Research Article

Gastro Retentive Bioadhesive Drug Delivery System – A Statin Group of Drug

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Accepted on: 02-09-2013; **Finalized on:** 31-10-2013.

ABSTRACT

The objective of this study was to develop sustained release mucoadhesive tablets of lovastatin by using hydrophilic polymers like chitosan, xanthan gum, karaya gum and HPMC K15M. Lovastatin is an anti-hyperlipidimic agent which has low bioavailability due to extensive first pass metabolism. It was sought to increase gastric retention time of lovastatin by development of sustained release mucoadhesive tablets leading to reduce fluctuation in the plasma concentration and improved bioavailability. Lovastatin tablets were prepared by wet granulation method the drug polymer mixtures were subjected to preformulation studies. FTIR studies showed that there was no interaction between drug and polymer. The granules were evaluated for angle of repose, bulk density, Carr's index, Hausner's ratio and the tablets were subjected to thickness, weight variation, drug content, hardness, friability, surface pH, swelling index, mucoadhesive strength and *In-vitro* studies. The results were found to be within the limits. The drug release studies were carried out for 12hours. In which formulation with combination of chitosan and karaya gum with the ratio of (1:1.5:1.5) was selected as an optimized formulation which have drug release of 98.89% in 12hours. Mathematical analysis of the release kinetics indicates that nature of drug release from the mucoadhesive tablets follows non-fickian diffusion mechanism. Formulation F9 was selected as optimized batch from all the formulations due to their improved bioavailability.

Keywords: Chitosan, Gastro-retention, Karaya gum, Lovastatin, Mucoadhesion, Non-Fickian diffusion, Xanthan gum.

INTRODUCTION

Controlled release drug delivery systems provide drug release at a predetermined, predictable rate and optimize the therapeutic effect of a drug by controlling its release in the body with lower and less frequent dosing. In order to maintain a constant drug level in either plasma or target tissue, release rate from controlled release system should be equal to the elimination rate from plasma or target tissue. The most conventional method to achieve a constant plasma level is the use of intravenous infusion. However, this would be inconvenient for most therapeutic situations so that other non-invasive route such as the oral or transdermal route is preferred. For conventional drug delivery systems, rate-limiting step in drug availability is usually absorption of drugs across a biological membrane such as the gastrointestinal wall. However in a sustained or controlled release product one aims for release of drug from the dosage form as the rate limiting step. Thus drug availability is controlled by the kinetics of drug release rather than absorption.[1]

Mucoadhesion is the state in which two materials, at least one biological in nature, are held together for an extended period of time by interfacial forces. It is also defined as the ability of a material (synthetic or biological) to adhere to a biological tissue for an extended period of time.[2]

Lipid lowering agents or anti hyperlipidemic agents are a diverse group of pharmaceuticals that are used in the treatment of hyperlipidemas. There are several classes of hypolipidemic drugs. They may differ in both their impact on the cholesterol profile some may lowers the low density lipoprotein(LDL) while others may preferentially increase high density lipoprotein(HDL).

In this study the main objective is to develop and evaluate mucoadhesive tablets of Lovastatin by employing various hydrophilic bioadhesive polymers such as xanthan gum, chitosin, karaya gum and HPMC K15 M for prolonged gastrointestinal absorption. The prepared tablets were evaluated for different parameters such as hardness, friability, weight variation, swelling index, in-vitro residence time and ex-vivo adhesive time.

MATERIALS AND METHODS

Lovastatin was collected as a gift sample from Aurobindo Pharma Ltdb Hyderabad, polymers are purchased from Yarrow Chem Products, Mumbai and all remaining excipients are purchased from Scientific Lab, Erode.

IR studies of Lovastatin with natural polymers Infrared spectra analysis[3]

Compatibility of the drug with the excipients was determined by subjecting the physical mixture of the drug and polymer of the main formulation to infrared spectral analysis. Any changes in chemical composition of the drug after the combining it with the polymers were investigated with IR spectral analysis.

Infrared spectrum of lovastatin was determined on Fourier transform infrared spectrophotometer using KBr pellet method. The base line correction was done using dried potassium bromide. Then the spectrum of the dried mixture of the drug and potassium bromide was done.

