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FORMULATION AND OPTIMISATION OF FAST DISSOLVING TABLETS OF VALSARTAN USING NATURAL SUPER DISINTEGRATING AGENTS

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ABSTRACT

The aim of this work was to develop a fast dissolving tablets of Valsartan drug by direct compression method using different natural and synthetic super disintegrants. The fast dissolving tablets of Valsartan were prepared by direct compression method. The physicochemical parameters like pre-compression and post-compression evaluation were performed as per pharmacopoeia standards and compatibility study was done by FTIR method. The release data were subjected to different models in order to evaluate their kinetics and release mechanism. Direct compression method using different natural and synthetic super disintegrants. The compatibility study of the drug with various polymers, IR spectra of drug and polymers were carried out. The FTIR spectral analysis showed that there was no drug interaction with formulations additives of the tablet as there is no variation and shift in bands, it can be justified there is no interaction between drug and polymer. The Solid dispersion with 1:3 ratio shows better aqueous solubility which explains better dissolution rate of the drug. Various batches of FDTs were prepared using selected ratio of SD. Pre compression parameters showed good flow properties. Post compression parameters like thickness, hardness, weight-variation, friability, wetting-time, water absorption ratio, disintegration time, drug content, *in-vitro* drug release study shown good results. Formulation F3 and F5 showed good results throught the study. Short term stability studies on the formulations F3 and F5 indicated that there are no significant change in the hardness, friability, disintegration time, drug content and *in-vitro* drug release study. The release kinetics data implies that the formulation was First order and Peppas models. From the results, it was concluded that the FDTs of valsartan containing seeds of *Plantago ovata* mucilage (F3) and leaves of *Hibiscus rosa sinensis* (F5) are showed disintegration time and *in-vitro* drug release study faster than the synthetic super disintegrants like croscarmellose sodium and crospovidone.

KEYWORDS: Fast dissolving drug delivery systems (FDDS); Solid dispersion (SD): Valsartan; *Hibiscus rosa sinensis (*HRS); *Plantago ovata* mucilage (POM).

INTRODUCTION

Among all routes of administrations, oral route have wide acceptance around 50-60% of total dosage forms. Solid dosage forms are popular because of their advantages like self-medication, pain avoidance, accurate dose, ease of administration. The more famous solid dosage forms are being tablets and capsules; but main drawback of this dosage forms is the difficulty to disintegrate or dissolve.[1] Therefore, recent advancement in novel drug delivery system have a better development in a convenient dosage form for administration and to achieve better patient compliance known as fast dissolving tablets (FDTs). Fast dissolving drug delivery systems were first developed in the late 1970s. These tablets are designed to dissolve or disintegrate the less than 60 seconds.[2]

United States Food and Drug Administration (USFDA), Fast dissolving tablets (FDTs) is defined as a solid dosage form containing medicinal element or active ingredient which disintegrate or dissolve rapidly within seconds when placed upon the tongue. Fast dissolving tablets are also named as mouth dissolving tablets, rapid dissolving, melt in mouth tablets, or dispersible tablets, rap melts, porous tablets, quick dissolving, quick melt and quick disintegrating tablets.[3] Addition of disintegrants in fast dissolving tablets, results in quick disintegration of tablets and improves dissolution. As disintegration plays an important role in a tablet's dissolution before the active drug substance is finally released from the tablet's structure in to the body; Therefore type, concentration, and efficiency of disintegrants to a large extent affects the disintegrant properties (e.g., disintegration time [DT] and the ratio of

crushing strength–friability to disintegration time [CSFR/DT]) of formulated tablet.[4]

Researchers are looking for a new, safe and effective disintegrating agents which can disintegrate tablets rapidly even at a tablet crushing strength of greater than 3.5 Kg. The wetting time of a molecule should have high polar component of surface free energy and the agents which meet these special requirements are called as superdisintegrants.[5] The ease of availability of these agents and the simplicity in the direct compression process suggest that their use would be a more profitable alternative in the preparation of FDTs than the sophisticated and patented techniques.[6]

MATERIALS AND METHODS

Materials

Valsartan was received as gift sample by Aarti Pharma, Mumbai Ltd., *Hibisicus rosa sinesis* and *Planatgo ovata* mucilage were extracted in pharmaceutical lab, croscarmellose sodium, crospovidone, mannitol, magnesium sterate, talc, sodium sachharine were used for the formulation of tablets. All reagents and chemicals used were of laboratory grade.

Preparation of Valsartan solid dispersions

The solid dispersions of Valsartan: β-Cyclodextrin were prepared by solvent evaporation method.

Solvent evaporation method

Weighed amount of Drug and carrier taken in ratio of 1:1, 1:2 and 1:3 (SD1, SD2, SD3). The polymer was dissolved in an adequate amount of methanol with constant vigorous stirring until get a clear solution. The solvent was then rapidly evaporated in hot air oven (up to about 50 °C) to form a uniform solid mass. The co-precipitate was crushed and stored in a desiccator until further use.

