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FORMULATION AND *IN-VITRO* CHARCTERIZATION OF PITAVASTATIN ORODISPERABLE TABLETS

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ABSTRACT

Objective: The aim of the present study was to develop and evaluate orodispersible tablets of Pitavastatin by direct compression method. **Material and methods:** Sodium starch glycolate (SCG), Crosscarmellose sodium and Cross-povidone were used as disintegrates to achieve the desired disintegration time required for orodispersible tablets. To mask the bitter taste of drug, aspartame was added. Lactose was used as sugar based multifunctional diluents. PEG-6000, Plasidone S-650 is solubility enhancer for active ingredient in different concentrations. The prepared tablets were evaluated for their physical (hardness, friability, weight variation), and functional (disintegration time) properties and for the drug content. The excipients were used in various concentrations in order to optimize the desired properties. SCG and Crosscarmellose sodium and Cross-povidone, used. **Results and Discussion:** From the data obtained, it is observed from the formulation containing Sodium starch glycolate 15mg in Formulation F8, shows Disintegration time in 30 seconds and the Percentage drug release is of 99.20 % at the end of 30min which satisfied all the tablet evaluation parameters for dispersible tablet. **Conclusion:** Hence, looking at all the satisfactory parameters F8 batch is selected as the optimized batch. Hardness and friability values were also optimized in the formulations to produce tablets of acceptable physical stability and mechanical strength. Weight variation and drug content of all formulations fully complied with the official specifications. The release profile of the optimized formula F8 fitted best to Korsemeyer-Peppas model with R2 value of 0.999.

KEYWORDS: Pitavastatin, orodispersible tablets, super disintegrants, Sodium starch glycolate (SCG), Crosscarmellose sodium and Cross-povidone.

INTRODUCTION

Orodispersible tablets

Solid dosage forms are well-liked because of the simplicity of administration, exact dosage, self-medication, pain evasion, and mainly the patient compliance. However, several people face trouble in swallowing the solid dosage forms. This intricacy in swallowing is considered dysphasia. Thus, these conventional dosage forms outcome in high occurrence of noncompliance and ineffective treatment with respect to swallowing particularly in the case of paediatrics, geriatric, or any mentally retarded patients.[1] Thus Orodispersible solid dosage forms are formulated to overcome the drawbacks. These are also called as orally disintegrating tablets, mouth-dissolving tablets, rapid-dissolving tablets, fast-disintegrating tablets, fast-dissolving tablets.[1]

Orodispersible are defined as tablets which are proposed to be positioned in the mouth where they disperse and disintegrate within 3 min prior to swallowing.[2] An Orodispersible tablet consists of super disintegrants, which assist them to break up the tablets within a minute in the existence in saliva without any complexity of swallowing. It offers numerous advantages with respect to its stability, administration in the absence of water, appropriate dosing, small packaging size, and management. Since the incorporation is taking place directly from the mouth, bioavailability of the drug improves. Drugs present in orodispersible tablets also avoid first pass metabolism.

Pitavastatin is an anti-hyperlipidaemic drug which acts by increase in uptake of low density lipids from blood into liver and further reduces cholesterol levels in blood. The drug is majorly prescribed to geriatric patients who possess swallowing difficulties, which enables the formulation of orodispersible tablets.

Superdisintegrant: Mechanism of release

Superdisintegrant is added to tablet and several encapsulated formulations to support the disintegration of the tablet into smaller fragments in aqueous surrounding which increases the surface area and endorse

an additional rapid discharge of the drug substance. They induce moisture diffusion and distribution of the tablet matrix.[3]

The release pattern of the orodispersible tablet is aided by the addition of superdisintegrant which gets swollen in contact with the aqueous environment and the swollen particles creates gaps and channels into which the fluid (saliva) enters and further fasten the release of drug into the oral cavity. This phenomenon completes within 3 minutes of administration (according to official standards).[4]

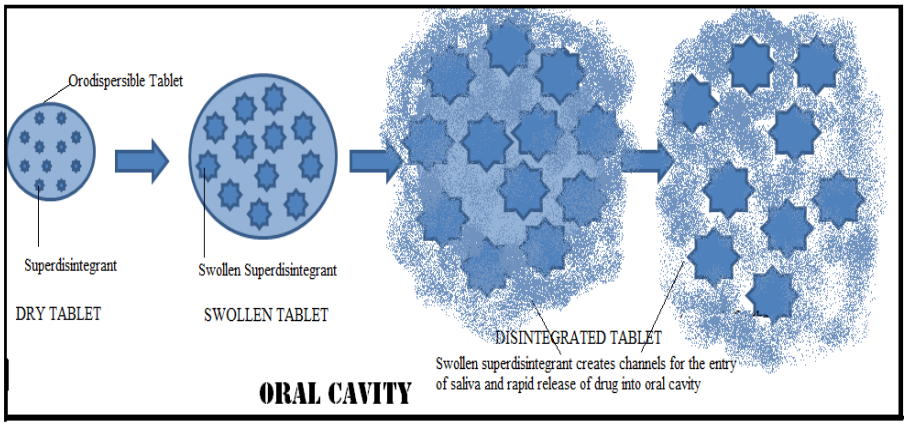

Fig. 1: Release pattern of orodispersible tablet

Types of superdisintegrants

Table 1: Types of Superdisintegrants[5]