Preparation of the Bio-Adhesive Tablet

The mucoadhesive tablets were prepared using different polymers alone and in combinations with varying ratios as summarized in table 1. Mucoadhesive tablets were prepared by wet granulation procedure involving two consecutive steps. The mucoadhesive drug and polymer mixture was prepared by homogeneously mixing the drug and polymers in a glass mortar for 15 min and then polyvinyl pyrrolidone was added as a binding agent up to the formation of mass. These mass was passed through the 8mm screen mess to form the granules. Then the formulated granules were dried in hot air oven at 60°C for 30mints. Magnesium stearate (MS) was added as a lubricant in the granules and mixed. The blended granules were then compressed 8mm length die concave punches on tablet compression machine. Each tablet contained 20 mg of Lovastatin, and the total weight of the each tablet was 200mg.

Table 1: Composition of Mucadhesive Tablets of Lovastatin

Ingredients (mg/tab)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Lovastain	20	20	20	20	20	20	20	20	20	20	20	20
Chitosan	40	60	-	-	-	-	30	-	30	30	-	-
Xanthan gum	-	-	40	60	-	-	30	30	-	-	30	-
Karaya gum	-	-	-	-	40	60	-	30	30	-	-	30
HPMC K15 M	-	-	-	-	-	-	-	-	-	30	30	30
Lactose	130	110	130	110	130	110	110	110	110	110	110	110
Magnesium Sterate	5	5	5	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5	5	5	5
Total (mg/tab)	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**

Table 2: Physico-Chemical Properties of Tablets

Formulation Code	Dimension		Hardness (kg/cm2)**	Friability (%)*	Weight variation (%) ***	Drug content (%w/w)*
	Diameter (mm)**	Thickness (mm)**				
F1	8.0±0.0	2.08±0.10	3.16±0.25	0.24±0.03	2.42	101.89±0.73
F2	8.0±0.0	2.17±0.12	3.33±0.25	0.34±0.07	1.42	98.67±0.26
F3	8.0±0.0	2.13±0.15	3.25±0.27	0.40±0.08	1.14	100.58±0.36
F4	8.0±0.0	2.12±0.07	3.08±0.20	0.37±0.07	1.93	98.70±0.55
F5	8.0±0.0	2.07±0.08	2.95±0.27	0.45±0.01	1.67	98.20±0.44
F6	8.0±0.0	2.25±0.14	3.13±0.25	0.34±0.04	1.72	99.53±0.56
F7	8.0±0.0	2.09±0.07	3.22±0.20	0.32±0.04	1.68	98.82±0.32
F8	8.0±0.0	2.07±0.08	2.97±0.19	0.45±0.02	1.74	98.98±0.71
F9	8.0±0.0	2.02±0.08	3.68±0.27	0.35±0.02	1.73	99.12±0.64
F10	8.0±0.0	2.15±0.14	3.23±0.25	0.34±0.04	1.72	99.53±0.56
F11	8.0±0.0	2.23±0.15	3.35±0.27	0.40±0.08	1.14	100.58±0.36
F12	8.0±0.0	2.17±0.08	3.82±0.19	0.45±0.02	1.74	98.98±0.71

*All the values are expressed as mean± SD, n=3; **All the values are expressed as mean± SD, n=6; *** All the values are expressed as mean± SD, n=20.

Evaluation of the Bio-Adhesive Tablets[4-6]

Dimension (Diameter and Thickness)

The Thickness and diameter permits accurate measurements and provide information on the variation between tablets. The thickness and diameter of the tablets was determined using a vernier caliper. Three tablets from each type of formulation were used and average values were calculated.

Uniformity of Weight

The weight variation test was done by taking 20 tablets randomly and weighed accurately. The composite weight divided by 20 provides an average weight of tablet. Not more than two of the individual weight deviates from the average weight by 10 % and none should deviate by more than twice that percentage. The average weight and standard deviation of the tablets were calculated.

Hardness

There is a certain requirement of hardness in tablets so as to withstand the mechanical shocks during handling, manufacturing, packaging and shipping. For each formulation, the hardness of 6 tablets was determined using the Monsanto hardness tester. The whole experiment was performed in triplicate. It is expressed in Kg/cm^2.

Friability

Friability is the measure of tablet strength. This test subjects a number of tablets to the combined effect of shock abrasion by utilizing a plastic chamber which revolves at a speed of 25 rpm for 4 minutes, dropping the tablets to a distance of 6 inches in each revolution. A sample of preweighed tablets was placed in Roche friabilator which was then operated for 100 revolutions. The tablets were then dedusted and reweighed. Generally considered and acceptable limit is loss of less than 1 % in weight. Percent friability (% F) was calculated.

