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ENHANCEMENT OF SOLUBILITY AND DEVELOPMENT OF FAST DISSOLVING ORAL FILM OF ATORVASTATIN

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ABSTRACT

The enhancement of dissolution rate and oral bioavailability of poorly soluble drugs remains one of the most challenging aspects of the drug development. Among the different methods of dissolution enhancement, Solid dispersion technology was found to be more successful with number of drugs. Solid dispersion of Atorvastatin with PEG 4000 was done by physical mixture method. Fast dissolving oral film containing Atorvastatin were prepared using solvent casting method. Total six formulations were prepared using varying amount of Sodium Starch glycolate and Cross-carmellose sodium. Percentage assay of different formulation was determined by U.V. vis Spectroscopy. The percentage assay of different formulation was in range of 95.23±0.65 to99.56±0.58%. The maximum percentage assay (99.56±0.58%) and less disintegration time were found in formulation F5 in fast dissolving oral film. The *in vitro* dissolution studies showed that Atorvastatin oral film formulation F5 showed maximum 89.98±0.25over a period of 15 min. Overall the results of the dissolution rate studies indicated greater dissolution rate of Atorvastatin from fast dissolving oral film.

KEYWORD: Atorvastatin, Solubility enhancement, fast dissolving oral film, evaluation.

INTRODUCTION

Solubility is the phenomenon of dissolution of solid in liquid phase to give a homogenous system and is one of the important parameter to achieve desired concentration of drug in systemic circulation for pharmacological response.[1] Poorly water-soluble drugs after oral administration often require high doses in order to reach therapeutic plasma concentrations.[2] The problem of swallowing tablets is more evident in geriatric and pediatric patients, as well as travelling patients who may not have ready access to water[3], to overcome this Oral fast

disintegrating drug delivery systems were developed, these systems were first developed in the late 1970s as an alternative to tablets, capsules and syrups for pediatric & geriatric patients who experience difficulties in swallowing traditional oral solid dosage forms.[4] These dosage forms either dissolve or disintegrate generally within a 3minute in mouth, without need of water.[5] Oral fast Disintegrating dosage form have started gaining popularity & acceptance as new drug delivery system because they are easy to administer & lead to better patient compliance.[6]

Fast dissolving oral films (FDOFs) is a type of oral drug delivery system for the oral delivery of the drug which was developed based on the technology of the transdermal patches.[7] This delivery system consists of a thin film of the size of a postage stamp, which is placed on the patient's tongue or mucosal tissue, where it instantly hydrates by absorbing saliva; the film then rapidly disintegrates and dissolves to release the drug for oral mucosal absorption.[8] 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.[9] Fast dissolving oral films were initially introduced in the market as breath fresheners and personal care products such as dental care strips and soap strips.[10,11]

Objective of the study were Enhance the solubility of drug using solid dispersion method, formulate and optimize Fast dissolving Film containing anti drugs, evaluate the film for the characteristics like physico-chemical, mechanical, organoleptic, *in-vitro* disintegration time, *in-vitro* dissolution studies, etc.

MATERIALS AND METHODS

Atorvastatin was obtained as gift sample from Bioplus life science, Bangalore. PVP purchased from S. D. Fine Chem. Ltd., Mumbai, Citricacid and HPMC from Qualigens fine chemicals, Mumbai, Sodium bicarbonate and Magnesium stearate from Chempure Pvt. Ltd and Talc and lactose purchased from Loba Chemie Pvt. Ltd Mumbai.

Methods

Preformulation Studies

Organoleptic evaluation: It was done by evaluation of sensory characters like taste, appearance, odor etc.

Solubility: Solubility can be defined as the property of a solute (solid, liquid, orgaseous chemical substance) to dissolve in a solid, liquid or gaseous solvent to form a identical solution of the solute in the solvent. The solubility of a substance is the quantity of that solute that will dissolve in a given quantity of solvent. It is an important parameter for dosage form designing. Approximately 10 mg of drug was weighed accurately and transferred to 5 different10 ml volumetric flasks. Different solvents (water, 0.1 N HCl, 0.1 N NaOH, ethanol, methanol, phosphate buffer pH6.8 and chloroform) were added to the flask respectively and the solubility was observed.

Loss on drying: Loss on drying was directly measured by IR moisture balance. Firstly the instrument was calibrated by rotating knob. Approximately 5 gram powdered drug was weighed accurately. The temperature was fixed at 100°C to 105°C for 5 minutes and constant readings was taken by setting the knob and % moisture was determined.

