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Research Article

Development and Evaluation of Fast Disintegrating Tablets of Valsartan for Orodispersible Using Superdisintegrants, Mannitol and Polyethylene Glycol 4000

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ABSTRACT

Over the past two decades, fast disintegrating tablets have gained global attention as a fast-rising alternative to conventional tablets by providing solutions to the limitations and disadvantages of earlier dosage forms administered orally. Valsartan sodium was formulated into tablets using the direct compression method. Different formulation batches were developed. Batches A1 to A3 contained fixed API, sodium starch glycolate, cellactose and mannitol in varying proportion; B1 to B3 contained fixed API, croscarmellose sodium, cellactose, and PEG 4000; C1 to C3, contained fixed API, SSG, cellactose, mannitol and PEG 4000 (50:50); D1 to D3 contained fixed API, CCS, cellactose, MN and PEG 4000 (50:50). The pre formulation characteristics of all powder mixtures showed good flow and compressibility properties. Batches A1 – A3 tablets containing mannitol were harder than B1 – B3 containing PEG 4000. From the results, C1 and D1 contained both MN and PEG 4000 in different proportion, PEG was responsible for lower tablet hardness, while both excipients played positive role in lowering disintegration time, C1 with average hardness and lower DT (47 .53 N, 6.44 s) will be adequate for FDT design for mouth disintegration on one hand, and A2 or A3 with hardness and DT :107.8 N, 7.21 s and 91.54 N, 6.80 s respectively could be best applied for the FDT intended to withstand rough handling transportation for commerce. The FTIR analysis of batches A to D showed no changes in the API peaks when compared with that of valsartan drug.

INTRODUCTION

Enhancement of drug solubility can therefore be seen as a very important method of improving bioavailability and efficiency, and is an important parameter to be considered in the formulation and development of orally administered drugs with poor aqueous solubility.

Various approaches have been used to improve drug solubility as well as dissolution of poorly aqueous soluble drugs and they include particle size reduction, micronization, solid dispersion, melt granulation, direct compression, nanosuspension, cryogenic techniques and micellar solubilisation. [1]

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Orally Disintegrating Tablets (ODTs)

The most common solid dosage forms are tablets and capsules, however a major disadvantage of these dosage forms for many patients, is the difficulty of swallowing, for which Water plays a crucial role. In most cases, people experience inconvenience in swallowing conventional dosage forms such as tablet when water is insufficient or unavailable, in the case of motion sickness and sudden episodes of coughing. For these reasons, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Orodispersible tablets are not only indicated for use in people who have swallowing difficulties, but also of high advantage to the general populace. Orodispersible tablets are those when placed on tongue, disintegrates instantaneously, releasing the drug, which dissolves or disperses in the saliva. The faster the drug dissolution, the quicker the absorption and onset of clinical

effect. Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form. The advantages of mouth dissolving dosage forms are increasingly being recognized in both, industry and academics.

Today ODTs are also called, quick disintegrating tablets, fast disintegrating tablets, fast dissolving tablets, porous tablets and rapidmelts. [2] The United States' Food and Drug Agency (FDA) classifies fast disintegrating tablets as ODTs. The United States Pharmacopoeia grades the formulation as an ODT if it has an in-vitro disintegration time of 30 seconds or less, while the European Pharmacopeia states that in-vitro disintegration time be within 180 seconds. The choice of reference exclusively depends on the official monograph method used. ODTs differ from other tablets placed or used in the mouth such as Buccal tablets, Sublingual tablets and Lozenges, in that it requires less than a minute to dissolve in the oral cavity.

Direct Compression

This technique can now be applied to ODTs because of the availability of improved tablet excipients, especially tablet disintegrants and sugar based excipients. Addition of disintegrants in ODTs, leads to quick disintegration of tablets and hence improves dissolution. In many fast dissolving tablet technologies based on direct compression, the disintegrants principally affect the rate of disintegration and hence the dissolution. The introduction of super-disintegrants and a better understanding of their properties have increased the popularity of this technology. Tablet disintegration time can be optimised by concentrating the disintegrants.

Mohire research group [3] prepared Metronidazole orodispersible tablets by three different techniques of taste masking and three different disintegrating agents‟ viz. sodium starch glycolate (SSG), Bamboomanna (BB), Chitosan (CHN) and combination thereof.

