min, releasing the drug and inactive ingredients. This fast dissolving action is primarily due to the large surface area of the film, which wets quickly when exposed to the moist oral environment. Most of the drug is swallowed with the saliva where

subsequent absorption takes place in the gastrointestinal tract. Fast dissolving films are a novel approach to get quick onset of action and to get immediate relief of the symptoms. Hence, fast dissolving films are the best formulations as they are soluble in saliva with in 1 minute releasing the drug and inactive ingredients [10]. Most of the drug is swallowed with saliva where subsequent absorption takes place in gastrointestinal tract [11]. The objective of the present study was to design and optimize the fast dissolving film of pravastatin sodium by casting method using hydroxy propyl methyl cellulose (HPMC), poly vinyl alcohol (PVA), Ocimum bacilicum mucilage powder, Xylitol, Mannitol, Sorbitol, PEG400, Propylene glycol, glycerin, aspartame and euginol and to optimize the concentration of PVA and ocimum bacilicum mucilage powder and xylitol for obtaining a film with satisfactory characteristics. Pravastatin sodium is used for the treatment of atherosclerosis and hyper lipidimia. Pravastatin sodium is structurally similar to the HMG, a substituent of the endogenous substrate of HMG-CoA reductase. Unlike its parent compound, mevastatin, and statins such as lovastatin and simvastatin, pravastatin sodium does not need to be activated *in vivo*. Its hydrolyzed lactone ring mimics the tetrahedral intermediate produced by the reductase allowing the agent to bind with a much greater affinity than its natural substrate. The bicyclic portion of pravastatin sodium binds to the coenzyme A portion of the active site. The absorption rate was 34% but the bioavailability is 45% due to its first pass effect, the half life of the drug was around 1.5-2 hours. Atherosclerosis, a disease which affects large and medium size arteries, is now a leading cause of death in many developed countries. The lesion characteristic of atherosclerosis is a localised plaque in the intima and is composed of cholesterol esters, proliferation of smooth muscle, deposition of fibrous proteins and calcification. Moreover in geriatric patients have difficulty of swallowing hence fast dissolving films for Pravastatin sodium was formulated.

MATERIALS AND METHODS

MATERIALS

Pravastatin sodium was obtained as a gift sample from Biocon laboratories. HPMC E3, HPMC E5, HPMC E6, PVA, xylitol, mannitol, sorbitol, PEG 400, glycerin, propylene glycol were procured from National Scientific products. Ocimum bacilicum seeds were obtained from local market. All the reagent and materials were of analytical or pharmacopoeia grade.

Drug polymer compatibility studies

Compatibility of drug with excipients was determined by carrying out FTIR studies. Infrared spectrum of Pravastatin sodium and physical mixture of drug and polymer was determined on Fourier Transform Infrared spectrophotometer (8400 S Shimadzu) using KBr dispersion method. The results were shown in (Figure 1 & 2).

Methods

General method of preparation of pravastatin sodium fast dissolving film by solvent casting method

Extraction of mucilage from ocimum bacilicum seeds [12].

a. Defatting by 12 hrs. Shaking with petroleum ether

The Ocimum seeds were kept in contact with petroleum ether in a stoppered conical flask for 12 h. The flask was kept on the electrical shaker for the continuous shaking. The material was then filtered out and dried at room temperature for complete removal of petroleum ether.

b. Extraction of mucilage:

The seeds were then soaked in distilled water for overnight. The swollen seeds were subjected to agitation by using mechanical stirrer (Remi electrotechnik Ltd.) with 1000 RPM for 2hrs. The agitated mass of seeds was then passed through the 8 folds of the muslin cloth.

c. Precipitation and drying of extracted mucilage in acetone

The filtrate was then precipitated in 3 volumes of acetone then spread on a glass tray and air dried. The dried material was then passed through mesh #30. The material was winnowed and again passed through mesh #60.

General method of preparation of pravastatin sodium fast dissolving film by solvent casting method [13].

Various trails were carried out to prepare the placebo films to optimize the concentration of polymer combination and film modifiers to obtain a film with satisfactory characteristics.