Melting point: It is one of the parameters for the purity of drugs. In case of pure chemicals, melting points are very sharp and constant. Since the drugs contain the mixed chemicals, they are described with certain range of melting point. A small quantity of drug was placed into a capillary tube, and then it was placed in the melting point determining apparatus containing liquid paraffin. The temperature of the liquid paraffin was gradual increased automatically and reading was taken at which sample started to melt till all sample gets melted.

Determination of λ_{max} of Atorvastatin

The λ_{max} of Atorvastatin was determined by running the spectrum of drug solution in double beam ultraviolet spectrophotometer. Accurately weighed 10 mg of drug was dissolved in 10 ml of 0.1 N HCl solutions in 10 ml of volumetric flask. The resulted solution 1000µg/ml and dilution to make it to a concentration range of 5-25 µg/ml. The spectrum of this solution was run in 200-400 nm range in U.V. spectrophotometer (Labindia-3000+). The spectrum peak point graph of absorbance of Atorvastatin versus wave length was shown.

Calibration curve of Atorvastatin Preparation of Standard Stock Solution

10mg of Atorvastatin was weighed accurately and transferred to 10 ml volumetric flask, and the volume was adjusted to the mark with the 6.8 pH buffer to give a stock solution of 1000 ppm or µg/ml.

Preparation of Working Standard Solution: From stock solutions of Atorvastatin 1 ml was taken and diluted up to10ml separate volumetric flask. From this solution 0.5, 1.0, 1.5, 2.0 and 2.5 ml solutions were transferred to 10ml volumetric flasks and make up the volume up to 10 ml with diluent, gives standard drug solution of 5, 10, 15, 20, 25µg/ml concentrations of Atorvastatin.

FT-IR Spectroscopy: Infra red spectrum is an important record which gives sufficient information about the structure of a compound. This technique provides a spectrum containing a large number of absorption band from which a wealth of information can be derived about the structure of an organic compound. There gi on from 0.8µ to 2.5µ is called near Infra-red and that from 15µ to 200µ is called Far infra-red region. Infra red spectroscopy is based on molecular vibrations caused by the oscillation of molecular dipoles.

KBr pellet: The concentration of the sample in KBr should be in the range of 0.2% to 1%. The pellet is much thicker than a liquid film, hence a lower concentration in the sample is required (Beer's Law). For the die set that you will be using, about 80 mg of the mixture are needed. Too high of a concentration causes usually difficulties to obtain clear pellets. The IR beam is absorbed completely, or scattered from the sample resulting to very noisy spectra.

Bulk Properties: Bulk density is defined as the mass of powder divided by the bulk volume. Bulk density largely depends on particle shape, as the particles become more spherical in shape, bulk density is increase. In addition as granules size increase, bulk density decrease. Bulk properties such as particle size, bulk density etc. of a solid form, are likely to change during process development. Therefore, comprehensive characterization of all Preformulation lots is necessary to avoid misleading predictions. Approximately 1 gram of powdered drug was accurately weighed and poured into the measuring cylinder carefully and level of the powdered drug without compacting was recorded. After that powdered drug was compressed by tapping the measuring cylinder for around 50 times on the palm and the compressed level was recorded. Finally the Bulk density was calculated in gm per ml gm/cc, by the formula:

Bulk density =Bulk Mass/Bulk Volume

Compressibility index (Carr's index): Compressibility index (C.I.) is an important measure that can be obtained from the bulk and tapped densities. Carr's index a material having values of less than 20% to 30% is defined as the free flowing material. It can be calculated as per given formula:

Moisture Content Determination: The titrimetric determination of water is based upon the quantitative reaction ofwater with an anhydrous solution of sulphur dioxide and iodine in the presence of abuffer that reacts with hydrogen ions. In the original titrimetric solution, known asKarl Fisher Reagents, the sulfur dioxide and iodine was dissolved in pyridine and methanol. The test specimen may be titrated with the reagent directly, or the analysis may be carried out by a residual titration procedure. The stoichiometry of the reaction is not exact, and the reproducibility of a determination depends upon such factors as the relative concentration of the reagent ingredients, the nature of the inert solvent used to dissolve the test specimen, and the technique used in the particular determination. Therefore, an empirically standardized technique is used in order to achieve the desired accuracy. Precision in the method is governed by the extent to which atmospheric moisture is excluded from the system. The titration of water is usually carried out with the use of anhydrous methanol as the solvent for the test specimen; however other suitable solvents may be used for special or unusual testspecimens. (Note: Now-a-days pyridine free Freagents are coming in which pyridine is replaced by the imidazole, because pyridine has carcinogenic effects).