Biswajit and Varun [4] have prepared orodispersible tablets of Amlodipine besylate by using three different disintegrants like crospovidone (Polyplasdone XL 10), Sodium starch glycolate (SSG), Croscarmellose sodium (Ac-De-Sol). Two method of preparation are used to formulate the orodispersible tablet of Amlodipine besylate like direct compression and sublimation method. Sublimation method showed good result as compare to direct compression. Thakur and Narwal [5] review on recent advancement in orally disintegrating preparations. The oral route is the most convenient route for the drug administration due to the highest component of compliance mainly the paediatrics and geriatrics.

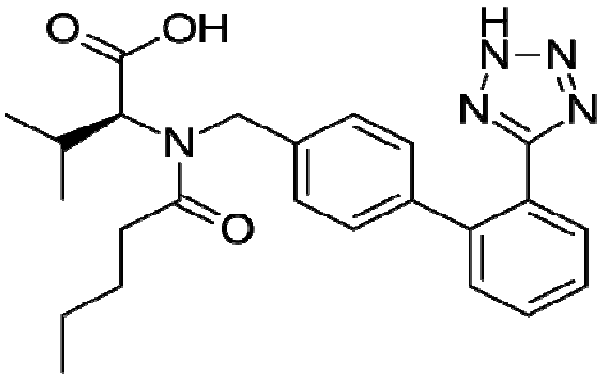
Shinde and co-worker [6] developed fast dissolving tablets of Cephalexin. A combination of superdisintegrants i.e. Sodium starch glycolate (SSG) and croscarmellose sodium (CS) were used along with camphor as a subliming material. Infrared (IR) spectroscopy was performed to identify the physicochemical interaction between drug and polymer. IR spectroscopy showed that there is no interaction of drug with polymer.

Pooja research team [7] Prepared and evaluate orodispersible tablets of Levocetirizine HCL to disintegrate in mouth (without the aid of water), to enhance the clinical effects and bioavailability through pre-gastric absorption.

Drug Profile – VALSARTAN

Valsartan is an antihypertensive; angiotensin receptor blockers (ARBs). Valsartan bioavailability is estimated as 25 %. It is Soluble in Ethanol, Dimethyl sulfoxide and Dimethlyformamide at 30mg/Ml. The solubility in water is 1.406mg/L at 25°C.

Structure:



Pharmacology:

It inhibits the pressor effect of an angiotensin II hormone, decreasing blood pressure. Angiotensin II is formed from Angiotensin I during a reaction catalysed by Angiotensin Converting Enzyme (ACE). Angiotensin II is the main pressor agent of the Renin-Angiotensin-Aldosterone System (RAAS), causing vasoconstriction, Aldosterone synthesis and release, cardiac stimulation, as well as the renal absorption of Sodium.

Sodium Starch Glycolate
Sodium starch glycolate (BP), Carboxymethylamylumnatricum (PhEur.), Sodium starch glycolate (USNF).

SSG is sparingly soluble in ethanol (95%), practically insoluble in water. In water, sodium starch glycolate swells to up to 300 times its volume.SSG is widely used in oral pharmaceuticals as a disintegrant in capsule and tablet formulations. It is commonly used in tablets prepared by either direct compression or wet granulation processes.

Croscarmellose Sodium
Croscarmellose sodium is cross-linked carboxymethyl cellulose sodium, it is insoluble in water. Although croscarmellose sodium rapidly swells to 4-8 times its original volume on contact with water. It's practically insoluble in acetone and ethanol.

Croscarmellose sodium is used in oral pharmaceutical formulation as a disintegrant for capsules, tablets and granules. In tablet formulation, croscarmellose sodium may be used in both direct compression and wet granulation processes.

Mannitol: Mannitol (BP).
It's a diluent for lyophilized preparations, sweetening agent, tablet and capsule diluent. Mannitol is soluble in water, alkalis, and ethanol (95%). It is practically insoluble in ether. In pharmaceutical preparations it is primarily used as a diluent (10-90% w/w) in tablet formulations. Mannitol may be used in direct compression tablet applications, for which the granular and spray dried forms are available, or in wet granulations. Mannitol is commonly used as an excipient in the manufacture of chewable tablet formulations because of its negative heat of solution, sweetness, and mouth feel.

Aerosil: Colloidal anhydrous silica (BP).
Aerosil sub-microscopic fumed silica with a particle size of about 15 nm. It is a light, loose, bluish-white-coloured, odourless, tasteless, non-gritty amorphous powder, which is practically insoluble in organic solvents, water, and acids, except hydrofluoric acid, soluble in hot solutions of alkali hydroxide. It forms a colloidal dispersion with water.