Extraction of mucilage from seeds of *plantago ovata* (*Isapghula seed*)[7]

Isapghula consist of dried seeds of *plantago ovata forskal. (Plantaginaceae).* It contains mucilage which is present in the epidermis of the seeds. The seeds of *plantago ovata* were soaked in distilled water for 48 hours. Then boiled for few minutes for complete release of mucilage in to water. The material was squeezed through muslin-cloth for filtering and separating out the marc. Then an equal volume of acetone was added to the filtrate so as to precipitate the mucilage. The separated mucilage was dried in an oven at temperature less than 60°C, to get a powder form.

Extraction of mucilage from *hibiscus rosa sinensis* leaves[8]

The fresh *Hibiscus rosa-sinensis* leaves were collected and washed with water to remove dirt's and debris. Leaves were powdered and soaked in water for 5-6 hours, boiled for 30 minutes and left stand for 1 hour to allow complete release of mucilage in to water. The mucilage was extracted using multi-layer muslin cloth to remove the marc from the solution. Acetone (in the volumes of three times to the volume of filtrate) was added to precipitate the mucilage. The mucilage was separated, dried in an oven at less than 50°C, collected, ground, passed through #80 sieve and stored in desiccator at room temperature for further use.

Characterization of solid dispersions

Phase solubility studies[9]

The solubility of both Valsartan drug: β-Cyclodextrin solid dispesrsions was determined in the water. The solubility of drug and solid dispersion was determined by taking an excess amount of drug (40mg) and SDs (equivalent to 40mg of drug) and adding them to100ml of water, in teflon-facing screw-capped vials. The samples were kept at equilibrium for a period of 48hrs in rotatory mechanical shaker. The supernatant fraction collected from the vials was filtered through a membrane filter and analyzed by UV-Visible spectrophotometer at a wavelength of 249 nm. Ratio optimization was done on the basis of the best solubility results obtained.

Product Yield

The production of yield of solid dispersions was calculated using the final product after drying with respect to the initial total weight of the drug and carrier used for the preparation of solid dispersion. Percent production yield were calculated as per the formula mentioned below,

$Py = Wo/Wt \times 100$

Where,

Py= Product yield,

Wo= Practical mass (solid dispersion)

Wt= Theoretical mass (carrier + drug)

Drug content

About 10 mg drug equivalent of SD was weighed accurately and transferred to 100 ml volumetric flask. From this stock solution (100 µg/ml), 1 ml was withdrawn and further diluted up to 10 ml with 1.2 pH. This solution was used for the assay for drug content by UV spectrophotometer at 249nm. Concentration of drug in stock solution was calculated by using calibration curve and from which percent drug content was calculated.

$\%\ \text{Drug content} = \text{Absorbance} \times D.F/100 \times 1000$

Where,

D.F= Dilution factor.

Dissolution study of solid dispersion with pure drug

In-vitro dissolution study of optimized SDs was carried out using Lab India Dissolution Apparatus (LABINDIADS 8000, India), Samples equivalent to 40 mg of VAL was hold in muslin cloth and then added 900ml phosphate buffer pH 1.2, maintained at 37±1 for at 0 rpm. 2ml of sample was withdrawn after specified time dissolution medium. Collected samples were analysed spectrophotometrically at measured wavelength of 249nm, and cumulative percent drug release was

calculated. Drug release profile was studied using percentage drug release versus time (hr) plot.

Formulation of fast dissolving tablets of Valsartan

Fast dissolving tablets of valsartan were prepared by direct compression method, in this powder blends of active ingredient or weighed equivalent weight of SD and suitable excipient, which flow uniformly in the die cavity and forms a firm compact was prepared as per the composition shown in the below table no. 04. Powdered drug was mixed with *Hibiscus rosa-sinensis* mucilage, Seeds of *plantago ovata* mucilage, Croscarmellose sodium, Cros-povidone, as a super disintegrants in 2.5%, 5%, mannitol used as a diluent, filler, to enhance compressibility, talc used as a glidant, magnesium stearate as a lubricant, sodium saccharin used as sweetener. All the powders were mixed well and compressed in single station tablet punching machine using 10 mm round shaped, flat punches to obtain the tablets. Each tablet weighed 200mg.

Standard calibration curve

Standard solution[10-11]

Standard calibration curve of Valsartan was prepared by dissolving accurately weighed 100mg of Valsartan in methanol solution in a 100ml volumetric flask and the volume was made up to 100ml by using methanol solution to obtain a stock solution of 1000µg/ml (SS-I). From this stock solution, 10ml withdrawn and diluted with 100ml by using methanol (SS-II). Appropriate aliquots were pipetted in to different 10ml volumetric flask and volumes were made up to 10ml with methanol. To get concentrations of 5, 10, 15, 20, 25, 30µg/ml. The absorbance of these drug solutions were measured at 249nm.

FTIR study

FTIR carried out by KBr disc method. KBr was dried in hot air oven at 60°C for 1hr. The samples were prepared by mixing it thoroughly with potassium bromide. This mixture was then placed in a scanning slot of Fourier Transform Infra-red (FTIR) spectrophotometer and scanned at range from 400 to 4000 cm-1 to obtain FTIR of API. The spectrum was then compared with the spectrum of reference standard.