Weight Variation

The weight variation test is done by taking 20 tablets randomly and weighed accurately. The composite weight divided by 20 provides an average weight of tablet. Not more than two of the individual weight deviates from the average weight by 10 % and none should deviate by more than twice that percentage. The average weight and standard deviation of the tablets were calculated.

Surface pH Study[7]

The surface pH of the mucoadhesive tablet was determined in order to investigate the possibility of any side effects in an oral cavity. As an acidic or alkaline pH may irritate the mucoadhesive mucosa, attempt was made to keep the surface pH close to the mucoadhesive pH. The tablets were allowed to swell for 2 h in 1 ml of distilled water. The surface pH was measured by bringing the electrode in contact with the surface of the formulations and allowing it to equilibrate for 1 min.

Table 3: Surface pH of Mucoadhesive Tablets

Formulation code	Surface pH*
F1	6.78±0.005
F2	6.70±0.025
F3	6.68±0.015
F4	6.64±0.025
F5	6.75±0.020
F6	6.94±0.015
F7	6.52±0.039
F8	6.64±0.040
F9	6.79±0.030
F10	6.83±0.015
F11	6.74±0.015
F12	6.79±0.030

*All the values are expressed as mean± SD, n=3.

In- Vitro Swelling Study (water uptake study) [8]

The tablets of each formulation were weighed individually (designated as W_1) and placed separately in petri dishes containing 2% agar gel. At regular intervals (1, 2, 3, 4, 5, 6, 7 and 8 hr), the tablets were removed from the petridishes and excess water was removed carefully by using filter paper. The swollen tablets were reweighed (W_2), the swelling index of each formulation was calculated using the formula;

$$\% \text{ Swelling Index } = \frac{w2 - w1}{w1} \times 100$$

Where, W_2- weight of tablet after particular time interval

W_1- initial weight of tablet

Evaluation of bio-adhesive strength of tablet [9-11]

Modified physical balance method

Measurement of adhesion force was determined by using goat gastric mucus membrane. The tissues were washed thoroughly with phosphate buffer solution (pH 6.8) then the membrane was tied to the glass slide using rubber band. The glass slide was kept in a beaker which was filled with phosphate buffer solution at 37°C±1°C in such way that buffer just reaches the surface of mucosal membrane and kept it moist. The tablet to be tested was stuck on the mucus membrane and allow for 5min for swelling and then by using clip to attach the tablet. Then the weight on the left hand side was slowly added in an increment of 0.5g till the tablet separated from the membrane. From bio-adhesive strength, the force of adhesion was calculated using the formula.

$$Force\ of\ adhesion\ (N) = \frac{Mucoadhesive\ strength}{100} \times 9.81$$

Ex-Vivo Mucoadhesion Time

The *ex-vivo* mucoadhesion time was examined after application of tablet over excised goat mucosa for 30sec after previously being secured on glass slab and was immersed in a basket of the dissolution apparatus containing around 750ml of phosphate buffer, pH 6.8 at 37°C±1°C . The paddle of the dissolution apparatus was adjusted at a distance of 5cm from the tablet and rotated at 25rpm. The time for detachment from the mucosa was recorded.

***In-Vitro* residence time**

The *In-vitro* residence time was determined using a locally modified USP disintegration apparatus. The disintegration medium was composed of 800ml of ph 6.75 isotonic phosphate buffer maintained at 37°C. A segment of porcine buccal mucosa, 3cm length, was glued to the surface of the glass slab, vertically attached to the apparatus. The mucoadhesive tablet was hydrated from the surface using 15ml pH of 6.8 and then the hydrated surface was brought in to the contact with the mucosal membrane. The glass slab was vertically fixed to the apparatus and allowed to move up and down so 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 (mean of triplicate determinations).

In-vitro drug release studies [12, 13]

The dissolution test apparatus (USP II) is used. The whole assembly is kept in a jacketed vessel of water maintained at 37°C±1°C. Bio adhesive tablet is stuck on to the bottom of the flask (so as to allow one sided release from the

tablet).The beaker is filled with 900ml of phosphate buffer. The vessel is maintained at 50rpm under stirring conditions by means of a paddle fabricated for the purpose in a dissolution apparatus. At various time intervals samples of dissolution medium are withdrawn and filtered through Whatman filter paper no: 42. It is replaced immediately with an equal amount of fresh buffer. The samples are then analyzed UV spectrophotometrically at 246 nm. Absorbance measured and % drug release is determined.