Aerosil is widely used in pharmaceuticals as its small particle size and large specific surface area give it desirable flow characteristics that are exploited to improve the flow properties of dry powders in a number of processes such as tableting. Aerosil is also used as a tablet disintegrant and as an adsorbent dispersing agent for liquids in powders.

MATERIALS
Valsartan Sodium (Zhucheng Haotian Pharma Co., Ltd), Sodium Starch Glycolate (Shanghai Macklin Biochemicals Co. Ltd China), Croscarmellose Sodium (Yuhao Chemicals Co. Ltd China), Cellactose (Molkerei MEGGLE Wasserburg GmbH & Co.KG), Polyethylene Glycol (PEG) 4000 (LobaChemiePvt. Ltd, Mumbai, India), Mannitol (Oxford Laboratory, Mumbai, India), Magnesium Stearate, Aerosil.

METHOD
Preparation of API and Excipients
The API (Valsartan) was used as received. The API and excipients mixes were prepared according to the table 1. Twelve different batches of tablets were prepared by varying the excipients contained in each batch as well as varying the quantity of excipients contained by different batches (A_1, A_2, A_3, B_1……D_3).

Standard Graph of Valsartan
Accurately weighed amount of 100 mg Valsartan was transferred into a 100ml volumetric flask. Twenty (20) millilitres of 0.1N hydrochloric acid (HCl) was added to dissolve the drug and volume was made up to 100 ml with the same solution. The resulted solution had the concentration of 1mg/ml which was labelled as 'stock'. From this stock solution 10ml was taken and diluted to 100 ml with 0.1N HCl having the concentration of 100 mcg/ml. Necessary dilutions were made by using this second solution to give the different concentrations of Valsartan (5 to 50 mcg/ml) solutions.

The absorbance of the above solutions was recorded at absorption maxima(249 nm) of the drug using double beam UV-Visible spectrophotometer. Standard graph was plotted between the concentration (on X-axis) and absorbance (on Y-axis). Similarly, standard graph was plotted with pH 6.8 phosphate buffer.

Formulation of ODTs
A table for the variation in excipients and quantity of API and excipients used per tablet produced in the formulation of the batches of ODT to be produced is given below:

Table 1: Tablet compression formula.

	BATCHES (MG/TABLET)											
Batch	A_1	A_2	A_3	B_1	B_2	B_3	C_1	C_2	C_3	D_1	D_2	D_3
API	40	40	40	40	40	40	40	40	40	40	40	40
SSG	7.5	17.5	26.5	-	-	-	7.5	17.5	26.5	-	-	-
CCS	-	-	-	7.5	17.5	26.5	-	-	-	7.5	17.5	26.5
CL	200	205	206	200	205	206	200	205	206	200	205	206
MN	100	85	75	-	-	-	50	42.5	37.5	50	42.5	37.5
PEG 4000	-	-	-	100	85	75	50	42.5	37.5	50	42.5	37.5
MS	5	5	5	5	5	5	5	5	5	5	5	5
AS	3	3	3	3	3	3	3	3	3	3	3	3
Total (mg/tablet)	355.5	355.5	355.5	355.5	355.5	355.5	355.5	355.5	355.5	355.5	355.5	355.5

API = Valsartan; **SSG** = Sodium Starch Glycolate; **CS** = Croscarmellose Sodium; **CL** = Cellactose; **MN** = Mannitol; **PEG 4000** = Polyethylene Glycol 4000; **MS** = Magnesium Stearate; **AS** = Aerosil.

One hundred (100) tablets were made per batch of excipient variation. All values in the table are given in milligrams (mg).

Direct Compression

Each tablet is expected to weigh 355.5mg, which is the total value of the weights of the API + Excipients. 355.5mg of powdered mixture was weighed and compressed using the single punch Carver hydraulic press, which was set to a compression force of one (1) metric tonne.

Evaluation of Powder Properties

Preformulation Analysis

Angle of Repose:

Angle of repose was determined by using funnel method. The accurately weighed blend is taken in a funnel. The height (h) of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of blend. The drug-excipient blend was allowed to flow through the funnel freely on to the surface. The diameter (d) of the powder cone was measured and angle of repose was calculated using the following equation.

$$\text{Tan } \Theta = h/r$$

Where Θ is the angle of repose, h and 'r' are height and radius of cone respectively.