The composition of various films is shown in (Table 1 & 2). The placebo films of the formulations F1 to F10 were prepared by solvent-casting method. Briefly, propylene glycol, glycerin, aspartame and various polymers were dissolved in a 12.5 ml of distilled water. HPMC and film modifier xylitol was soaked in 12.5 ml water for 4 h and then uniformly dispersed to obtain a dispersion. Aqueous solution and the polymeric dispersion were mixed and stirred for 1 hour on magnetic stirrer to

obtain a homogenous dispersion and kept for 1 hour to remove all the air bubbles entrapped. 25 ml of the dispersion was cast onto petry dish, the dispersion was dried in a tray drier (Sapphire Machines, Mumbai, India) at 40–45 °C. The films were carefully removed from petri plates and cut into desired shape of dimensions 2×2 cm². The formulations F11-F13 containing mannitol, sorbitol and PEG400 respectively as plasticizer were casted by the same procedure. The formulations F14 and F15 were casted by increasing the concentrations of film modifier (xylitol). The films were rapped in aluminium foil and stored in an air tight glass bottle. The films were evaluated for imperfections and cuts, peelability without rupturing, folding endurance and cracking and surface roughness.

Table 1: Composition of Pravastatin Sodium Fast Dissolving Films

Ingredients	Purpose										
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Pravastatin sodium	Anti-hyperlipidemic	40mg	40mg	40mg	40mg	40mg	40m	40mg	40mg	40mg	40mg
HPMC E3 w/v	polymer	2%									
HPMC E5 w/v	polymer		2%								
HPMC E6 w/v	Polymer			2%			1%	1%			
PVA w/v	Polymer				2%		1%		1%	1.5%	1.5%
Ocimum bacilicum mucilage w/v	polymer					2%		1%	1%	0.5%	0.5%
Aspartame w/v	sweetner	0.125 %	0.125 %	0.125 %	0.125 %	0.125 %	0.125 %	0.125 %	0.125 %	0.125 %	0.125 %
Xylitol w/v	Film former	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%
Propylene glycol w/v	Plasticizer	1.35 %	1.35 %	1.35 %	1.35 %	1.35 %	1.35 %	1.35 %	1.35 %	1.35 %	1.35 %
Glycerin w/v	Humectant and plasticizer	1.6%	1.6%	1.6%	1.6%	1.6%	1.6%	1.6%	1.6%	1.6%	1.6%
Eugenol %v/v	Flavouring Agent	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%
Distilled water	Solvent	25ml	25ml	25ml	25ml	25ml	25ml	25ml	25ml	25ml	25ml

Table 2: Composition of Pravastatin Sodium Fast Dissolving Films Developed from the Optimized Formula F10

Ingredients	Purpose	F11	F12	F13	F14	F15
Pravastatin sodium	Anti-hyperlipidemic	40mg	40mg	40mg	40mg	40mg
PVA w/v		1.5%	1.5%	1.5%	1.5%	1.5%
Ocimum bacilicum mucilage w/v	Polymer	0.5%	0.5%	0.5%	0.5%	0.5%
Aspartame w/v	Sweetner	0.125%	0.125%	0.125%	0.125%	0.125%
Xylitol w/v	Film former				1.4%	2.4%
Mannitol w/v	Film former	0.4%				
Sorbitol w/v	Film former		0.4%			
PEG 400 w/v	Plasticizer			0.4%		
Propylene glycol w/v	Plasticizer	1.35%	1.35%	1.35%	1.35%	1.35%
Glycerin w/v	Humectant and plasticizer	1.6%	1.6%	1.6%	1.6%	1.6%
Eugenol w/v	Flavouring Agent	0.3%	0.3%	0.3%	0.3%	0.3%
Distilled water	Solvent	25ml	25ml	25ml	25ml	25ml

RESULTS

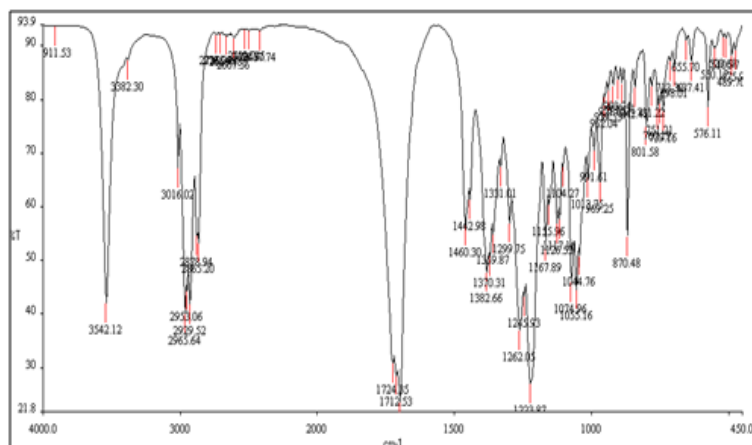


Figure 1: FTIR Spectra of Pravastatin Sodium:

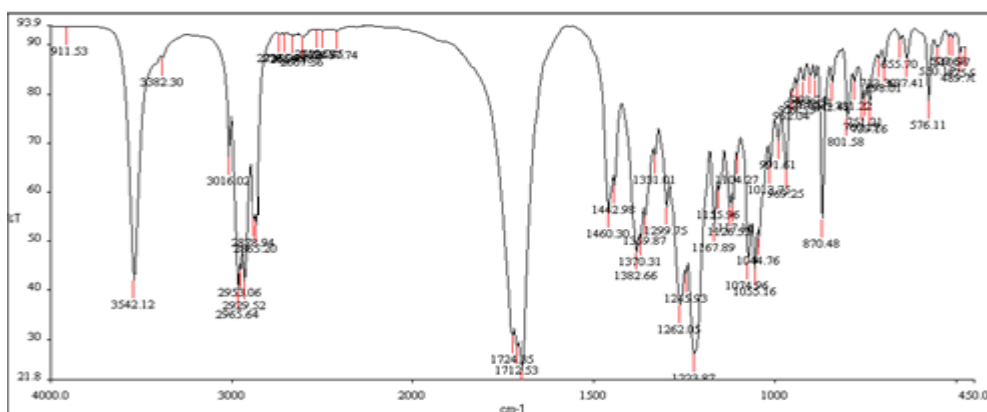


Figure 2: FTIR Spectra of Optimized Formulation (F14)

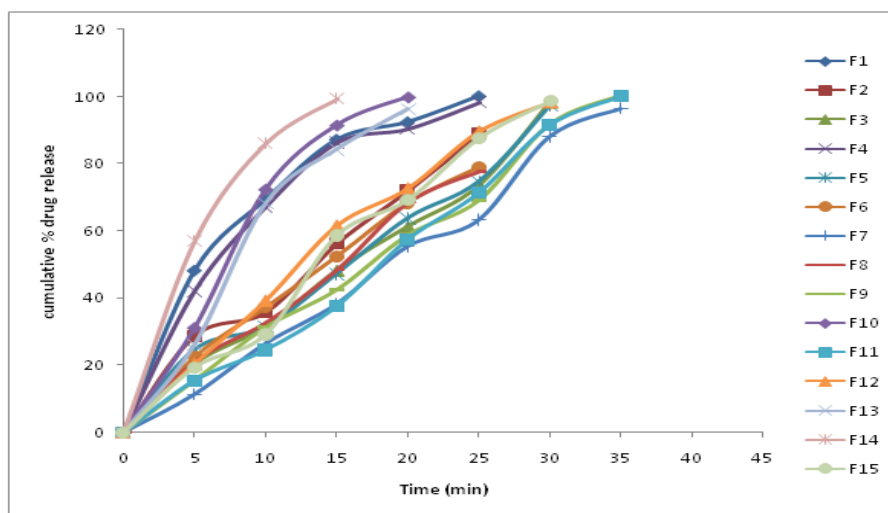


Figure 3: Cumulative % Drug Release Profile of Pravastatin Sodium Fast Dissolving Films of Formulations F1 to F15

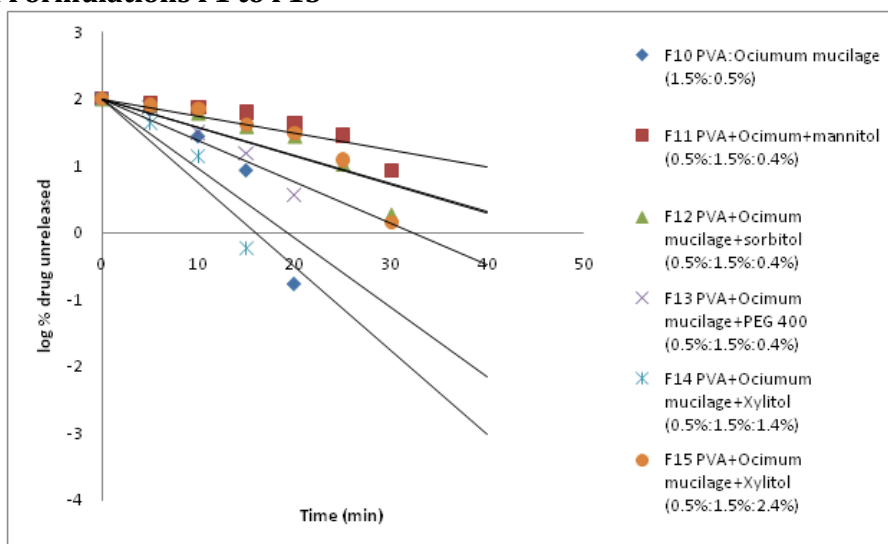


Figure 4: First Order Plots of Pravastatin Sodium Fast Dissolving Films of Formulations F10 to F15