Nature of Polymers	Polymers
Natural	Pectin, Mucin, Agar, Alginic acid, Casein, Gelatin, Schizophillan, Carrageenin
Semi synthetic	Methyl cellulose(MC), Hydroxylethyl cellulose(HEC), Hydroxypropyl methyl cellulose(HPMC), Hydroxyethyl methyl cellulose(HEMC), Corboxymethyl cellulose(CMC)
Synthetic	Povidone, Polyethylene glycol(PEG), Polyvinyl pyrolidine(PVP), Crospovidone, Polyvinyl alcohol(PEA)

MATERIALS AND METHODS

Materials

Pitavastatin was obtained from NATCO Pharma Pvt. Ltd, Hyderabad as gift sample. Lactose and magnesium stearate were obtained from Yarrow Chemicals, PEG-6000 from LKM International, Crosscarmellose Sodium, Aspartame, Plasidone S-630 and Talc were procured from Sisco research Laboratories. Sodium starch glycolate and cross-povidone were obtained from Hetero Chemicals, Hyderabad.

Equipments

Tablet Compression machine-Single Rotary 16 stations (Karnavati Engineering Ltd., India), Automatic tablet dissolution apparatus USP-I & USP- II (Lab India), Electronic thickness measurement apparatus (Lab India), Friability tester (Stereo Lab Hyderabad), Tablet hardness tester (ACG World Wide), Bulk density apparatus (Technofour Electronics), Flodex tester (ACG World Wide), Multi mill (Pharma Chem Machineries) and Sifter (Grovers Group).

Methods

Study of the drug

The drug information such as solubility, melting point (capillary tube method) and organoleptic properties of the drug are compared as with Indian Pharmacopoeia.

U.V Spectrophotometric study

Preparation of Solutions

Stock solution of (10 µg/ml) Pitavastatin was prepared in 0.1 HCL buffer solutions. The solution was kept in a 10 mm fused silica cuvette. The UV spectrum was recorded in the range of 200-400nm on UV-visible spectrophotometer at 1cm, slit width. It showed a maximum absorption at 227.0nm.

Procedure

100mg pure drug was taken in 100ml volumetric flask and the volume is made up with buffer solution (Stock Solution). From the stock solution 1ml is taken and diluted to 10ml in a 10ml volumetric flask (Dilution 1). 1ml is obtained from first dilution and diluted to 10ml in a 10ml volumetric flask to get 10µg/ml concentration of solution. Likewise 20, 40, 60, 80 and 100 µg/ml dilutions were prepared and scanned at 227nm.

Drug – Polymer Incompatibility Studies

FTIR - Study

FTIR study was carried out to ensure compatibilities between drug and polymers. Infrared spectrum of Pitavastatin was determined by using KBr dispersion method. The base line correction was done by using dried potassium bromide. Then the spectrum of dried mix of drug and potassium bromide was run followed by

drug with various polymers by using FTIR spectrophotometer. The spectrum obtained with the substance being compared with reference spectrum.

Preparation of blend

Pitavastatin, sodium starch glycolate, crospovidine, Crosscarmellose sodium, Plasidone S -630, Lactose and aspartame was sifted through 24 mesh & ingredients such as magnesium stearate, Talc were added and the powder blend was passed through 60 mesh.[6]

Evaluation of Micromeritics properties of the blend

Bulk density

An accurately weighed powdered mix from each formula is introduced in to a measure and was shaken to eradicate any agglomerates. The volume occupied by the powder was measured which results in determining bulk volume. It is determined using the following formula.[7]

$$Bulk\ Density\ (\rho b) = \frac{Mass\ of\ the\ Powder\ (M)}{Bulk\ Volume\ (Vb)}$$

Tapped density

An accurately weighed powdered mix from each formula is introduced in to a measure and was shaken to remove any gaps. The measuring cylinder was tapped until no alteration in volume was noted which gives the tapped volume. It is determined by using the following formula.[7]

$$Tapped\ Density\ (\rho t) = \frac{Mass\ of\ the\ Powder\ (M)}{Tapped\ Volume\ (Vt)}$$

Hausner's ratio

It determined by using following formula

$$Hausner's\ ratio = \frac{Bulk\ Density\ (\rho b)}{Tapped\ Density\ (\rho t)}$$

A hausner ratio less than 1.25 shows good flow while greater than 1.5 shows poor flow.

Carr's compressibility index

It is a simple guide that can be determined on minute quantities of powder. The compressibility index of the formulation was determined by using following Carr's compressibility index equation.[8]

$$Carr's\ Index = \frac{\rho t - \rho b}{\rho t} \times 100$$

The values are cross checked with standard table.