Bulk Density:

Apparent bulk density was determined by pouring a weighed quantity of blend into graduated cylinder and measuring the volume and weight. Bulk density was calculated by using the following formula:

Bulk density = Weight of the powder/Volume of the packing

Tapped Density:

Tapped density was determined by transferring a known mass of drug-excipient blend into graduated cylinder. The cylinder was allowed to fall under its own weight onto a hard surface from a height of 10 cm at 2 second intervals. The tapping was continued until no further change in volume was noted. Tapped density was calculated by using the following formula:

Tapped density = Weight of the powder/Volume of the tapped packing

Compressibility Index:

The compressibility index of the blends was determined by calculation using the following formula:

Compressibility Index (%) = [(TD – BD) x 100/TD]

Hausner's Ratio:

Hausner's ratio also indicates the flow properties of powder/granules. This can be calculated by using the following formula:

Hausner's ratio = (Tapped density x 100) / (pour density)

Evaluation of Tablet properties

Evaluation of Tablets:

All the formulated FDTs were subjected to the following quality control tests:

Weight Variation:
The weight variation test was carried out in order to ensure uniformity in the weight of tablets in a batch. First, the total weight of 20 tablets from each formulation was determined and the average was calculated. The individual weight of each tablet was also determined. The deviations of each tablet from the mean were calculated, and the USP maximum % difference allowed (5 %) for tablets average weight greater than 324 mg was applied.

Hardness:
The hardness of tablet is an indication of its strength. It was measured as the crushing strength, i.e., the force required to break the tablet across its diameter. The force was measured in kg and the hardness of 3 -6 kg/cm^2 is considered to be satisfactory for uncoated tablets by British Pharmacopoeia. Crushing strength of ten (10) tablets from each batch was determined by Monsanto hardness tester.

Friability Test:
Friability test was carried out to access the ability of the tablet to withstand abrasion in packaging, handling and transport. Roche friabilator was employed to determine the friability of the tablet samples from each batch of the formulations. Twenty (20) tablets from each were weighed and transferred into the friabilator. The rotation was set at 25 rpm for 4 minute, after which the tablets were removed collectively, dedusted and weighed. The percentage lost in weight, i.e., friability, was calculated using the formula:

$$\% \text{ Friability} = [(W_1 - W_2) \times 100] / W_1$$

Where, W_1 is the weight of tablets before the test; W_2 is the weight of the tablets after the test.

Wetting Time:
A 6ml of distilled water containing acridine orange (a water-soluble dye) was placed in a petri dish of 10 cm diameter. A piece of tissue paper folded twice was placed in the petri dish. Tablets were carefully placed in the centre of the petri dish and the time required for water to reach the upper surface of the tablet was noted as the wetting time. The test results are presented as mean value of three determinations.

Drug Content Uniformity
Standard Preparation
An accurately weighed amount of pure valsartan (100mg) was transferred into 100mL volumetric flask. It was dissolved and made up to volume with phosphate buffer of PH-6.8 to 100ug/mL concentration of the standard stock solution. Various working concentrations (10, 5, 2.5, 1.25 ug/mL) were made by further dilution with the same medium and absorbance was measured at 273 nm. A standard calibration curve was first established to quantify the drug.

Sample Preparation
Three tablets were weighed individually then placed in a mortar and powdered with a pestle. A 100 mg powdered valsartan were transferred into buffer solution. The solution was filtered through 0.45µm membrane and absorbance was measured at 273 nm after suitable dilution.

Calculation
The amount of ciprofloxacin present in tablet can be calculated using the formula:

$$AT/AS \times SW/100 \times 100/St \times AV$$

Where,
AT = Absorbance of sample preparation
AS=Absorbance of standard preparation
SW=Weight of ciprofloxacin working standard (mg)
St =Weight of ciprofloxacin tablet (mg)
AV=Average weight of tablet (mg)

Disintegration
The disintegration times of the tablets were determined in distilled water at 37± 0.5 ^{0}C using the Apex disintegration testing apparatus. Four tablets from each batch were employed for this evaluation. One tablet was placed in each tube and the Basket rack positioned in 1L beaker of distilled water at 37±0.5 ^{0}C in a manner that the tablet remained 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement. The basket containing the tablets was then operated at a rate of 30 cycles per Minute. Then the disintegration time for each formulation was determined.