Preparation of Solid Dispersions

Optimization of Drug: Polymer Ratio: In order to optimize the drug is to polymer ratio, we have prepared the matrices by both i.e. physical mixture method and solid dispersion method.

Physical mixture method: All the ingredients were weighed accurately and passed through sieve no. 85 in order to obtain powder of fine particle size with narrow size distribution. The physical mixture of drug with carrier PEG 4000 was prepared in different concentration by slightly grinding the drug and carrier in mortar for 2 min. The drug: PEG 4000 ratio which was taken as 1:1, 1:2, 1:3 and 1:4 respectively. Then the resultant powder was passed through sieve no 60 and was stored in desiccators for 2-6 hrs to carry out further analysis. The prepared physical mixture was subjected to spectrophotometric study.

Preparation of solid dispersion of Atorvastatin

For the preparation of Atorvastatin-PEG 4000 solid dispersion by conventional method, PEG 4000 was weighed and melted at 58°C (±1°C) and a measured amount of Atorvastatin was added and stirred. After solidification at room temperature, sample was pulverized with use of a pestle and mortar and sieved through a 400-mm mesh. 10mg of Atorvastatin-PEG 4000 powder (containing 10mg of Atorvastatin and 10mg of PEG 4000) was used for further investigations.

Evaluation of dispersion granules

Percentage drug content: For the determination of Atorvastatin calcium content, dispersion granules equivalent to 10 mg of Atorvastatin calcium, were weighed and extracted with 10 ml of methanol by mechanical mixing for 5min followed by centrifugation at 10,000 rpm for 5 min on a centrifuge. The supernant was filtered through 0.45µmembrane filter, and the filtered solutions were suitably diluted and analyzed for Atorvastatin at 248nm using a validated UV spectrophotometric method.

Formulation development of oral film of Atorvastatin

Casting process of fast disintegrating oral film

Various methods are available for casting of oral films. This is fast disintegrating oral film hence on the laboratory scale solvent casting technique was adopted for formulation of films.

Solvent casting technique: Drug (Atorvastatin) containing fast dissolving films were fabricated by the solvent casting method. The optimized amount of HPMC was dissolved in 5ml of water and stirrer continuously for 1 hour, optimized amount of Plasticizer and drug were dissolved in 95% ethanol and then added to the polymeric solution, the optimized amount of drug was dissolved in 2ml of water and kept on sonication for proper dispersion. Polymeric solution was stirred for 30 min using magnetic stirrer and was kept in undisturbed condition till the entrapped air bubbles were removed. The aqueous solution was casted in a glass moulds having 2.5 x 2.5 cm X 10 films are and was dried at controlled room temperature (25°-30°C, 45 % RH) as well as at increased temperature (microwave oven). The film took approximately 48 hr to dry at controlled room temperature. The dried film was carefully removed from the glass plates and was cut into size required for testing. The films were stored in air tight plastic bags till further use.

Parameter Selection for Formulation of Oral Film

Size of Film: Sizeoftongueisabout2.5x2.5cm, to provide sufficient space for dissolving in oral cavity by putting film on tongue for swishing or hydrating with saliva, size 2.5x2.5cm were concluded as unit dose of Film.

Fabrication of film casting glass reservoir: Film casting glass reservoir is most important glass ware which was fabricated keeping view the following aspect:

- No. of films in one batch
- Holding capacity of formulation solution for drying
- Scrapping-of films from Film casting glass reservoir

- Easy to positioned horizontally with gravity for uniform formation of film

  A 15.0 x 5.0 cm sized Film casting glass reservoir was fabricated having depth of 0.5cm. This sized Film casting glass reservoir will produce twelve 2.5x2.5cm.

Amount of solution for formulation: 30.0 ml solution was calculated for further study, because this will produce 200 micrometer depth for solvent evaporation and sufficient numbers of films for further evaluations.

Temperature and time of drying: Preliminary study suggests that 40+/- 1.0 degree centigrade for 12 hrs adequately dry the film. Speed of mixing at magnet stirrer 200 +/- 10 RMP speed for first 30 minutes were optimized for entire study and 5minutes for all in gredients with same speed were finalized.