Angle of repose

It is determined by using the funnel method. The precisely weighed powder is taken in a funnel. The altitude of the funnel is adjusted in such a way that the tip of the funnel just touched the apex of the stack of the powder. The powder was allowed to run through the funnel freely onto the surface. The diameter of the powder can be measured to determine the angle of repose.

It was calculated using the following equation.[8]

$$\tan\theta = \frac{Height\ of\ Pile\ (h)}{Radius\ of\ pile\ (r)}$$

$$Angle\ of\ repose\ (\theta) = \tan -1\frac{h}{r}$$

Where 'h' and 'r' are the height and radius respectively of the powder cone.

Tablet preparation

Selection of PEG Blend

Fast melt tablets of Pitavastatin are prepared using melt granulation technique. The first step involved is selection of PEG blend comprising of PEG 6000 and Plasidone S-630 having a melting point approximately to body temperature 37°C.[8]

PEG blend was prepared by mixing F1-F3 PEG 6000 1 : 5, 1 : 8, 1 : 10, with F4-F6 Plasidone S-630 at ratios of 1 : 5, 1 : 8, 1 : 10. All the ratios were weighed and add remaining Excipients mixed together. Remaining F7-F9 Formulations are only plain formulation different super disintegrates using this formulations. The blends were melted on water bath at 50-60°C until homogenized, and then removed from the water bath and triturated until congealed. The melting point of resultant mixtures was determined using melting point apparatus.[9]

Environment Condition: Room Temperature (25^0C), RH – 65%.

Manufacturing Characteristics: Machine: Karnavati – Total 16 stations.

Direct compression

Ingredients such as Pitavastatin was sifted through 24 mesh, & ingredients such as sodium starch glycolate, crospovidine, Crosscarmellose sodium, Plasidone S-630, Lactose and aspartame, magnesium state, Talc were passed through 60 mesh. The above ingredients were mixed in 10 min. and lubricants were added to the above ingredients. The lubricated blend was compressed by using oval shaped 7.0 mm punches.[10]

Tablet evaluation

Thickness

The Thickness and diameter were used to measure and provide information on the variation between tablets. The thickness of the tablets was determined using a digital Vernier calipers. Three tablets from each formulation were used and mean values of thickness were calculated.

Hardness

The hardness of tablets was determined by using Monsanto Hardness tester and it is expressed in Kg/cm^2. The whole experiment was performed in triplicate.

Friability

The friability of the tablet was determined by using Roche friabilator. Twenty tablets are initially weighed W_1 and transferred into the friabilator. The friabilator was operated at 25 rpm for 4 minutes. The tablets were weighed again (W_2). The percentage of friability was calculated by using following formula.[11]

$$\%\ Friability = \frac{Initial\ Weight - Final\ Weight}{Initial\ Weight} \times 100$$

Disintegration

The test was carried out as per USP- 2008. One tablet was placed in six tubes of the basket and 0.1 N HCL buffer is used as the disintegration solution. The temperature of the liquid was maintained at $37^0C \pm 2^0C$.

Weight variation

20 tablets were selected unbiased and weighed accurately. The weight divided by 20 provides an average weight of tablets. Not more than two of the individual weight deviates from the average weight by 10 % and none should deviate by more than double that percentage. Standard deviation and average weight were calculated.[11]

Uniformity of Dispersion Test

Two dispersible tablets were placed into a 250 ml glass beaker containing 100 ml purified water and tablet was allowed to disintegrate for few seconds and the solution was stirred by using a glass rod. The obtained dispersion was passed through a sieve no. 12.

Wetting time

A portion of filter paper folded twice and placed in a small petridish containing 5ml of distilled water, the tablet was placed on the paper, and the time for complete wetting of the tablet was measured in seconds. The wetted tablet was then weighed. Wetting time, S, was determined by using following formula.[11]

$$S = \frac{Wb - Wa}{Wb} \times 100$$

Where,

Wa – weight of the tablet before water absorption.

Wb – weight of the tablet after water absorption.

Uniformity of content

The drug content in each formulation was determined by mixing 10 tablets and powder equivalent to 10 mg was added in 100ml of 0.1 N HCL buffer followed by stirring for 10 minutes. The solution was filtered through a 0.45µ filter paper, diluted suitably and the absorbance of resultant solution was measured by using UV-Visible spectrophotometer at 276.0 nm.[12]

Determination of moisture content by Karl Fisher Apparatus

50 ml of methanol was taken in a dried titration flask and it was titrated with KFTS to obtain moisture free flask. 10 tablets were blended to get fine powder and 0.5 gm of powder sample was transferred to titration flask it was titrated with KFTS solution to the end point and moisture content was calculated by the following formula.[13]

$$\%\ of\ Water = \frac{Volume\ of\ KFTS\ consumed \times f}{Weight\ of\ the\ sample\ in\ mg} \times 100$$

***In-vitro* drug release**

There are no standard methods yet developed for determining the *in-vitro* drug release for dispersible tablets. The release rate of dispersible tablets of Pitavastatin was carried out using rotating paddle apparatus (USP Type II).[13] The dissolution medium consisted of 900 ml of 0.1 N HCL buffer. The release study was performed at $37^0C \pm 0.5^0C$ with a rotation speed of 25 rpm. The 5ml of sample was withdrawn at time interval of 5, 10, 15, 20, 25 minutes up to 30 min and replaced with 5 ml of dissolution medium. The amount of Pitavastatin released was determined by UV Spectrophotometer at 276.0nm.[14]

Kinetics of *In-vitro* Drug Release

Release kinetics data was applied to kinetic models such as zero order, first order, Higuchi and Korsmeyer-Peppas.[15]

1) Zero order

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

$Q_t = Q_0 + K_0t$

Where,

Q_t - amount of drug dissolved in time t,

Q_0 - initial amount of drug in the solution (most times, $Q_0 = 0$).