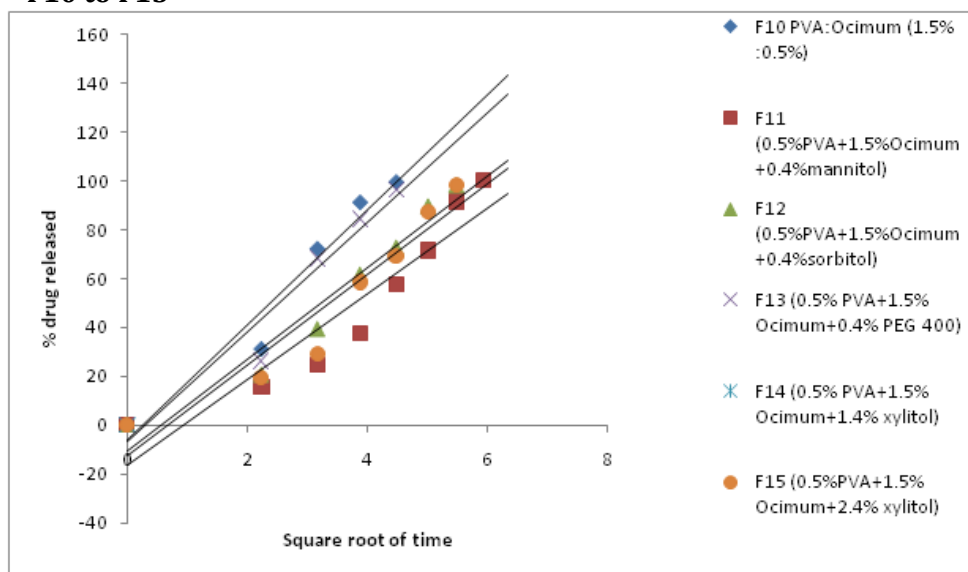


Figure 5: Higuchi Plots Of Pravastatin Sodium Fast Dissolving Films Of Formulations F10 To F15

Evaluation of films: [14]

Appearance:

All the prepared films were checked for their appearances either they are

transparent or opaque or presence of air bubble. The prepared films were shown in figure.



**F10 (PVA: Ocimum)
(1.5%:0.5%)
+ 0.4% xylitol**



**F14 (PVA: Ocimum)
(1.5%:0.5%)
+ 1.4%xylitol**

Figure 6: Picture of FDFS Prepared By Using PVA and Ocimum Bacilicum Mucilage Powder

Weight variation:

Ten films were randomly selected and their average weight was obtained. Individual films were weighed and compared with the average weight for the deviation.

Thickness:

The thickness of a film can be measured by micrometer or screw gauge at different strategic locations (at least 5 locations). This is essential to determine uniformity in the thickness of the film as this is directly related to the accuracy of dose in the film.

Folding endurance test:

Folding endurance is determined by repeated folding of the film at the same place till the film breaks. The number of the times of the film is folded without breaking is computed as the folding endurance value

Moisture uptake:

The percent moisture absorption test was carried out to check the physical stability and integrity of the films at high humid conditions. In the present study the moisture absorption capacities of the films were determined in the following manner. The films were placed in the dessicator containing saturated solution of aluminium chloride, keeping the humidity inside the dessicator at 79.5 % R.H. After 3 days the films were taken and weighed the percentage moisture absorption of the films was found.

Tensile strength& Percent elongation:

This mechanical property was evaluated using the Instron universal testing instrument (Model F. 4026, Instron Ltd., Japan) with a 5 kg load cell. Film strips in a special dimension and free from air bubbles or physical imperfections were held between two clamps positioned at a distance of 3 cm. During measurement, the strips were pulled by the top clamps at a rate of 100 mm/min; the force and elongation were measured when the film broke. Results from film samples, which broke at and not between the clamps, were not included in the calculations. Measurements were run in triplicate for each film. Two mechanical properties, namely, tensile strength and percentage elongation were computed for the evaluation of the film. Tensile strength is the maximum stress applied to a point at which the film specimen breaks and can be computed from the applied load at rupture

$$\text{Tensile stress}(S) = \frac{\text{Applied force}}{\text{Cross sectional area}} = \frac{m \cdot g}{b \cdot t}$$