Selection and optimization of film forming agents: Two film forming agents and one co-film forming were selected for this research work. The concentration of film forming was important to form a proper thickness for appropriate packaging and handling of oral films. Concentration of film forming agent is optimized on the basis of thickness and appearance of film.

Optimization of formulations

Table 6.5: Selection and Optimization of Film Forming Agents.

Name of ingredients (mg for 12 strips)	F1	F2	F3	F4	F5	F6
API Equivalent to 120 mg	240	240	240	240	240	240
HPMC	250	500	750	250	500	750
Glycerin	-	-	-	-	-	-
PEG-400	100	100	100	100	100	100
SSG	150	200	-	-	-	-
CCS	-	-	150	200	-	-
CP	-	-	-	-	150	200
Aspartame	50	50	50	50	50	50
Citricacid	100	100	100	100	100	100
DMwaterqsto(ml)	30	30	30	30	30	30

Dose calculations

Width of the plate = 5cm

Length of the plate = 12cm

No. of 2.5x 2.5 cm^2 films present whole plate = 12

Each film contains 20mg of drug

12 no. of films contains mg of drug ? = 10×12 = 120mg

The amount of drug added in each plate was approximately equal to 120mg

Evaluation of prepared Film

Thickness: The thickness of patches was measured at three different places using a vernier caliper.

Weight uniformity: For each formulation, three randomly selected patches were used. For weight variation test, 10 films from each batch were weighed individually by digital electronic balance and the average weight was calculated.

Folding Endurance: This was determined by repeatedly folding one film at the same place until it broke. The number of times the film could be folded at the same place without breaking cracking gave the value of folding endurance.

Percentage of Moisture Content: The films were weighed individually and kept in desiccators containing activated silica at room temperature for 24 hrs. Individual films were weighed repeatedly until they showed a constant weight. The percentage of moisture content was calculated as the difference between initial and final weight with respect to final weight.

Drug Content Analysis: The patches (n=3) of specified area were taken into a 10 ml volumetric flask and dissolved in methanol and volume was made up with 10 ml methanol. Subsequent dilutions were made and analyzed by UV spectrophotometer at 248 nm.

Disintegrating time: The most important criteria of present work are to that dosage form should be dissolved within few seconds. The incorporation of super disintegrating agent to minimizes the disintegrating time. Three super disintegrating agent were selected for this work.

***In-vitro* dissolution study:** The *in-vitro* dissolution test was performed using the USPXXX dissolution apparatus II (Paddle with sinker). The dissolution studies were carried out at 37±0.5°C; with stirring speed of 50 rpm in 900 ml phosphate buffer (pH 6.8). Film size required for dose delivery (2.5×2.5cm^2) was used. Five ml aliquot of dissolution media was collected at time intervals of 1, 2, 5, 10 and 15 minutes and replaced with equal volumes of phosphate buffer (pH 6.8). The collected samples were filtered through 0.45 µm membrane

filter and the concentration of the dissolved Atorvastatin calcium was determined using UV-Visible spectrophotometer at 248 nm. The results were presented as an average of three such concentrations.

Stability studies: Stability studies were carried out with optimized formulation which was stored for a period of one, two and three months at 40 ± 2 ^{O}C temperature and 75 ± 5 % relative humidity for a period 3 months. The % Assay of formulation was determined by U.V. spectrophotometer using calibration curve method. The % assay of film was found to slightly decrease at higher temperature.

RESULTS AND DISCUSSION

Preformulation Study

Physical evaluation: It was found that Atorvastatin is white powder and Taste was bitter. It was found that Atorvastatin was slightly soluble in water, freely soluble in ethanol and methanol, soluble in 0.1NHCl and Chloroform, and sparingly soluble in 0.1N NaOH and phosphate buffer pH 6.8.

Loss on drying: The percentage of loss on drying of Atorvastatin was found 1.482%**.**

Melting point: Melting point was determined 158-160 ^{o}C for Atorvastatin.

Determination of λ_{max} of Atorvastatin

The absorption maxima of Atorvastatin were determined by running the spectrum of drug solution in double beam ultraviolet spectrophotometer.