K_0 - zero order release constant expressed in units of concentration/time.

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

2) 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.

$$\log C = \log C_0\ n\ Kt / 2.303$$

Where,

C_0 -initial concentration of drug

K - First order constant

t -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.

3) Higuchi model

The first example of a mathematical model aimed to describe drug release from a matrix system was proposed by Huguchi in 1961. Initially conceived for planar systems, it was then extended to different geometrics and porous systems.[15] This model is based on the hypotheses that,

- Initial drug concentration in the matrix is much higher than drug solubility.
- Drug diffusion takes place only in one dimension (edge effect must be negligible).
- Drug particles are much smaller than system thickness;
- Matrix swelling and dissolution are negligible.
- Drug diffusivity is constant.
- Perfect sink conditions are always attained in the release environment.

Model expression is given by the equation

$$Ft = Q = A\sqrt{D(2C - Cs)Cs\,t}$$

Where,

Q- is the amount of drug released in time t per unit area A,

C -is the drug initial concentration,

Cs- is the drug solubility in the matrix media

D- is the diffusivity of the drug molecules (diffusion coefficient) in the matrix substance.

4) Korsmeyer Peppas model

To find out the mechanism of drug release, first 60% drug release data were fitted in Korsmeyer Peppas model.

$$Mt/M\infty = Ktn$$

Where,

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

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

The n value is used to characterize diverse release for cylindrical shaped matrices. In this model, the value of n characterizes the release method of drug as described should only be used. To study the release kinetics, data obtained from in vitro drug release studies were plotted as log collective percentage drug release versus log time.[16]

The value of n indicates the drug release mechanism related to the geometrical form of the delivery system, if the exponent n = 0.5, then the drug release mechanism is Fickian diffusion. If n < 0.5 the mechanism is quasi-Fickian diffusion, and 0.5 < n < 1.0, then it is non-Fickian or anomalous diffusion and when n = 1.0 mechanism is non Fickian case II diffusion, n> 1.0 mechanism is non Fickian super case II.

Stability Studies

Stability testing is an integral part of formulation development. It generates information on which to base proposals for the shelf lives of drug substances and products and their recommended storage conditions. Stability data also are a part of the dossier submission to regulatory agencies for licensing approval.

Stability testing ensures that a drug substance will be safe and effective throughout the shelf life of the product. However, meeting the potency and purity profiles recognized in the compendia can be challenging as pharmaceutical products become increasingly complex and diverse.

The optimized formulation F8 packed in PVC blister pack then, they were stored at three different temperatures $4^0C\pm2^0C$, $27^0C\pm2^0C$ and $45^0C\pm2^0C$ for 45 days at RH 75±5%. At 15 days intervals, the tablets were evaluated for their physical appearance, drug content and drug excipients compatibility at specified intervals of time.

RESULTS AND DISCUSSION

Study of the drug

Pitavastatin is an odorless white powder with melting point 178^0C. Pitavastatin is freely soluble in water. Depending on the saturation solubility data the dissolution media selected for Pitavastatin was water 42 mg/L (at 25^0C).

U.V Spectrophotometric study

Serial of dilutions were made from standard working solution with distilled water to get concentration from 20 to 100 µg / ml and the absorbance was measured at 276.0nm.

Table 2: Absorbance for Pitavastatin dilutions in distilled water

S. No	Concentration (µg/ml)	Absorbance
1	20	0.1608
2	40	0.3192
3	60	0.4756
4	80	0.6405
5	100	0.8010

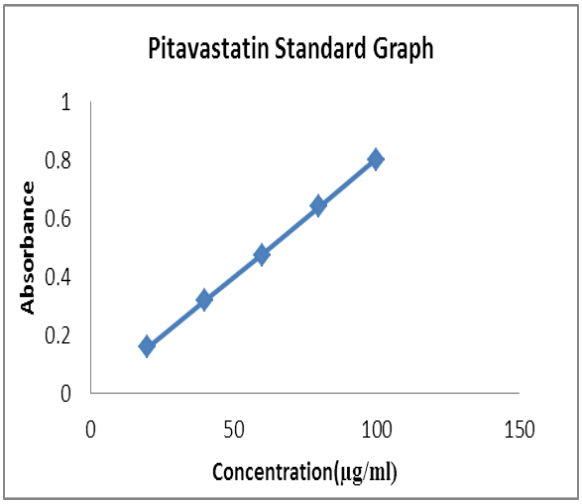

Fig.2: Pitavastatin standard calibration curve

Drug – Polymer Incompatibility Studies

From the following figures, it can be seen that, the major functional group peaks observed in spectra's of drug with all the polymers remains unchanged as compared with spectra of Pitavastatin. So from the above IR spectra it can be observed that there is no interaction between Pitavastatin and polymers used in the formulations.