Table 4: Percentage swelling index of Tablets

Code	Time (hours)					
	0	1	2	4	6	8
F1	0	298.64±2.25	381.60±0.90	525.84±2.37	722.94±3.40	632.11±3.54
F2	0	351.51±2.35	402.35±2.77	582.97±3.31	795.53±3.25	712.92±2.87
F3	0	153.99±0.60	241.04±1.17	407.45±3.08	562.72±1.22	551.88±2.84
F4	0	167.88±0.49	273.65±0.12	450.34±1.76	584.28±2.24	578.67±1.86
F5	0	130.64±2.31	198.34±1.18	321.32±0.44	462.11±1.16	317.23±1.32
F6	0	138.22±0.47	211.66±0.13	384.37±1.77	491.87±1.07	415.17±1.18
F7	0	291.64±2.25	374.60±0.90	512.84±2.37	634.94±3.40	601.11±3.54
F8	0	259.51±2.35	398.35±2.77	547.97±3.31	663.53±3.25	573.92±2.87
F9	0	226.24±2.86	343.03±2.56	505.83±2.26	621.11±1.59	554.41±1.54
F10	0	340.64±2.15	465.60±0.90	661.84±2.17	794.94±2.10	783.11±2.14
F11	0	309.51±2.15	422.35±2.37	601.97±2.11	775.53±2.25	755.92±2.87
F12	0	298.24±2.81	381.03±2.12	573.83±2.16	741.11±1.51	712.41±1.42

*All the values are expressed as mean± SD, n=3

Table 5: Effect of bioadhesive polymers on bioadhesive strength and bioadhesive force

Formulation code	Mucoadhesive strength (g)*	Mucoadhesive Force (N)*	*Ex-Vivo* Mucoadhesion time (hrs)*	Mucoadhesion Retention time (hrs)*
F1	18.53±0.060	1.81±0.005	5 hours	More than 3hours
F2	18.39±0.062	1.80±0.005	5 hours	More than 3hours
F3	19.91±0.055	1.95±0.007	More than 7 hours	More than 3hours
F4	20.62±0.090	2.02±0.008	More than 7 hours	More than 3hours
F5	16.39±0.060	1.60±0.006	More than 6 hours	More than 3 hours
F6	17.78±0.071	1.74±0.005	More than 6 hours	More than 3 hours
F7	19.82±0.072	1.94±0.005	5 hours	More than 3hours
F8	17.72±0.087	1.73±0.085	5 hours	More than 3hours
F9	20.82±0.062	2.04±0.072	More than 7 hours	More than 3hours
F10	21.39±0.060	2.08±0.006	More than 8 hours	More than 3hours
F11	21.78±0.071	2.13±0.005	More than 8 hours	More than 3hours
F12	22.82±0.072	2.23±0.005	More than 8 hours	More than 3hours

Table 6: *In-vitro* dissolution study of formulations F1-F12

Batch No	1 hr	2 hrs	4 hrs	8 hrs	10 hrs	12 hrs
F1	23.29±0.46	39.23±0.34	56.29±0.52	85.46±0.74	97.23±0.34	----
F2	21.48±0.78	32.23±0.68	49.19±0.47	83.67±0.68	95.36±0.68	----
F3	14.87±1.24	28.75±0.47	43.79±0.64	77.46±0.48	90.75±0.47	94.79±0.64
F4	12.09±1.22	27.96±0.84	41.46±0.74	75.76±0.64	88.96±0.84	92.48±0.74
F5	12.86±1.09	26.11±0.48	42.71±0.53	71.49±0.84	86.76±0.48	----
F6	8.86±0.75	18.82±0.57	39.21±1.06	73.11±0.98	83.23±0.57	98.03±1.06
F7	25.32±.68	37.18±0.38	52.16±1.04	83.16±0.78	98.18±0.38	----
F8	24.82±.54	40.65±0.47	58.37±1.12	84.49±0.81	96.65±0.47	----
F9	8.94±0.74	19.2±0.24	35.12±0.98	73.14±0.34	83.41±0.24	98.89±0.98
F10	9.86±0.75	17.38±0.68	46.67±0.84	65.86±0.75	78.38±0.68	93.67±0.84
F11	11.32±.68	19.49±0.74	47.46±0.67	71.32±.68	82.49±0.74	94.46±0.67
F12	7.82±.54	16.98±0.84	39.61±1.03	62.82±.54	73.16±0.84	90.79±1.03