Dissolution
The USP, 2000 dissolution apparatus basket method was adopted. Six tablets were taken for the study of dissolution pattern of the tablets. A

900 ml of the 0.1 N HCL solutions was used as the dissolution medium. The revolution of the basket was maintained at 50 rpm and the temperature of the medium was set at 37± 0.5° C. The dissolution was carried for a period of one hour. A 5mL menstrum was removed at designated intervals (5, 10, 15, 20, 25, 30, 45 and 60 minutes) filtered and subjected to UV-spectrophotometer analysis of the drug content, while replacing the withdrawn sample with fresh 0.1 N HCL solution. The absorbance of the samples was measured and total drug concentration determined.

Characterization

Fourier Transform Infrared Spectroscopy (FT-IR):

The interaction between drug and excipients was studied by using FTIR spectroscopy. FTIR spectroscopy was employed to ascertain the compatibility between Valsartan and the selected excipients. Solid admixtures were prepared by mixing the pure drug with potassium bromide, each formulation excipient separately in the ratio of 1:1 and stored in airtight containers at 40°C/75%RH and 60°C/75%RH.Potassium bromide, the pure drug and the excipients were heated to 105°C for one hour in a hot air oven to remove the moisture content. FTIR spectrum of Valsartan was compared with FTIR spectra of drug – excipients mixture.

RESULTS

Analysis of Powder Properties

The powder mixtures of the batches were analysed and the necessary parameters were determined as shown below:

Table 2: Showing results of the properties of powder mixtures.

Batch	Flow Rate (g/s)	Angle of Repose (°)	Bulk Density (g/mL)	Tapped Density (g/mL)	Compressibility Index (%)	Hausner's Ratio
A_1	3.86	14.62	0.432	0.537	19.55	1.24
A_2	4.82	16.36	0.428	0.556	23.02	1.30
A_3	4.60	18.00	0.429	0.619	30.70	1.44
B_1	0.27	34.49	0.261	0.372	29.84	1.43
B_2	0.30	30.60	0.265	0.337	21.37	1.27
B_3	0.43	24.90	0.266	0.338	21.30	1.27
C_1	0.78	26.29	0.272	0.349	22.06	1.28
C_2	1.28	24.23	0.278	0.353	21.25	1.27
C_3	1.38	27.79	0.299	0.374	20.05	1.25
D_1	2.08	24.55	0.295	0.380	22.37	1.29
D_2	2.62	20.16	0.284	0.375	24.27	1.32
D_3	2.78	26.57	0.305	0.384	20.57	1.26

Result of Standard Calibration Curve

Table 3: Showing results for absorbance of Valsartan at different concentrations

S. No	Concentration (µg/ml)	Absorbance
1	5	0.159
2	10	0.208
3	15	0.318
4	20	0.428
5	25	0.512
6	30	0.605
7	35	0.718
8	40	0.860
9	45	0.932
10	50	1.009

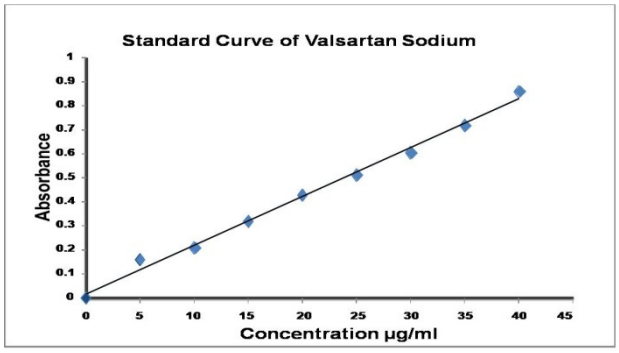


Figure 1: Standard Calibration Curve of Valsartan at different concentration

Analysis of Tablet Properties

After directly compressing the tablets of each batch, the tablets were analysed and the properties determined. The results are given below:

Table 4: Showing results of the properties of tablets formulated.

Batch	Weight (mg)	Crushing Strength (N)	Friability (%)	In-vitro Disintegration time (s)	Content Uniformity (%)
A_1	0.350±0.04	143.80±20.20	1.59	13.35±1.15	98.40±2.60
A_2	0.313±0.02	107.80±10.10	1.04	7.21±0.20	100.30±4.20
A_3	0.325±0.01	91.54±5.20	1.09	6.80±0.23	98.60±2.20
B_1	0.350±0.02	11.30±2.10	0.00	10.88±1.10	98.00±2.20
B_2	0.332±0.03	17.82±3.12	0.18	16.11±1.20	99.10±0.20
B_3	0.317±0.01	23.23±3.20	0.30	19.23±0.90	98.50±1.10
C_1	0.345±0.02	47.53±1.12	0.65	6.44±0.20	99.17±0.10
C_2	0.338±0.02	27.53±2.11	0.97	7.50±0.50	98.20±0.60
C_3	0.334±0.03	22.61±1.20	1.03	9.60±0.90	98.80±1.00
D_1	0.323±0.01	43.07±2.01	1.08	11.50±0.75	102.18±2.11
D_2	0.327±0.02	26.03±1.00	1.01	22.90±1.20	97.80±2.00
D_3	0.320±0.02	18.93±2.01	1.00	36.70±2.20	98.70±0.90