Pre compression parameters[12-13]

Pre-compression studies were carried out by standard methods. The flow property were characterized in terms of angle of repose, bulk density, tapped density, carr's index, hausner's ratio.

Post compression parameters[14]

Compressed tablets were then evaluated for thickness, hardness, weight variations and friability. Diameter and thickness were measured by using digital vernier caliper. Hardness was measured by Monsanto type hardness tester. Weight variation is carried out in single pan balance. Friability testing was done by using Roche friabilator.

Wetting time [15]

The method was applied to measure tablet wetting time. A piece of tissue paper folded twice was placed in a small petridish (i.d. = 6.5cm) containing 10ml water, a tablet was placed on the paper, and the time for complete wetting was measured. Three trials for each batch were performed and standard deviation was also determined.

Water absorption ratio[15]

A piece of tissue paper folded twice was placed in a small petridish containing 6ml of water. A tablet was put on the paper and time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R was determined using following equation. Three tablets from each formulation were performed and standard deviation was also determined.

R = 100(Wa – Wb)/Wb

Where,

Wb – weight of tablet before absorption,

Wa – weight of tablet after absorption.

***In-vitro* disintegration time[15]**

The process of breakdown of a tablet in to a smaller particles is called as disintegration. The *in-vitro* disintegration time of a tablet was determined using disintegration apparatus as per I.P specifications.

I.P specifications: Place one tablet in each of 6 tubes of the basket. Add a disc to each tube and run the apparatus using pH 1.2 maintained at 37°± 2°C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the pH 1.2 maintained at 37° ± 2°C. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded.

Drug content [16]

Three tablets weighed and crushed in a mortar then weighed powder contain equivalent to 100mg of drug transferred in 100ml of phosphate buffer pH 1.2. Subsequently, the solution in volumetric flask was filtered, suitable dilutions will be carried out. And final solution were analysed at 249nm using UV- visible spectrophotometer Shimadzu UV- 2450, Japan.

***In-vitro* drug release study[16]**

In-vitro drug release was studied using Lab India Dissolution Apparatus (LABINDIA DS 8000, India), in 900ml phosphate buffer pH 1.2, maintained at 37±1℃ for 30 minutes, at 50 rpm. 5ml of sample was withdrawn after specified time dissolution medium. Collected samples were analysed spectrophotometrically at measured wavelength of 249nm, and cumulative percent drug release was calculated. Drug release profile was studied using percentage drug release versus time (hr) plot.

Kinetic study[17]

The rate and mechanism of release of acyclovir from the prepared floating tablets were analyzed by fitting the dissolution data into following equations.

Zero order kinetic $Qt = Q0 + k0t$

First Order Kinetics $InQt = InQ0 – k1$

Higuchi's Model $Qt = kH\sqrt{t}$

Hixon-Crowell $Q01/3 – Qt1/3 = kst$

Peppas Model $Qt/Q\infty = kktn$

Where,

Qt: amount of drug released in time t, Q0: initial amount of drug in the Tablet, Qt/Q∞: fraction of drug released at time t, k0; k1; kH; kk; ks: release rate constants, n: the release exponent indicative of the mechanism of drug release.

Stability studies [18]

Stability studies of pharmaceutical products were done as per ICH guidelines. These studies are designed to increase the rate of chemical or physical degradation of the drug substance or product by using exaggerated storage conditions. In order to determine the change in *in-vitro* release profile on storage, stability study of formulation code F3-F5 was carried out at 40°C in a humidity chamber having 75% RH. Samples were withdrawn at regular intervals during the study of 60 days. Formulations are evaluated for change in hardness, friability, disintegration time, drug content and *in-vitro* drug release pattern.

RESULTS AND DISCUSSION

The λmax of Valsartan was found to be 249 nm against Methanol. The standard calibration curve results were shown in Table no 04 and Figure. no. 01. The standard curve shows slope of 0.0302 and correlation coefficient of 0.9993. The curve was found to be linear in concentration range of 5 – 30 µg/ml at 249 nm.

Table no. 01: Composition of fast dissolving tablets of valsartan.

Ingredients (mg)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Valsartan	40	---	---	---	---	---	---	---	---
VAL SD	---	160	160	160	160	160	160	160	160
P.O.M	---	5	10	---	---	---	---	---	---
H.R.S.	---	---	---	5	10	---	---	---	---
C.C.S	---	---	---	---	---	5	10	---	---
C.P	---	---	---	---	---	---	---	5	10
Mannitol	154	29	24	29	24	29	24	29	24
Mg stearate	2	2	2	2	2	2	2	2	2
Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Saccharin Na	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5

Each tablet weighs 200mg.

VAL SD: Valsartan solid dispersion

H.R.S: *Hibiscus rosa-sinensis.*

P.O.M: *Plantago ovata* mucilage.

C.C.S: Croscarmellose Sodium.