Where, S = tensile stress in 980 dynes/cm²

m = mass in grams

g = acceleration due to gravity (980 dynes/cm²)

b = breadth of strip in centimeters

t = thickness of strip in centimeters

Percent elongation

When stress is applied, a strip sample stretches and this is referred to as strain. Strain is basically the deformation of strip divided by original dimension of the sample. Generally elongation of strip increases as the plasticizer content increases.

$$\text{Strain}(E) = \frac{\text{Total elongation}}{\text{Original length}} \times 100 = \frac{L - L_0}{L_0} \times 100$$

Where, L = length after force was applied
L₀ = original length

Content uniformity

The content uniformity of dosage units of the oral film preparation was tested for verapamil HCl using UV spectroscopy. According to the USP standards, the contents of preparations should lie between the limits 90% and 110%. The film of area 2x2 cm² was cut and dissolved in distilled water and the remaining volume was made up with distilled water to 100ml in 100ml volumetric flask. Then 1 ml was withdrawn from the solution and diluted to 10ml. The absorbance of the solution was taken at relevant nm and concentration was calculated. By correcting dilution factor, the drug content was calculated by UV spectrophotometry at 238nm.

Surface pH

The film to be tested was placed in a Petri dish and was moistened with 0.5 ml of distilled water and kept for 30 s. The pH was noted after bringing the electrode of the pH meter in contact with the surface of the formulation and allowing equilibration for 1 min. The average of three determinations for each formulation was done.

Disintegration test

Disintegration test was performed to ensure the disintegration of film in water. One film from each formulation was introduced into the one tube of disintegration apparatus USP. A disc was placed on the tube. The assembly was suspended in a beaker containing simulated saliva and the apparatus was operated until the film disintegrated. The results of evaluation studies were represented in (Table 3).

In vitro dissolution test

The dissolution test was performed according to the USP type II Paddle apparatus. Dissolution medium was 900 mL of simulated salivary phosphate buffer (pH 6.8) at 37±0.5°C with a rotation rate of 50 rpm. 5 ml aliquots of samples were taken with a time interval of 5 min and the same volume of fresh of phosphate buffer (pH 6.8) was replenished. Pravastatin Sodium concentrations were assayed spectrophotometrically at 238 nm. The cumulative release profiles of all the formulations were represented in (figure 3).

Data analysis**Kinetic Data / Model fitting**

Drug release mechanisms and kinetics are two characteristics of the dosage forms which play an important role in describing the drug dissolution profile from a dosage forms and hence there *in vivo* performance. The dissolution data obtained is fitted to mathematical models and the best fit is obtained to describe the release mechanism of the drug. A number of mathematical models have been developed to describe the drug dissolution kinetics from drug delivery system *e.g.*, First order (log cumulative % drug remaining versus time), Zero order (cumulative % drug release versus time) Higuchi (cumulative % drug release versus square root of time); and Hixon crowel model ($w_0^{1/3} - w_t^{1/3}$ versus time). The order and mechanism of release of optimised formulation was shown in (Figures 4 and 5) respectively [15,16].

Stability studies

The stability study of the optimized formulation of fast dissolving film was carried out under different environmental conditions. The film was packed in the aluminium foil and stored in stability chamber for stability studies at 2-8°C (45%RH) 25-30°C (60% RH) and 45-50°C (75% RH) for a period of 45days. The films were characterised for drug content and other parameters during the stability study period. The results were shown in (Table 4) [17].