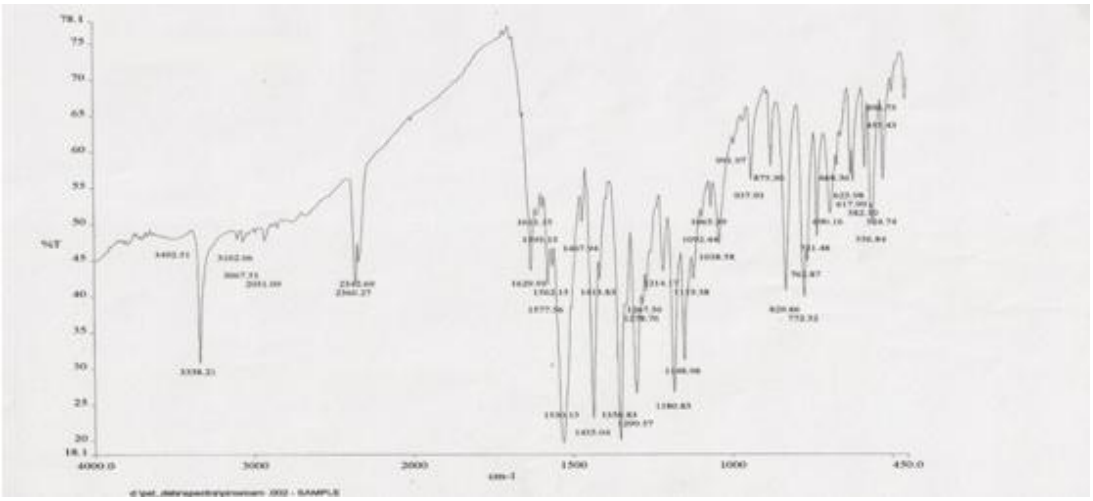

Fig. 3: Infra Red Spectrum of Pure Pitavastatin

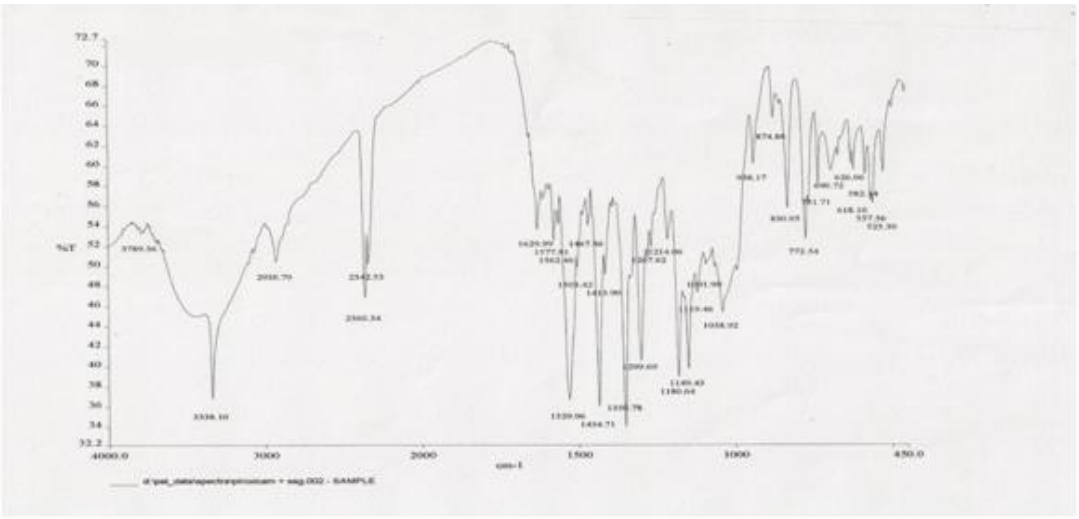

Fig. 4: Infra Red Spectrum of Pitavastatin with Sodium Starch Glycolate

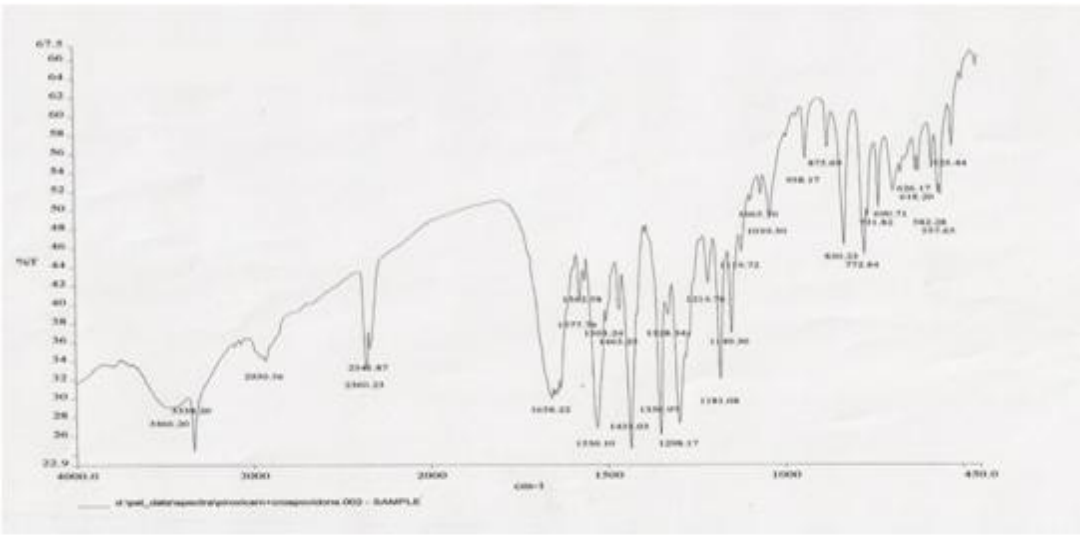

Fig. 5: Infra Red Spectrum of Pitavastatin with Crospovidone

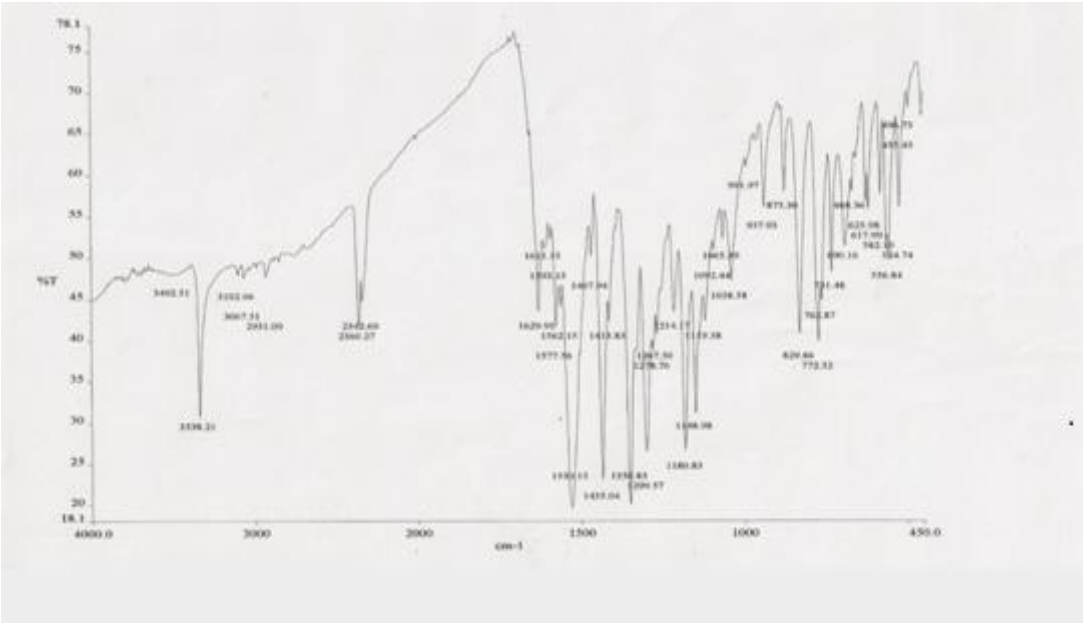

Fig. 6: Infra Red Spectrum of Pitavastatin with Croscarmellose Sodium

Evaluation of Micromeritics properties of the blend

The Bulk density of the formulations was measured by graduated cylinder. The bulk density was found in the range 0.188– 0.232kg/cm^3.

The Tapped density of the formulations was measured by graduated cylinder. The Tapped density was found in the range 0.214– 0.252 gm/cm^3.

The Compressibility of the formulations was measured using bulk density and tapped density data, compressibility index was calculated. It was found in the range 7.14 – 13.02%, which indicates an excellent flow.

The Hausner's ratio of formulations was measured using bulk density and tapped density data, Hausner's ratio was calculated. It was found in the range 1.07 – 1.15, which specifies good flow properties.

Angle of repose ranged from 22.29 to 25.26, the flow properties of powder blend in all formulations exhibit good flow characteristics.

Table 3: Micromeritic properties of the blend

Formulation No.	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Compressi-bility Index (%)	Hausner Ratio	Angle of repose (θ°)
F1	0.1956	0.2143	8.695	1.09	22.33
F2	0.1883	0.2152	12.500	1.14	22.29
F3	0.1934	0.2236	13.02	1.15	24.15
F4	0.2237	0.2500	10.52	1.11	23.48
F5	0.2255	0.2505	10.00	1.11	25.26
F6	0.2162	0.2328	7.1428	1.07	22.78
F7	0.2255	0.2505	10.00	1.11	22.48
F8	0.2327	0.2521	7.6923	1.08	24.72
F9	0.2250	0.2500	10.00	1.11	23.62

Tablet evaluation

Physical property evaluations

Tablets were prepared using direct compression technique. Since the material was free flowing, tablets were obtained of uniform weight, due to uniform die fill tablets were obtained in the range with acceptable weight variations as per Indian Pharmacopoeia specifications which is less than 0.75%.