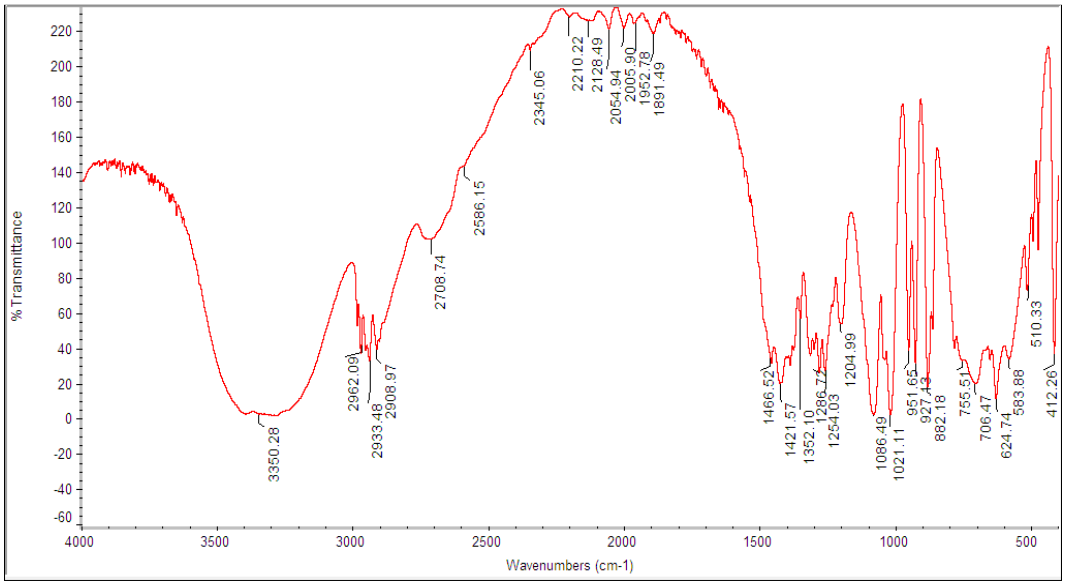


Figure 2: FT-IR spectra of D(-) Mannitol

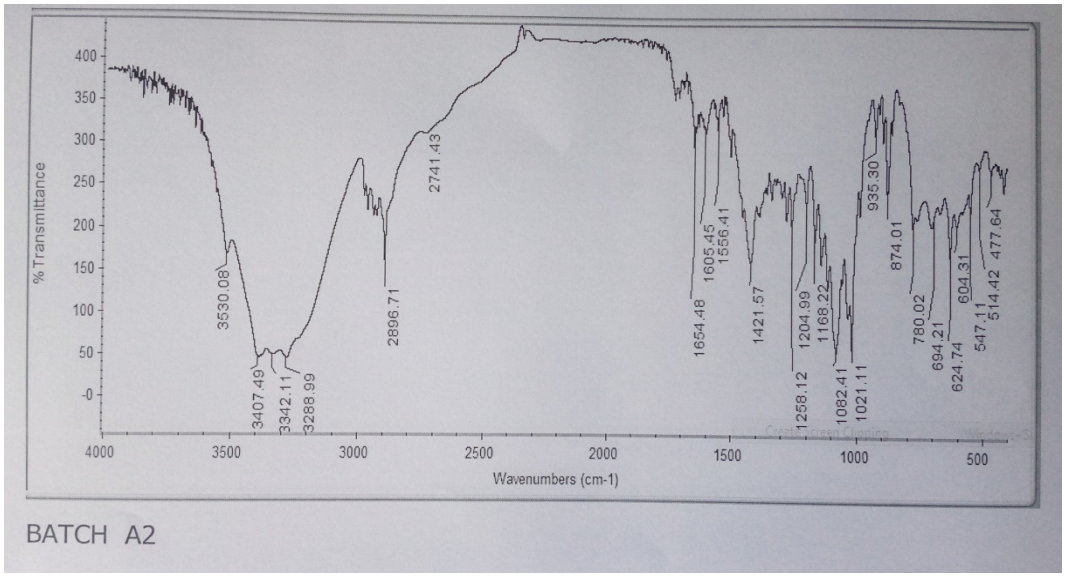


Figure 3: FT-IR spectra of Batch A_2

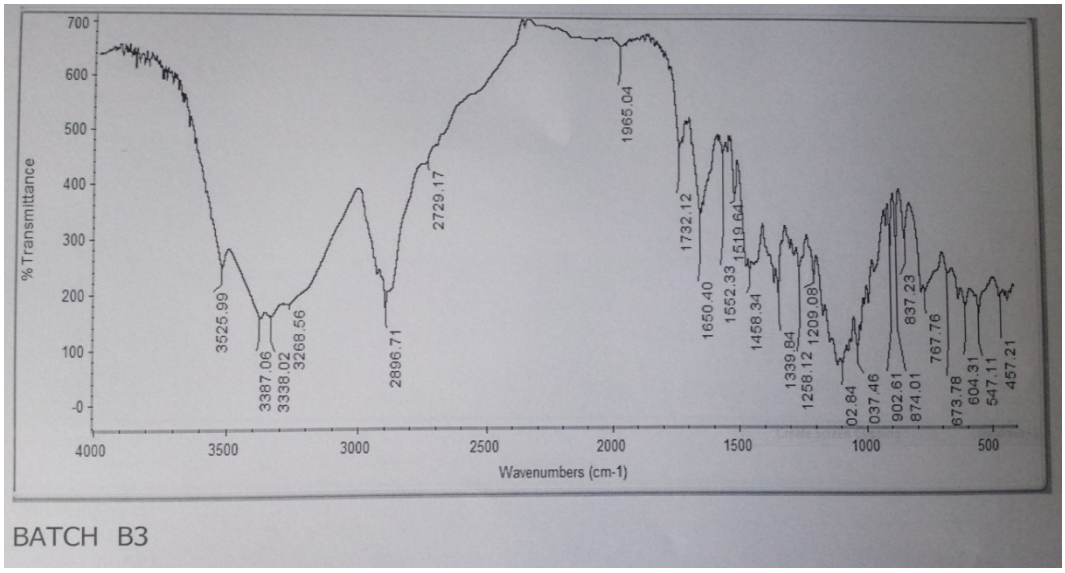


Figure 4: FT-IR spectra of Batch B_3

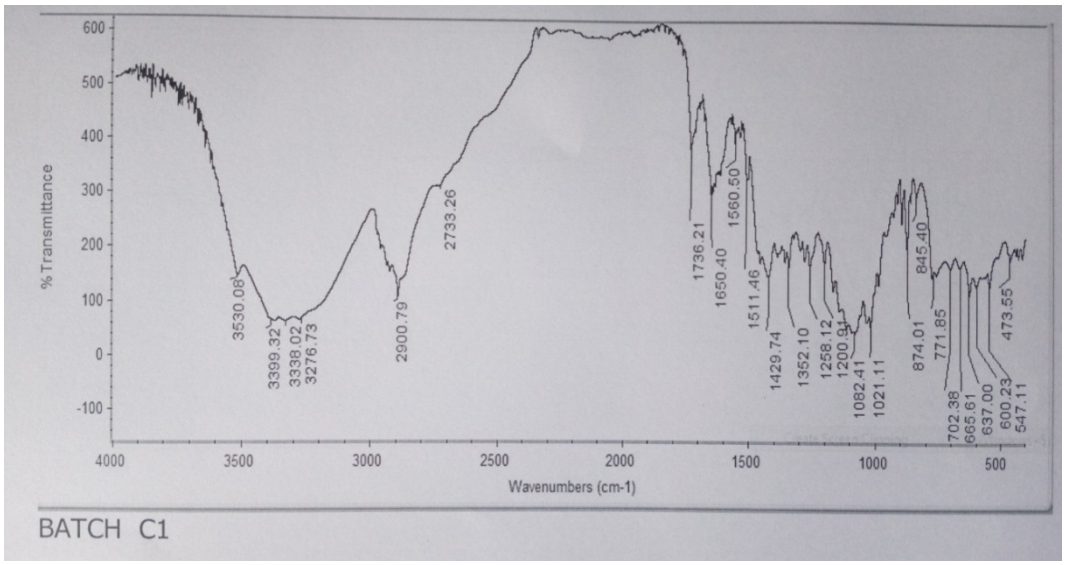


Figure5: FT-IR spectra of Batch C_1

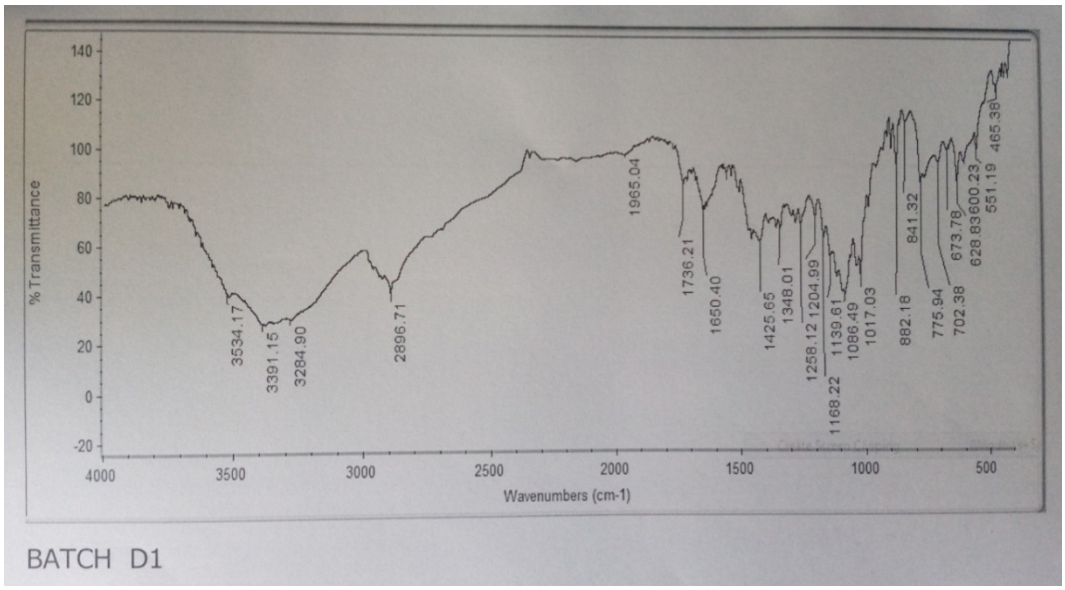


Figure6: FT-IR spectra of Batch D_1

DISCUSSIONS

Preparation of Valsartan ODT was attempted at formulating rapid dissolving tablets. In the current study, the excipients were varied across batches to give optimum compressibility to the tablets by direct compression.

Evaluation of Powder Properties

The properties of the triturated powder mixtures were evaluated with parameters like Flow rate, Angle of Repose, Compressibility Index and Hausner's ratio for their suitability for direct compression. The Flow rate was found to