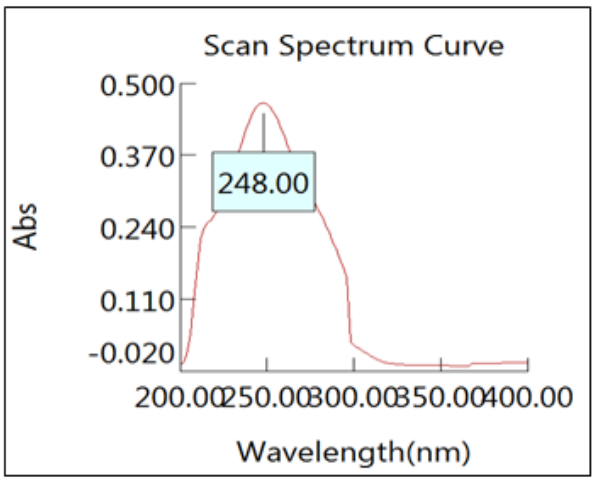

Figure 7.2: Determination of λmax of Atorvastatin at 248nm.

Calibration curve of Atorvastatin

Table no.7.7: Readings for Calibration curve of Atorvastatin.

Standard Conc. (□g/ml)	Rep-1	Rep-2	Rep-3	Rep-4	Rep-5	Mean
5	0.098	0.099	0.097	0.098	0.098	0.098
10	0.198	0.199	0.198	0.199	0.197	0.1982
15	0.295	0.296	0.295	0.298	0.299	0.2966
20	0.389	0.389	0.391	0.398	0.399	0.3932
25	0.498	0.498	0.499	0.497	0.498	0.498
Correlation Coefficient (r^2)	0.999	0.999	0.999	0.999	0.999	0.999
Slope (m)	0.019	0.019	0.019	0.019	0.019	0.019
Intercept (c)	0	0	0	0	0	0

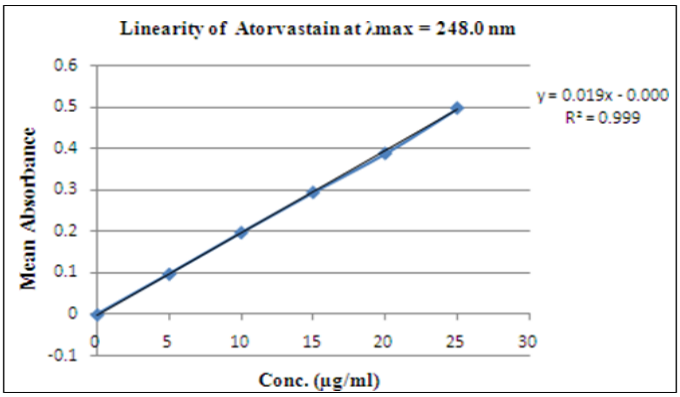

Figure 7.3: Calibration Curve of Atorvastatin.

Table no.7.8: Stastical Data for Linearity.

S. no.	Parameter	Atorvastatin
1	Linearty Range	5-25 µg/ml
2	Regression Equation	Y=0.019x+0.000
3	Correlation Coefficient	0.999

Identification Test FT-IR Spectroscopy

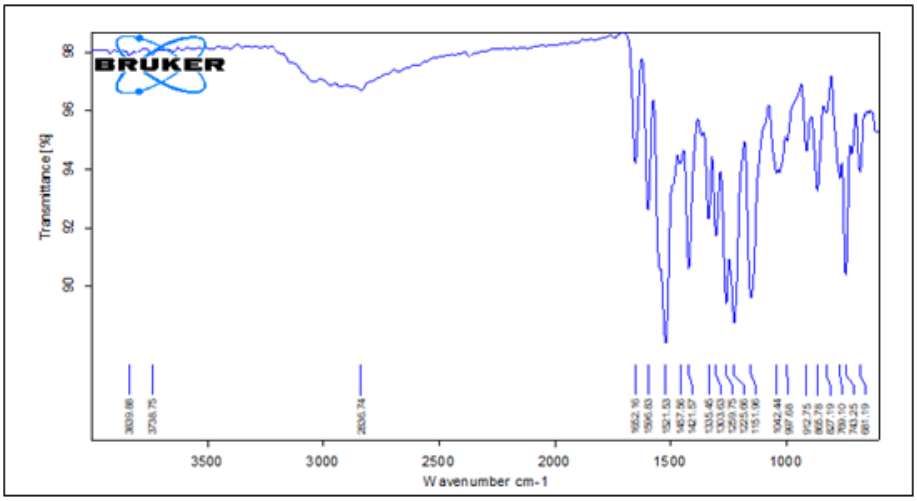

Figure no.: FT-IR Spectrum of Pure Drug (Atorvastatin).