Tablets thickness was evaluated by using digital Vernier caliper. The thickness of the tablets was found in the range 5.3 – 6.0 mm. Uniformity in thickness was obtained due to uniform die fill.

Tablet hardness was evaluated by using Monsanto Hardness tester. Hardness of the tablets was found in the range 3.12 – 3.71 Kg/cm2. Uniform hardness was obtained due to equal compression force.

Tablets were evaluated by using Roche Friabilator and friability of tablets was observed in the range 0.26-0.79.

Tablets were evaluated for disintegration time in the IP disintegration apparatus. The disintegration time was found in the range 29 – 33 sec.

The tablets were evaluated for the uniformity dispersion in which all the tablets were dispersed in few seconds in purified water and all the formulations were under the IP limits.

Tablets were evaluated for wetting time test. The wetting time was found in the range 54–59 sec.

Table 4: Physical property evaluations of the tablet

Formulation No.	Weight variation	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Disintegration time (sec)	Wetting time (sec)
F1	148±2.34	5.7	3.50	0.75	33.47	54.54
F2	150±3.5	5.7	3.48	0.77	31.56	55.56
F3	149±4.2	6.0	3.42	0.34	29.91	54.46
F4	151±1.3	5.8	3.58	0.33	35.42	56.37
F5	148±1.5	5.7	3.68	0.26	33.45	59.35
F6	149±0.9	5.9	3.71.	0.65	29.25	54.25
F7	151±0.7	5.6	3.45	0.79	33.25	59.90
F8	150±1.2	5.4	3.36	0.46	31.24	56.08
F9	152±0.4	5.3	3.12	0.33	29.35	52.05

Uniformity of content

Tablets were evaluated for content uniformity by using assay method. The drug was obtained in the acceptable limit. The drug content was found in the range 95–101%.

Table 5: Content Uniformity.

Formulation No.	Assay value in % w/w
F1	101
F2	100
F3	95
F4	98
F5	100
F6	99
F7	100
F8	99
F9	101

Determination of moisture content by Karl Fisher Apparatus

Table 6: Moisture content determination

Formulation No.	Moisture content (% w/w)
F1	2.1
F2	2.2
F3	1.8
F4	2.2
F5	2.3
F6	2.7
F7	2.0
F8	1.9
F9	2.3

***In-vitro* drug release**

In-vitro drug release studies were conducted for the formulation using USP dissolution apparatus type-II (paddle) at 25 rpm. The percentage drug release at the end of 30 min. was found in the range 90–99 %.

Comparing F1-F9 formulations F8 have shown a good release pattern.

Table 7: Comparative Dissolution Profile of Pitavastatin dispersible tablets in 0.1 N HCL Buffer Solutions

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
5	24.2	29.21	30.10	33.15	35.05	35.25	36.46	41.02
10	37.02	40.05	38.15	47.05	41.08	45.31	49.36	53.10
15	46.5	53.32	51.02	50.24	44.12	55.46	53.08	61.24
20	66.63	58.05	54.06	62.14	62.53	71.38	77.13	80.61
25	75.12	64.02	78.12	75.31	82.14	73.15	90.22	94.05
30	83.14	74.08	84.08	95.05	94.09	96.26	97.34	99.20

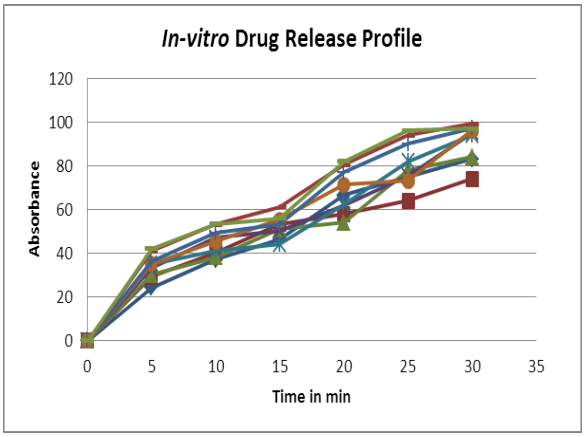

Fig.7: Comparative Dissolution Profile of Pitavastatin dispersible tablets in 0.1 N HCL Buffer Solutions.

Kinetics study

The release profile of the optimized formulation F8 fitted best to Korsmeyer-Peppas model with R^2 value of 0.965. As the n value for the Korsmeyer-Peppas model was found to be greater than 1, it follows case-2 transport.

Table 8: Dissolution Kinetics of optimized formulation F8.