C.P: Crospovidone

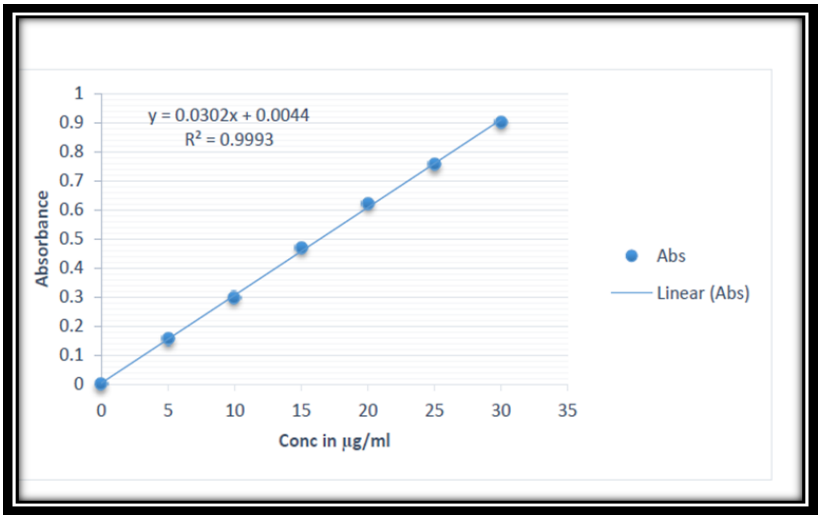


Fig. 01: Standard calibration curve of valsartan.

The prepared SD's were subjected for solubility study to evaluate the effect of carrier on the aqueous solubility of Valsartan and result of phase solubility analysis are shown in Table No. 2(b) from the result of phase

solubility analysis it can be clearly established that the carrier like β-Cyclodextrin is having very good solubility enhancing property. The aqueous solubility of drug increased significantly with increasing concentration of the carriers. On the basis of the phase solubility determination, the solubility of the 1:3 ratio was found to be 0.089mg/ml and 0.097mg/ml and fold is increase by 3.02 and 3.84 more than that of drug. The 1:3 ratio of solid dispersion was used for the further formulation and evaluated the *in-vitro* dissolution profiles of the drug and solid dispersion are shown in Table No 03 and Figure no. 03 Drug exhibited a slow dissolution, where as solid dispersion showed a marked enhancement in dissolution rate. Thus, dissolution up to 78.36 and 95.28% was recorded with solid dispersion in 30 min.

Table no. 02 (a): Results of phase solubility study.

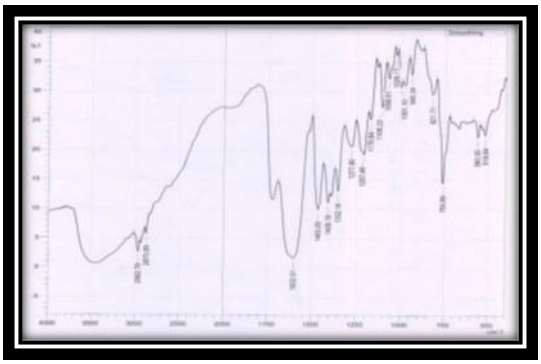
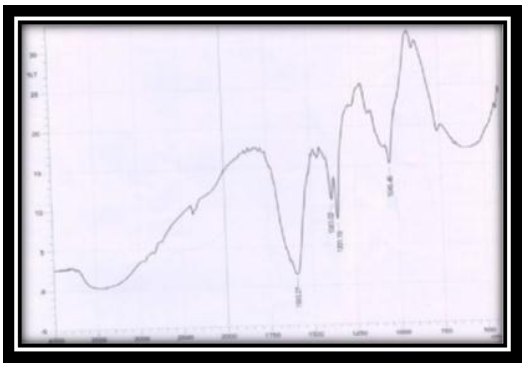
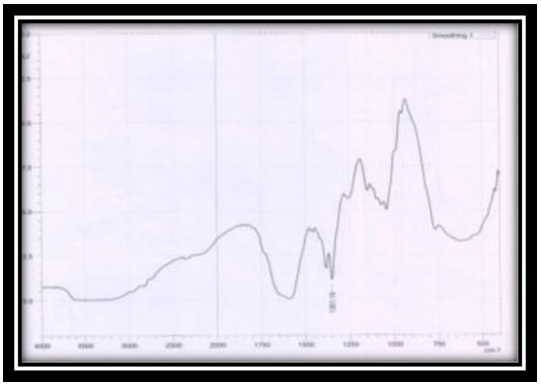
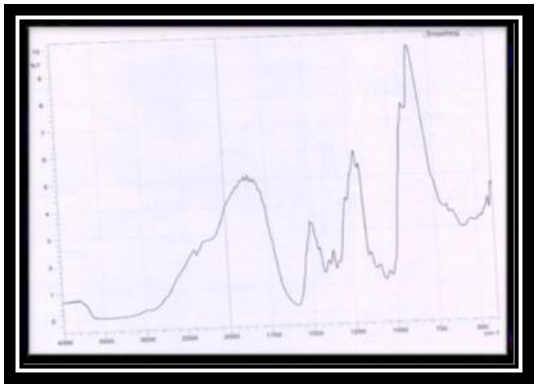
Sl. No	Drug	Polymer	Ratio	Solubility (mg/ml)±S.D	Fold Increase in solubility
1	Valsartan	-------	---	0.023	1 fold
2	Valsartan	β-Cyclodextrin	1:1	0.052	1.92 fold
3	Valsartan	β-Cyclodextrin	1:2	0.076	2.71 fold
4	Valsartan	β-Cyclodextrin	1:3	0.097	3.84 fold

Table no. 02 (b): Solid dispersion of drug content (%).