Bulk density of Atorvastatin

Table No.7.3: Bulk density of Atorvastatin.

S. no.	Bulk mass	Bulk volume	Bulk density	Avg. Bulk density
1.	1gm	1.9 ml	0.526 g/ml	
2.	1gm	1.9 ml	0.555 g/ml	0.526g/ml
3.	1gm	1.9 ml	0.526 g/ml	

Tapped density of Atorvastatin

Table no.7.4: Tapped density of Atorvastatin.

S. no.	Bulk mass	Tapped volume	Tapped density	Avg. tapped density
1.	1gm	1.5ml	0.666 g/ml	
2.	1gm	1.5ml	0.666 g/ml	0.666g/ml
3.	1gm	1.4ml	0.714g/ml	

Compressibility index (Carr's index)

Table no.7.5: C.I. of Atorvastatin.

S. no.	Bulk density	Tapped density	C. I.
1.	0.76g/ml	0.90g/ml	21.02

Hausner's ratio

Table no.7.6: Hausner of Atorvastatin.

S. no.	Bulk density	Tapped density	Hausner's ratio
1.	0.76g/ml	0.90g/ml	1.26

Moisture Content Determination: The Moisture content of Atorvastatin was found **0.0433%**

Solubility Enhancement by Solid Dispersion

Table no.: Percentage cumulative drug release of physical mixture.

S. no.	% Solubility Enhancement				
Absorbance	**1:1**	**1:2**	**1:3**	**1:4**	**Pure Drug**
	0.320	0.252	0.159	0.305	0.134
% Solubility Enhancement	238.806	188.0597	118.6567	227.6119	--

Therefore 1:1 ratios were found to be superior and were used for further evaluation purpose.

Drug content

Table no.: Results of drug content.

Formulation	Label claim	Amount found*	Label claim (%)	S.D.	%RSD
Physical mixture	10mg	9.98	99.80	0.125	0.135

***Average of three determination

EVALUATION OF PREPARED FILM

General Evaluation

Table no.: General Evaluation of prepared Film.

Formulation code	General Appearance	Thickness (µm)	Weight (mg)
F1	Translucent	98 ± 4	110 ± 2
F2	Translucent	102 ± 6	115 ± 5
F3	Translucent	105 ± 5	118 ± 6
F4	Translucent	95 ± 7	112 ± 7
F5	Translucent	98 ± 8	116 ± 8
F6	Translucent	105 ± 9	118 ± 9

Folding Endurance, Tensile strength & % Age Elongation

Table no.: Result of Folding Endurance, Tensile strength & % Age Elongation.

Formulation code	Folding endurance (Times)	Disintegrating time (Sec.)	Tensile strength (kg/cm^2)	Percentage of Moisture Content	% Assay
F1	150±8	100±5	0.965	1.25±0.32	97.85±0.45
F2	165±9	95±8	0.895	1.65±0.15	98.89±0.32
F3	162±7	105±6	0.652	1.98±0.45	95.65±0.56
F4	152±6	115±4	0.985	0.92±0.65	96.65±0.45
F5	145±8	68±6	0.965	1.65±0.58	99.56±0.58
F6	189±9	91±5	0.978	1.45±0.89	95.23±0.65

Optimized Formulation

The most important criteria of present work are to that dosage form should be dissolved within few seconds. The incorporation of super disintegrating agent to minimizes the disintegrating time. Three super disintegrating agent were selected for this work.

Table no.: Results of Optimized formulation F-5.

Name of Ingredients	Composition(mg) Per Strip
API	240
HPMCK15	500
Glycerin	-
PEG-400	100
SSG	-
CCS	-
CP	150
Aspartame	50
Citric acid	100
DM water qs to	30

***In-Vitro* release study of optimized formulation F-5**

Table no. : *In-Vitro* release study of optimized formulation F-5

S. no.	Time (Min.)	Cum % Drug release
1.	1	30.25 ± 0.52
2.	2	38.89 ± 0.45
3.	5	50.25 ± 0.32
4.	10	65.56 ± 0.65
5.	15	89.98 ± 0.25