Time (Sec)	Square root of time	Log time	% drug released	Log % drug released	% drug remaining	Log % drug remaining	Time(sec)
0	0	-	0	-	100	2	0
5	2.236068	0.69897	41.02	1.6129957	58.98	1.770704768	5
10	3.162278	1	53.1	1.7250945	46.9	1.671172843	10
15	3.872983	1.176091	61.24	1.7870352	38.76	1.588383768	15
20	4.472136	1.30103	81.64	1.911903	18.36	1.263872677	20
25	5	1.39794	94.05	1.9733588	5.95	0.774516966	25

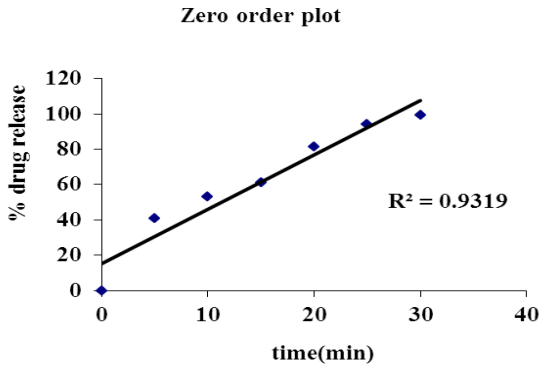

Fig. 8: Zero order kinetics of optimized formulation F8.

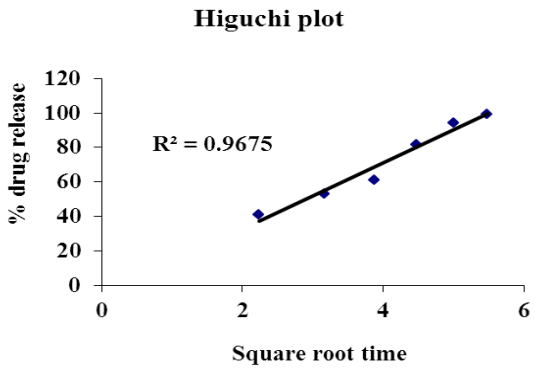

Fig. 10: Higuchi kinetics of optimized formulation F8.

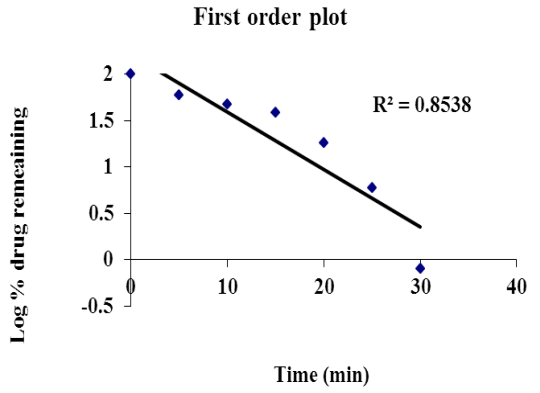

Fig.9: First order kinetics of optimized formulation F8.

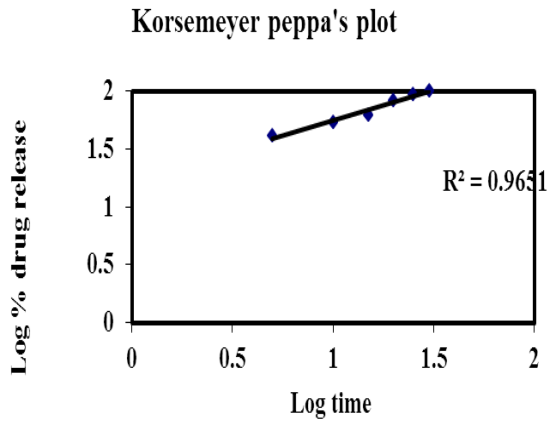

Fig. 11: Korsemeyer peppa's kinetics of optimized formulation F8.

Stability studies

According to ICH guidelines, 45 days stability study at $4^0C \pm 2^0C$, $27^0C \pm 2^0C$ and $45^0C \pm 2^0C$ for 45 days at RH 75±5% of optimized formulation (F8) 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 $4^0C \pm 2^0C$, $27^0C \pm 2^0C$ and $45^0C \pm 2^0C$ for 45 days at RH 75±5%.

Table 9: Stability studies of Pitavastatin tablets.

Parameters	After 15 days	After 30 days	After 45 days
Physical appearance	No change	No change	No change
Weight variation (mg)	150±0.5	149±2.5	149±4.23
Thickness (mm)	5.2	5.1	5.1
Hardness (kg/cm^2)	3.4	3.3	3.2
Friability (%)	0.41	0.43	0.43
Drug content (%/tablet)	99.9	99.81	99.0
Wetting time (sec)	58.96	60.12	65.51
Disintegration time (sec)	34.19	39.13	45.05
Percentage drug release	99.20	98.56	98.00

CONCLUSION

From the data obtained, it is observed from the formulation containing Sodium starch glycolate 15mg in Formulation F8, shows disintegration time in 30 seconds and the Percentage drug release is of 99.20 % at the end of 30min. which satisfied all the tablet evaluation parameters for dispersible tablet. Hence, looking at all the satisfactory parameters of F8 batch formulation is selected as the optimized batch. The release profile of the optimized formula F8 fitted best to Korsmeyer-Peppas model with R_2 value of 0.999.

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