Sl. No.	Drug	Polymer	Ratio	Drug content (%)
1.	Valsartan	β-Cyclodextrin	1:1	95.62±0.48
2.	Valsartan	β-Cyclodextrin	1:2	97.16±0.44
3.	Valsartan	β-Cyclodextrin	1:3	97.49±0.28

Table no. 03: Dissolution study of pure drug and valsartan solid dispersions.

Sl. No.	Time (min)	% Drug release	
		Drug	VAL+β-Cyclodextrin
1.	5	9.25%	22.65%
2.	10	13.42%	39.41%
3.	15	19.85%	67.52%
4.	20	23.53%	75.18%
5.	25	26.72%	87.63%
6.	30	30.34%	95.28%

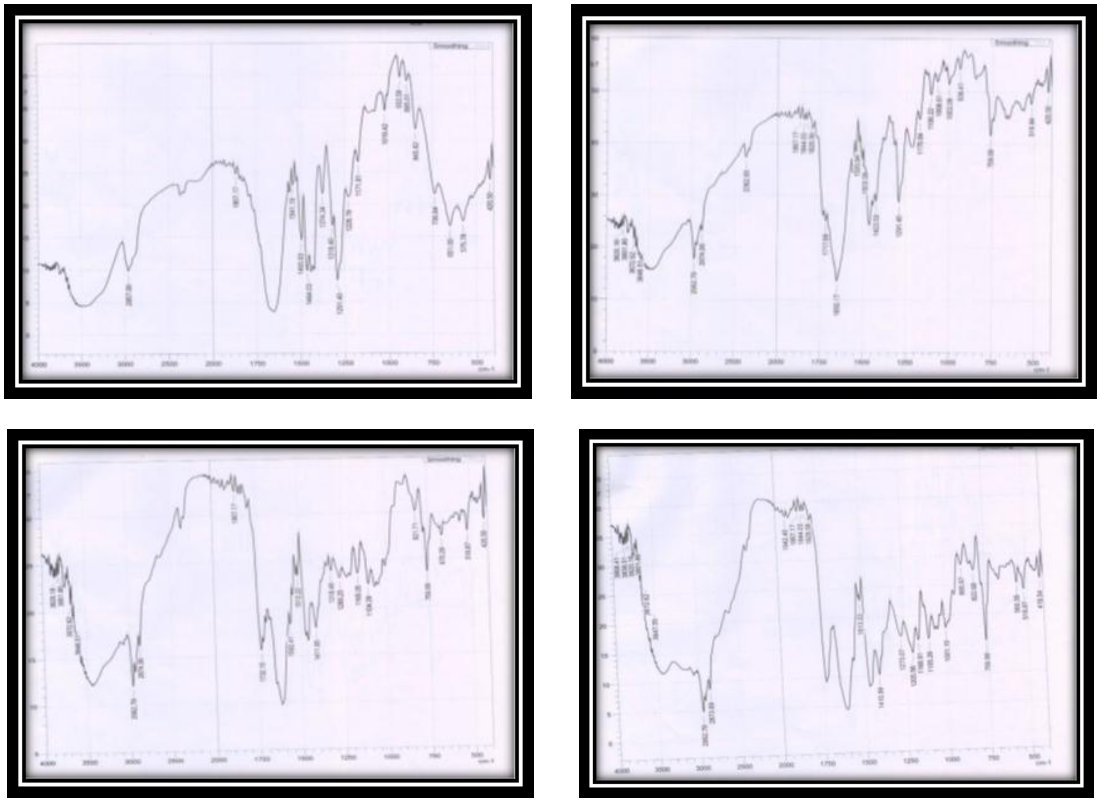


Fig. no. 02: (a): FTIR Spectrum of Valsartan, (b): FTIR Spectrum of *Plantago ovata* mucilage, (c): FTIR Spectrum of *Hibiscus-rosa sinensis*, (d): FTIR Spectrum of Croscarmellose sodium, (e): FTIR Spectrum of Crospovidone (f): FTIR Spectrum of Valsartan + Croscarmellose sodium, (g): FTIR Spectrum of Valsartan + Crospovidone, (h): FTIR Spectrum of Valsartan + *Hibiscus rosa-sinensis*, (i): FTIR Spectrum of Valsartan + *Plantago ovata* mucilage.