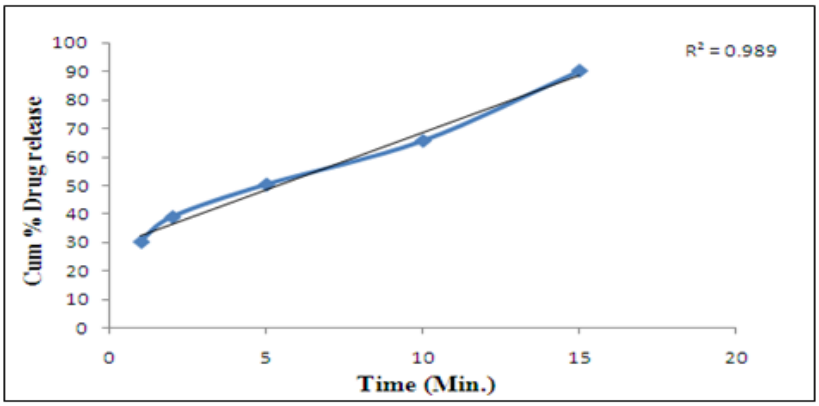

Figure no.: *In-Vitro* release study of optimized formulation.

Stability studies: Minor difference was found between evaluated parameters before and after ageing/storage and all was in acceptable limits. Therefore formulation remains stable for sufficient time.

DISCUSSION

Fast dissolving oral film are those when put on tongue disintegrate/dissolve/disperse instantaneously releasing the drug which dissolve or disperses in the saliva with Their characteristic advantages such as administration without water, anywhere, anytime lead to their suitability to geriatric and pediatric patients. Atorvastatin is prescribed to treatment of hypertension. Therefore, a new Atorvastatin calcium preparation that is useful for swallow function deficient patients is needed. Keeping an objective an attempt is made to develop fast dissolving oral film of Atorvastatin.

The preliminary study showed that Atorvastatin is White to off-white and Odorless powder. It is freely soluble in methanol and ethanol and soluble in 0.1N Hydrochloric acids, Phosphate buffer pH 6.8, and slightly soluble in water the melting point was in the range of 158-160^{o}C which is compliance with the standard value of as per Indian Pharmacopoeia. Identification of Atorvastatin was performed by UV/VIS Spectroscopy. The 10µg/ml solutions of Atorvastatin

calcium was scanned in the range of 200-400nm todetermine the λ_{max} for drug. The λ_{max} of Atorvastatin was found to be 248nm. Fromthe respective stock solution (1mg/ml) different concentration of 5, 10, 15, 20 and 25µg/ml Atorvastatin was prepared and scanned in UV region. Their absorbances were noted at 248.0 nm and calibration curve was plotted as absorbance vs concentration and their linearity range was determined.

This work deals with the investigations carried out on the preparation and characterization of fast dissolving oral film containing Atorvastatin with increase its oral bioavailability. Fast dissolving oral film oral film containing Atorvastatin were prepared using solvent casting method. Total six formulations were prepared using varying amountof Sodium Starch glycolate and Croscarmellose sodium. The prepared Oral film was further evaluated for disintegration time, and uniformity of drug content, and *In-vitro* Release Studies. Percentage assay of different formulation was determined by U.V. vis Spectroscopy. The percentage assay of different formulation was in range of 95.23 ± 0.65 to 99.56 ± 0.58%. The maximum percentage assay (99.56 ± 0.58%) and less disintegration time were found in formulation F-6 in fast dissolving oral film. The optimized formulation of batch F-6 subjected to further *Invitro* drug release.

CONCLUSION

The enhancement of dissolution rate and oral bioavailability of poorly soluble drugs remains one of the most challenging aspects of the drug development. Among the different methods of dissolution enhancement, Solid dispersion technology was found to be more successful with number of drugs. Solid dispersion of Atorvastatin with PEG 4000 was done by physical mixture method. Among the polymers used tested PEG-4000 gave highest enhancement of dissolution rate and efficiency of Atorvastatin (1:1 ratio). Further fast dissolving oral film of Atorvastatin were conveniently formulated by solvent casting method. The *in vitro* dissolution studies showed that Atorvastatin oral film formulation F5 showed maximum 89.98 ± 0.25 over a period of 15 min. Overall the results of the dissolution rate studies in dictated greater dissolution rate of Atorvastatin from fast dissolving oral film.

CONFLICTS OF INTEREST

There are no conflicts of interests.

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