Table 7: Drug release kinetic studies of Mucoadhesive tablets

Formulation code	Zero order	First order	Higuchi	Korsemeyer-peppas		Best fit model
	R	R	R	R	n	
F1	0.952	0.930	0.998	0.996	0.608	Higuchi
F2	0.995	0.163	0.993	0.993	0.637	Zero
F3	0.974	0.972	0.993	0.993	0.748	Higuchi
F4	0.974	0.979	0.991	0.984	0.806	Higuchi
F5	0.988	0.968	0.995	0.994	0.806	Higuchi
F6	0.993	0.845	0.995	0.994	0.964	Higuchi
F7	0.997	0.162	0.991	0.992	0.579	Zero
F8	0.940	0.938	0.999	0.995	0.577	Higuchi
F9	0.995	0.797	0.989	0.997	0.963	Higuchi
F10	0.977	0.910	0.986	0.979	0.909	Higuchi
F11	0.977	0.937	0.993	0.985	0.867	Higuchi
F12	0.989	0.917	0.990	0.988	0.964	Higuchi

Table 8: Stability studies of Mucoadhesive tablets

Characteristic	Initials	1 Month	2 Month	3 Month
Hardness (kg/cm2)*	3.68±0.27	3.65±0.19	3.6±0.20	3.59±0.21
Drug content (mg/tablet)*	99.12±0.64	98.89±0.52	98.24±0.35	98.07±0.20
Bioadhesive Force (N)*	1.78±0.07	1.76±0.04	1.73±0.05	1.71±0.03
In-vitro drug release at 12 hour*	98.89±0.98	98.38±0.32	97.85±0.10	97.53±0.17

Drug release kinetics [14]

To study the release kinetics of *in-vitro* drug release, data was applied to kinetic models such as zero order, first order, Higuchi and Korsmeyer- Peppas.

Zero order

Drug dissolution from dosage forms that do not disaggregate and release the drug slowly can be represented by the equation:

$$C = k_0 t$$

K_0 - is the zero order release constant

To study the release kinetics, data obtained from in vitro drug release studies were plotted as cumulative amount of drug released versus time.

First order

This model has also been used to describe absorption and/or elimination of some drugs, although it is difficult to conceptualize this mechanism on a theoretical basis. The release of the drug which followed first order kinetics can be expressed by the equation

$$\log C = \log C_0 \, nKt/2.303$$

where,

C_0 - is the initial concentration of drug

K - is the first order constant

t - is the time in hrs.

The data obtained are plotted as log cumulative percentage of drug remaining vs. time which would yield a straight line with a slope of -K/2.303.

Higuchi

It describes the release of drugs from insoluble matrix as a square root of time dependent process based on Fickian diffusion.

$$Q = Kt_2^1$$

Where, K is the constant reflecting the design variables of the system. Hence drug release rate is proportional to the reciprocal of the square rot time.

Korsmeyer Peppas

It derived a simple relationship which described drug release from a polymeric system equation. To find out the mechanism of drug release, first 60% drug release data were fitted in KorsmeyernPeppas model.

$$M_t / M_\infty = K.t^n$$

Where,

Mt / M∞ - is a fraction of drug released at time t,

k- Is the release rate constant and n is the release exponent.

Stability Study[15]

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, enabling recommended storage conditions, re-test periods and shelf-lives. Generally, the observation of the rate at which the product degrades under normal room temperature requires a long time. To avoid this undesirable delay, the principles of accelerated stability studies are adopted.

Formulations were selected for stability on the basis of the In-vitro drug release profile. The formulations were subjected to accelerated stability studies as per ICH (The International Conference of Harmonization) guidelines i.e. 25°C/60% RH and 40°C/75% RH in air tight high density ethylene bottles for 3 months in thermostated ovens. Tablets were evaluated for the different physicochemical parameters i.e. content uniformity, hardness, bioadhesive strength, and percentage of drug release.

RESULTS AND DISCUSSION

Bioadhesive tablets of Lovastatin were formulated by wet granulation techniques using polymers like Chitosan, Xanthan gum, Karaya gum, and HPMC K 15M with the formulation codes F1,F2,F3,F4,F5,F6,F7,F8,F9,F10,F11 and F12 were prepared all the formulation were evaluated for their various physical parameters given in the table-2 .The thickness and hardness of the tablets were in the range of 2.02mm-2.25mm and 2.95-3.82 Kg/cm^2 respectively .The values of weight variation was within limit. Drug content was in the range of 98.20%-101.89% indicating good content uniformity prepared formulation. The friability of the tablets was also within the range 0.24%-0.45%.