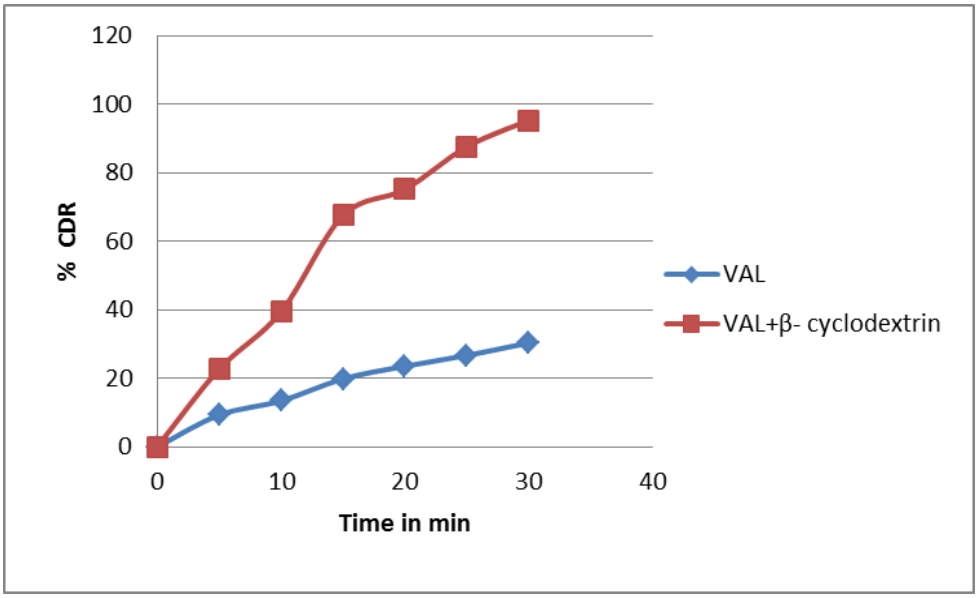


Figure no 03: % Cumulative drug release of valsartan and valsartan + β-cyclodextrin.

The compatibility study was performed by IR Spectroscopy to study the interaction of polymers with Valsartan. The FTIR spectroscopy was employed to ascertain the compatibility between drug and polymers. All the IR spectra shown in Figure. No.02 from (a) to(i). By correlation, interpreting the results, it indicates that drug is compatible with formulation components. The FTIR spectral analysis showed that there was no drug interaction with formulations additives of the tablet as there is no variation and shift in bands, it can be justified there is no interaction between drug and polymer.

Prepared tablets were evaluated for Pre and Post compression parameters. Angle of repose was performed

by funnel method. All the formulations were found in the range of 22.61° to 29.52°. All formulation shown within and nearby 30°, which indicates good free flowing properties and results were shown in Table. No.05. The bulk density and Tap density results were shown in the Table No.05. Bulk density was found to be in range of 0.4725 gm/ml to 0.4945 gm/ml, and Tapped density was found to be 0.5351 gm/ml to 0.5813 gm/ml, for Valsartan formulations. The values obtained lies within the acceptable range and not much difference were found. This result helps in calculating the % Carrs of the powder. The percentage of Carrs index of powder mix was determined by carrs compressibility index. The % compressibility of all the formulations lies within the range of 13.51% to 15.14%. The results were shown in Table. No. 05. Hausner's ratio is an indirect index of ease of powder flow. The values were lies within the range of 1.1563 to 1.1775 which indicates all formulations were showing the good flow properties and results were shown in Table. No.05. The tablet thickness was found to be 3.43±0.10 mm to 3.70±0.10 mm and the results was found to be within the limits. The results were depicted in Table. No 06. The tablet thickness was found to be 3.43±0.10 mm to 3.70±0.10 mm and the results was found to be within the limits. The results were depicted in Table. No.06. The wetting time of all the formulations was found to be 12.00±1.00 sec to 49.66±2.88 sec. The results were depicted in Table. No.07. The water absorption ratio of all the formulations was found to be 19.29±0.34 % to 97.57±1.0 %. The results were depicted in Table. No.07. The disintegration time of all the formulations was found to be 15.33±2.08 sec to 249.00±1.00 sec. The results were depicted in Table. No.07. The drug content estimation data for all the formulations were found to be 95% to 97.66%. The results were depicted in Table. No.07.

Table no. 04: absorbance data for the standard calibration curve of valsartan in methanol at 249 nm.

Sl. No.	Concentration in µg/ml	Absorbance at 249nm
1	0	0
2	5	0.155
3	10	0.299
4	15	0.469
5	20	0.621
6	25	0.756
7	30	0.901

Table no. 05: Physical properties of valsartan formulations.

Formulation.	Angle of Repose. (ɵ)	Bulk- Density. (gm/ml)	Tap- Density. (gm/ml)	Carrs Index. (%)	Hausner Ratio.
F1	25.19	0.4921	0.5691	13.53	1.1564
F2	23.62	0.4945	0.5718	13.51	1.1563
F3	27.49	0.4725	0.5532	14.58	1.1707
F4	29.52	0.4804	0.5657	15.07	1.1775
F5	28.92	0.4944	0.5813	14.94	1.1757
F6	25.64	0.4829	0.5613	13.96	1.1623
F7	22.61	0.4852	0.5655	14.19	1.1654
F8	28.84	0.4727	0.5351	15.14	1.1700
F9	27.67	0.4921	0.5713	13.86	1.1609

Table no. 06: Evaluated for thickness, hardness, uniformity of weight variation, friability.