Table 3: Evaluation Parameters of Films of Formulations F-1 To F-15

Formulation code	Film for min g capacity	Appearance	Thickness* (mm)	Folding Endurance	Tensile strength* (Kg/cm ²)	% Elongation*	Surface pH*	Weight variation* (mg)	Invitro disintegration time *(sec)	Assay (%)	% moisture content
F1	+++	Transparent	0.444 ±0.004	73±0.42	0.623 ±0.021	14.93 ±0.324	6.48±0.027	0.935 ±0.004	12±1.6	97.74 ±0.23	1.024 ±0.002
F2	+++	Transparent	0.485 ±0.006	70±0.41	0.603 ±0.024	15.75 ±0.124	6.52±0.014	0.942 ±0.002	21±2.3	95.80 ±0.21	1.973 ±0.006
F3	+++ +	Transparent	0.476 ±0.01	79±0.36	0.609 ±0.019	12.92 ±0.312	6.54±0.021	0.958 ±0.001	26±1.5	97.32 ±0.12	1.426 ±0.003
F4	+++	Transparent	0.34±0.007	75±0.23	0.625 ±0.015	13.21 ±0.241	6.59±0.029	0.911 ±0.001	9±1.1	98.62 ±0.08	1.473 ±0.001
F5	+++ +	Transparent	0.318 ±0.006	77±0.12	0.627 ±0.028	17.11 ±0.124	6.56±0.024	0.932 ±0.004	15±1.2	97.69 ±0.34	2.016 ±0.004
F6	+++	Transparent	0.35±0.012	71±0.81	0.631 ±0.017	12.44 ±0.312	6.61±0.025	0.941 ±0.008	30±1.5	95.61 ±0.11	2.346 ±0.005
F7	+++	Transparent	0.428 ±0.008	78±0.34	0.639 ±0.024	13.16 ±0.214	6.65±0.027	0.945 ±0.005	32±1.6	95.53 ±0.02	2.675 ±0.004
F8	+++	Transparent	0.385 ±0.012	76±0.45	0.684 ±0.032	12.44 ±0.312	6.69±0.028	0.956 ±0.002	23±1.8	98.29 ±0.23	1.874 ±0.006
F9	+++	Transparent	0.335 ±0.012	72±0.32	0.621 ±0.027	15.33 ±0.188	6.75±0.041	0.955 ±0.001	28±1.2	97.65 ±0.22	2.995 ±0.003
F10	+++ +	Transparent	0.365 ±0.012	81±0.12	1.143 ±0.034	10.69 ±0.421	6.91±0.021	0.963 ±0.003	6±1.5	96.78 ±0.87	2.452 ±0.004
F11	++	Whitish	0.385 ±0.012	72±0.02	0.636 ±0.046	12.91 ±0.542	6.78±0.032	0.986 ±0.004	8±1.9	99.12 ±0.32	2.018 ±0.002
F12	+++	Transparent	0.377 ±0.012	77±0.22	0.629 ±0.062	11.74 ±0.112	6.82±0.044	0.937 ±0.002	10±1.2	97.98 ±0.14	2.432 ±0.001
F13	++	Transparent	0.359 ±0.012	78±0.11	0.639 ±0.071	14.77 ±0.116	6.89±0.023	0.925 ±0.002	11±1.6	98.23 ±0.32	2.321 ±0.002
F14	+++ +	Transparent	0.363 ±0.012	85±0.19	2.679 ±0.065	17.94 ±0.221	7.05±0.004	0.905 ±0.001	5±1.4	99.88 ±0.43	2.998 ±0.003
F15	+++	Transparent	0.372 ±0.012	79±0.16	2.435 ±0.046	13.66 ±0.032	7.01±0.002	0.991 ±0.002	12±1.2	97.64 ±0.12	2.992 ±0.001

All the values are represented as Mean ± SD (n=5)

DISCUSSION

Drug polymer compatibility studies:

From the FTIR spectra of pure drug (**Figure 1**) and drug-excipients mixture it was found that drug and excipients were compatible with each other as there was no interference of peaks or existence of extra prominent peaks. Peaks of spectrum of pure drug were compared with the peaks of the spectra of physical mixtures of drug and polymers. It was observed that characteristic IR absorption peaks of Pravastatin sodium were not altered in physical mixture without any change in their position. This ruled out the drug-polymers interaction indicating the drug is compatible and stable in the formulation. This result showed in (**Figure 2**).

Screening of the Polymers for Formulation of Placebo Fast Dissolving Films

Among all the formulations the formulation F10 with PVA: Ocimum bacilicum mucilage powder (1.5%: 05%) showed best film forming ability with xylitol(0.4%) as film modifier.

Screening of the Film Modifiers for Formulation of Placebo Fast Dissolving Films

film modifiers manitol, Sorbitol and PEG 400 were used respectively at a concentraion of (0.4%). Amongst various film modifiers, xylitol showed best ability to improve film forming properties of PVA and ocimum bacilicum as compared to the other film modifiers like mannitol, sorbitol and PEG 400. incorporation of mannitol in films resulted in white patches whereas xylitol and sorbitol containing films had good film characteristics. However, xylitol was selected for the film formation due to its more negative heat of solution and lesser hygroscopicity as compared to sorbitol. The agents with more negative heat of solution are expected to give more cooling sensation in the mouth.

Evaluation of fast dissolving films:

The evaluation parameters of prepared films were showed in the (**Table 3**).

Film forming capacity:

Among all the polymes and their combinations used, combination of PVA : Ocimum bacilicum mucilage powder showed best film forming ability.