Surface pH Study

The results showed that the surface pH of all the tablets was within the range of 6.52-6.94 given in the table-3. These results indicated that there is no risk of mucosal damage or irritation while administering these formulations on mucoadhesive mucosal region.

Swelling index

Batch F1-F2 formulated with the polymer chitosan shows maximum of 795% swelling in 8 hrs, batch F3-F4 formulated with the polymer xanthan gum shows maximum of 584 % swelling in 8hrs, batch F5-F6 formulated with the polymer karaya gum shows maximum swelling index of 494% in 8 hr, the formulations F7-F9 formulated with the combination of natural polymers shows swelling index between 621%-663%. And the formulations F10-F12 formulated with the combination of natural polymers with HPMC K15M shows good swelling index of 741%-794% the results was given in the table 4.

Bio-adhesive strength

All the formulation shows good mucoadhesion. The In-vitro bioadhesive strength study was performed on the modified physical balance to measure the force (N) required for detaching the tablet and the results was given in the table 5. The bioadhesion characteristics were affected by the type and concentration of the bioadhesive polymers. Viscosity of the polymer also affects the bioadhesive strength of the tablet. Chitosan batch (F1, F2), Xanthan gum batch (F3, F4) and karaya batch (F5, F6) shows good mucoadhesion and the formulations with the combination of natural polymers with HPMC K15M shows highest adhesive strength.

Ex-Vivo Mucoadhesion Time

Ex-Vivo Mucoadhesion time of all formulation (F1-F12) calculated by modified dissolution apparatus. In all the formulation *Ex-vivo* mucoadhesive time increased more than 6 hrs except formulations F1, F2, F7 it was decreased because of chitosin which displayed a much lower hydration capacity and a higher rate of erosion. But the F9 formulation with the combination of karaya gum with chitosan shows mucoadhesion time of 7 hours as compared with the other formulation contains chitosan.

In-Vitro Drug Release

From the overall dissolution profiles, it was concluded that the drug release rate decreased as the concentration of the polymer increased, in batches (F1-F6) which was also affected by the type of polymer used. And in batches (F7-F9) formulation F9 with combination of chitosan with karaya gum shows extended drug release which is the best in all the formulations. And in batches (F10-F12) with combination of natural polymers with synthetic polymer decreases the drug release. The results were given in the table 6.

Drug Release Kinetics

The dissolution data of the all the formulations was subjected to the different model such as zero- order, first order, Korsmeyer- peppas and matrix- Higuchi diffusion models and the results was given in the table 7. The release kinetic is best explained by the Higuchi diffusion model by all the formulations except the formulations F2 and F7 follows zero-order kinetics. The values of n (diffusion exponent) were estimated by linear regression of log cumulative % drug release Vs log time (t) of different formulations. The obtained values of n lie between 0.5 to 1.0 in all the formulations exhibiting a non- fickian release behavior controlled by combination of diffusion and chain relaxation mechanism. The optimized formulation F9 showed the sustained drug release according to the Higuchi diffusion model.

Stability study

According to ICH guidelines, 3months stability study at 4°C ± 2°C, 27°C ± 2°C and 45°C ± 2°C for 30 days at RH 75±5% of optimized formulation (F9) was carried out. It showed negligible change over time for parameters like

appearance, drug content, dissolution and assay etc., No significant difference in the drug content between initial and formulations stored at 4°C ± 2°C, 27°C ± 2°C and 45°C ± 2°C for 45 days at RH 75±5% for 3months.

CONCLUSION

Review of the literature indicates that gastro retentive drug delivery systems can be used to increase the gastric residence time of dosage form, which led to an increased bioavailability of various drugs. Thus, in the present investigation, an attempt was made to deliver lovastatin via an oral bio-adhesive drug delivery system to the vicinity of the absorption site by prolonging the gastric residence time of the dosage form. For the formulation of the oral bio-adhesive tablet, various hydrophilic polymers and their combinations were used in varying concentrations.

Tablets were subject to various evaluation parameters such as Hardness, Friability and Drug content, surface pH, Bio-adhesive strength study, and In-vitro drug release study and drug release kinetics. It was revealed that tablets of all batches had acceptable physical parameters. Tablets of batch F9 have good mucoadhesion along with In-vitro drug release. The formulation Batch F9 was selected as an optimized batch. The present study shows that the hydrophilic gums obtained from natural sources can be used for designing a bio-adhesive Control release drug delivery system.

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Source of Support: Nil, **Conflict of Interest:** None.