Formulation.	Thickness. (mm) ± SD	Hardness. (kg/cm2) ±SD	Weight Variation. (mg) ± SD	Friability. (%) ± SD
F1	3.43±0.10	2.63±0.15	196.9±1.72	0.65±0.12
F2	3.50±0.10	2.66±0.11	197.5±1.71	0.62±0.07
F3	3.63±0.11	2.76±0.05	197.3±2.16	0.55±0.14
F4	3.53±0.05	2.60±0.10	197.7±1.63	0.58±0.04
F5	3.53±0.15	2.60±0.10	197.3±1.83	0.41±0.12
F6	3.70±0.10	2.70±0.10	196.9±2.02	0.61±0.06
F7	3.63±0.15	2.80±0.00	196.8±1.61	0.61±0.03
F8	3.60±0.10	2.50±0.10	197.0±2.00	0.69±0.02
F9	3.63±0.10	2.63±0.15	197.7±1.88	0.50±0.02

Table no. 07: Evaluated for wetting-time, water absorption ratio, disintegration time, drug- content.

Formulation.	Wetting Time. (Sec)± SD	Water absorption Ratio. (%)± SD	Disintegration Time. (sec)± SD	Drug Content. (%)
F1	49.66±2.88	19.29±0.34	249.00±1.00	95.00
F1	22.00±1.00	90.33±0.27	25.33±1.52	96.50
F1	12.00±1.00	97.57±1.0	15.33±2.08	96.83
F1	24.33±1.52	88.56±1.77	30.33±1.52	97.16
F1	14.00±1.00	95.77±0.65	17.66±1.52	97.66
F1	29.66±0.57	67.92±0.30	33.00±2.00	95.33
F1	22.66±1.15	86.70±0.42	26.33±1.52	96.00
F1	23.33±1.52	72.83±0.63	29.00±1.00	96.50
F1	21.66±0.57	84.27±0.38	24.33±1.52	97.33

Drug release profile was studied using percentage drug release versus time (hr) plot. The results were depicted in Table No.08 and Figure no 4 and 5. Formulations F1, F2, F3, F4 and F5 showed 28.94%, 93.47%, 96.06%, 92.54%, and 95.59%. Release of drug respectively at 30min. Formulations F6, F7, F8 and F9 showed 91.37%, 94.25%, 91.66% and 93.53%. respectively. Among all formulations, F3 and F5 showed faster release of drug.

Table. no. 08: *In-vitro* dissolution study.

Time (Min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
5	11.07%	23.85%	38.07%	22.05%	38.52%	21.42%	38.82%	22.05%	26.55%
10	14.28%	35.52%	68.87%	46.91%	67.26%	46.01%	69.78%	46.92%	53.83%
15	21.67%	65.27%	81.05%	75.08%	83.62%	74.32%	81.83%	75.23%	82.62%
20	23.52%	77.12%	92.99%	85.91%	90.28%	82.89%	85.05%	85.73%	85.77%
25	26.68%	90.55%	95.01%	88.91%	92.43%	88.92%	93.17%	88.80%	90.52%
30	28.94%	93.47%	96.06%	92.54%	95.59%	91.37%	94.25%	91.66%	93.53%

F1:- Without adding any superdisintegrants.
F2:- *Plantago ovata* mucilage (2.5%).
F3:- *Plantago ovata* mucilage (5%).
F4:- *Hibiscus-rosa sinensis* (2.5%)
F5:- *Hibiscus-rosa sinensis* (5%).
F6:- Croscarmellose Sodium (2.5%).
F7:- Croscarmellose Sodium (5%).
F8:- Crospovidone (2.5%).
F9:- Crospovidone (5%).

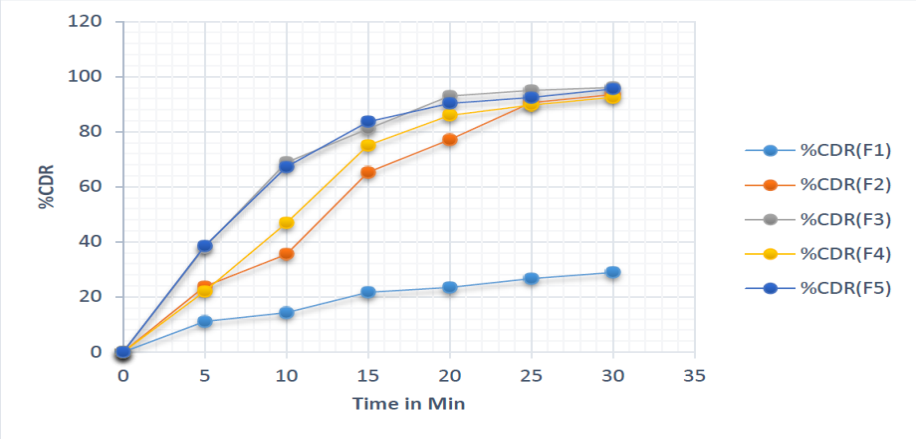


Fig. no. 04. Cumulative percentage drug release vs time of f1 to f5.

F1:- Without adding any superdisintegrant and solid dispersions.
F2:- *Plantago ovata* mucilage (2.5%).
F3:- *Plantago ovata* mucilage (5%).
F4:- *Hibiscus-rosa sinensis* (2.5%).
F5:- *Hibiscus-rosa sinensis* (5%).