Appearance:

The physical appearance of various formulations was determined by visual inspection under black and white background .All the prepared films showed transparency except formulation F11 due to the presence of mannitol (**Figure 6**).

Thickness:

This is essential to ascertain uniformity in the thickness of the film as this is directly related to the accuracy of dose in the strip. Low SD values in the film thickness measurements ensured uniformity of thickness in each formulation. Differences in thickness of films may due to differences of viscosities of polymeric solutions. The thickness was gradually increases with the amount of polymers. Films containing HPMC were thicker than films containing PVA. Thickness of the prepared films was in the range of 0.318 ± 0.006 to 0.485 ± 0.006 mm.

Folding endurance:

The results indicated that the films would not break and would maintain their integrity with general folding when used. Folding endurance of the prepared films were in the range of 70 to 85. Lower folding endurance of films may due to less viscosity of the polymeric solution and formed films were very thin.

Tensile Strength:

Tensile Strength of the prepared films was in the range of 0.603 ± 0.024 to 2.679 ± 0.065 .

% Elongation:

% Elongation of the prepared films was in the range of 10.69 ± 0.421 to 17.94 ± 0.221 .

Surface pH:

The surface pH of fast dissolving films 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 oral mucosa Surface pH of the prepared films were in the range of 6.48 ± 0.027 to 7.05 ± 0.004 . It assured that there will not be any kind of irritation to the mucosal lining of the oral cavity.

weight variation:

weight variation of the prepared films were in the range of 0.905 ± 0.001 to 0.991 ± 0.002

Invitro Disintegration Time:

As expected, increase in the polymer concentration increases disintegration time. While for a fixed polymer quantity, higher

PVA content resulted in faster disintegration of the films. Films formed by combination of PVA and Ocimum bacilicum had shown good disintegration properties than HPMC and PVA films. Invitro Disintegration Time of the prepared films were in the range of 5 to 32 seconds.

Assay:

Homogeneous uniform drug distribution is one of the important characteristic of a fast dissolving film that ensures the uniform reproducible release of the drug from the film % drug content of the prepared films were in the range of 95.53% to 99.88%. Estimation of drug content indicated that the drug is uniformly distributed throughout the films, evidenced by the low values of the SD.

Moisture Content:

Moisture content of the prepared films were in the range of $1.024 \pm 0.002\%$ w/w to $2.998 \pm 0.003\%$ w/w. The films could not be differentiated on the basis of moisture uptake.

In vitro drug release:

Being the fast disintegrating formulations the release rates of all the formulations were very rapid. It was noticed that the films got hydrated rapidly and began to dissolve the drug within minutes. This may be due to the water solubility of the drug and the polymer. The water soluble filler xylitol was reported to be used as inert carrier to form a high water soluble dispersion with active agents. Films formed by higher viscosity of polymer had shown slower dissolution rate this might be due to the increase level of polymer, results in formation of high viscosity gel layer caused by more intimate contact between the particles of polymer results in decreased in mobility of drug particles in swollen matrices, which leads to decrease in release rate. From the *In vitro* drug release (**Figure 3**), it was observed that in formulation containing a single polymer, the drug release was found to be faster from films containing PVA as a polymer when compared with the films containing HPMC lower viscosity resulted in a faster release of drug. The drug release was found to be faster from films containing PVA and

ocimum bacilicum mucilage powder than the films containing HPMC and ocimum bacilicum mucilage powder. It was found that addition of xylitol at a concentration of 1.4% resulted in faster drug release from the films. The release of the drug from its film formulations can be ranked in the following descending order: **F14 > F10 > F13 > F1 > F4 > F15 > F12 > F2 > F8 > F6 > F11 > F3 > F5 > F9 > F7**

Data analysis: Kinetic Data / Model fitting:

The *In vitro* data was fit to different equations and kinetic models to explain permeation profiles. Model fitting data was represented in. The coefficient of correlation of each of the kinetics was calculated and compared. From the Regression coefficient value it was concluded that it follows first order kinetics (**Figure 4**).

The data was further treated as per Higuchi's equation (**Figure 5**). indicated that the drug released by diffusion predominated with the formulation.

Stability study:

There were no physical changes in appearance and flexibility. After subjecting the optimized formulation (F14) to the Accelerated Stability Studies, the results were shown (**Table 4**) that there were no major changes in Drug Content and *In Vitro* Drug Release. Hence the formulation was found to be stable.