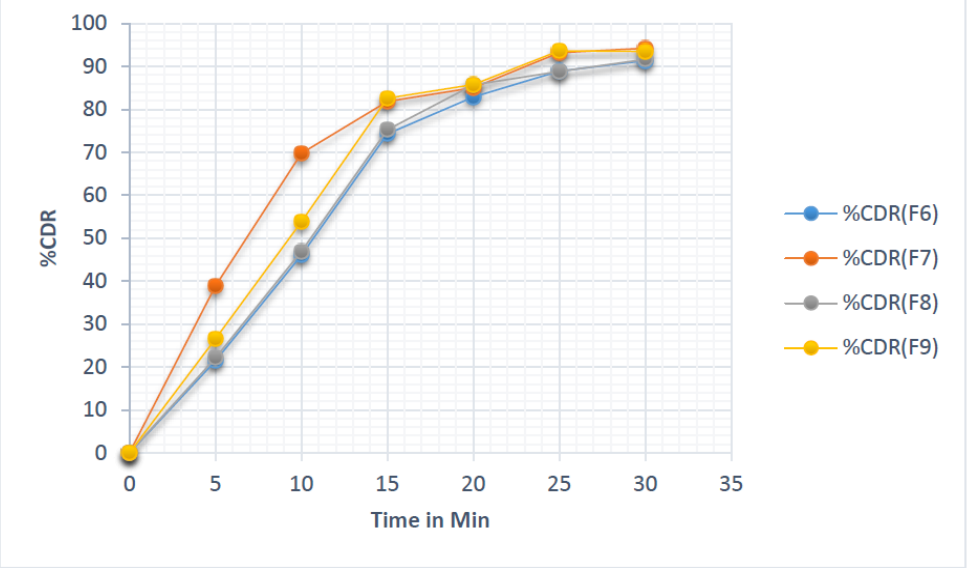


Figure. no. 05: Cumulative percentage drug release vs time of f6 to f9.

f6:- Croscarmellose Sodium (2.5%).
F7:- Croscarmellose Sodium (5%).
F8:- Crospovidone (2.5%).
F9:- Crospovidone (5%)

The *in-vitro* drug release data of the fast dissolving tablets were evaluated kinetically, by Zero order, First order, Higuchhi, Peppas, Hixon crowen model. The data were processed for regression analysis using PCP DISSO V3 Software. The regression coefficient (R) value for Zero order, First order, Higuchhi, Peppas, Hixon crowen models for all the formulations were shown in Table. No.07. The formulations F1, F2, F4, F6 and F8 follows Peppas model and formulations F3, F5, F7 and F9 are follows First order kinetics. The release of drug may be depends on disintegration time.

On the basis of drug content, *in- vitro* release study, disintegration time and wetting- time results, formulations F3 and F5 were subjected for stability studies as per ICH guidelines. The results observed were not much varied in integrity of the tablets at different temperature conditions. There was no significant change in hardness, friability, disintegration-time, drug content and *in-vitro* release study. The results were depicted in Table. No.10 and 11.

Table. no. 09: Kinetics of drug release of valsartan fast dissolving tablet.

Code.	Zero Order. (R value)	First Order. (R value)	Higuchhi. (R value)	Peppas. (R value)	Hixon Crowen. (R value)	Best Fit Model.
F1	0.9307	0.9870	0.9339	0.9936	0.9329	Peppas.
F2	0.9762	0.9640	0.9799	0.9844	0.9787	Peppas.
F3	0.8458	0.9849	0.8600	0.9627	0.8554	First Order.
F4	0.9403	0.9694	0.9461	0.9708	0.9442	Peppas.
F5	0.8374	0.9841	0.8518	0.9624	0.8471	First Order.
F6	0.9435	0.9695	0.9492	0.9716	0.9474	Peppas.
F7	0.8258	0.9833	0.8411	0.9576	0.8361	First Order.
F8	0.9374	0.9690	0.9432	0.9695	0.9419	Peppas.
F9	0.9073	0.9745	0.9153	0.9604	0.9127	First Order.

Table no. 10: Stability studies of f3 formulation at 40°c± 2°c / 75% rh±5%. (p.o.m 5%).

Parameter.	0-Days.	15-Days.	30-Days.	60-Days.
Hardness. (kg/cm^2)	2.76	2.76	2.60	2.55
Friability (%)	0.55	0.55	0.49	0.49
Disintegration time. (Sec)	15.33	14	14	13
Drug-Content. (%)	96.83	96.79	96.76	96.21
In-vitro drug release. (%)	96.06	96.01	95.98	95.91

Table. no. 11: Stability studies of f5 formulation at 40°c± 2°c / 75% rh±5%. (h.r.s 5%).

Parameter.	0-Days.	15-Days.	30-Days.	60-Days.
Hardness. (kg/cm^2)	2.60	2.60	2.50	2.50
Friability (%)	0.41	0.41	0.39	0.36
Disintegration time. (Sec)	17.66	17	16	16
Drug-Content. (%)	97.66	97.02	96.96	97.00
In-vitro drug release. (%)	95.59	95.52	95.48	95.45

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