CONCLUSION

The fast-dissolving oral films of Pravastatin sodium prepared using different film-forming materials by the solvent-casting method which is simple and cost effective. Films showed satisfactory drug dissolution and acceptable physico-mechanical characteristics. Amongst all formulae, the formulation F14 showed the faster dissolution rate with satisfactory physico chemical parameters. Films were found to be stable at accelerated stability conditions. In the present work, it can be concluded that the fast dissolving films formulation can be an innovative and promising approach for the delivery of Pravastatin for the treatment of hyperlipidemia.

Table 4: Parameters after Accelerated Stability Study of Formulation F14

Parameters after Accelerated Stability Study of Formulation	Temperature Maintained at 40 ± 2°C ; Relative Humidity (RH) Maintained at 75%±5%RH			
	Initial	After 1 month	After 2 months	After 3 months
Drug Content (%)	99.89±0.20	99.80±0.12	99.71±0.12	98.69±0.10
In Vitro Drug Release (%)	99.28±0.34	99.15±0.32	99.01±0.12	98.88±0.13

REFERENCES

1. S.P Vyas., Roop K.Khar., controlled oral, administration, in., controlled drug delivery concepts and advances, 1st edition, vallab prakasham publications, Delhi, 2002.
2. Loyd V.Allen., Nicholas G. Popavich., Howard C. Ansel., Dosage form design biopharmaceutical and pharmacokinetic considerations, In; Ansel's pharmaceutical Dosage Forms and Drug Delivery Sustems, 8th edition, Bl publicatuons, 2006.
3. Renuka sharam , R.K. Parikh, M.C. Gohel and M.M.Soniwala .(2007) Development of taste masked film of Valdecocix for oral use. Indian J. Pharm.Sci., 69(2):320-323.
4. Seager, H. Drug delivery products and zydus fast dissolving dosage forms J. Pharm. Pharmacol. 1998, 50,375.
5. Mashru, R.C., Sutarya, V.B., sankalia, M.G and Parikh P.P., Development and evaluation of fast-dissolving film of salbutamol sulphate. Drug Develop. Ind. Pharm., 2005,31,25.
6. A.C. Liang and L.H.Chen, "Fast Dissolving Intra oral Drug Delivery Systems," Exp. Opin.Ther.Patents 11(6),2001,981-986.
7. S.Borsadia,D.Ohalloran, and J.L.Osborne, "Quick Dissolving Films:Anovel Approach to Drug Delivery, DrugDel.Technolo., 3 (3), 2003,84-90.
8. J.Klanke, "Dissolution Testing of Orally Disintegrating Tablets," Dissol.Technol.,10(2),2003,6-8.
9. S.R.Parakh and A.V.Gothoskar, " A Review of Mouth DissolvingTalet Technolgies," Pharm.Technol.,27 (11),2003,92-100.
10. Chen X, Ji ZL, Chen YZ:TTD: Therapeutic Target Database.Nucleic Acids Res.2002 Jan1;30(1):412-5.
11. Renuka Mishra, Avani Amin, Formulation Development of Taste Masked Rapidly Dissolving films of Cetrizine Hydrochloride. Pharmaceutical Technology.2009;volume33,Issue2,pp.48-56.
12. Sunil Mistry, Biswal PK, B Mishra, S Sahoo. Isolation, Characterization and Pharmaceutical evaluation of the mucilage from Polyalthia suberosa leaves. International Journal of PharmTech Research 2010; 2: 1455-1459.
13. Murata, Y, Isobe, T, Kofuji, K, Nishida, N. Preparation of fast dissolving films for oral dosage from natural polysaccharides. Materials. 2010; 3(8):4291- 4299.
14. Mashru. R.C, Sutariya. BC, Parikh, PP., Development and evaluation of fast dissolving films of Salbutamol sulphate. Drug Development Indian Pharmaceutics. 2005; 35: 25-34.
15. Higuchi W I, Stenhle R G; Rheometric study of particle-particle interactions in suspensions. J of Pharm Sciences. 1965; 64:265-269.
16. Korsmeyer R W, Gurny R, Doelker E, Bur P and Peppas N A; Mechanism of solute release fromporous hydrophilic polymers. Int. J. of Pharmacy. 1983; 15:25-35.
17. Tadao. T, Hirotaka. Y, Naoki. I, Kazuyuki. H, Mayumi. Y, Yasutomi. K, Yoshinovi. J., Preparation of fast dissolving oral thin film containing Dexamthasone. European Journal of Pharm. Biopharmaceutics, 2009; 73(3): 361-5.