be 0.27g/s at lowest for B_1 and 4.82g/s at highest for A_2. The Angle of repose obtained was 14.62° at lowest for A_1 and 34.49° at highest for B_1. All batches contain uniform amount of valsartan and cellactose. In addition, batches A1 –A3 contain MN and SSG, (Table 1 and 2), they showed better flow. Batches B1 - B3 contain PEG 4000 and CCS, and showed poor flow this is due to the waxy nature of the PEG. Batches C1 – C3 containing MN, PEG and SSG showed improved flow properties over B batches. This improved flow was possible due to inclusion of MN in the formula. Batches of D contained MN, PEG and CCS showed better flow characteristics than the Bs and Cs batches. All batches expressed good compressibility.

The bulk density and tapped density range were between 0.261g/mL to 0.432g/mL and 0.337g/mL to 0.619g/mL respectively. These values indicate good packing for all batches A – D powder mixes.

Evaluation of Tablet Properties

The RDTs/FDTs were prepared and have a white colour appearance with a circular, flat surfaced shape. All tablets passed the weight variation test and were found within the USP acceptable limit of ±10%. The results for tablet hardness were of the range 11.30N to 143.80N (Table 4). Tablet formulations must show good mechanical strength with sufficient hardness in order to handle shipping and transportation. Friability values were within the range of 0.00% to 1.59% (Table 4). The results obtained are all within the USP acceptable range of less than 1% weight loss, indicating adequate tablets mechanical integrity and strength. According to the United States Pharmacopoeia, all of the tablet's formulations should disintegrate completely within 30 seconds which indicates rapid disintegration. The disintegration time recorded ranged from 6.44 seconds to 36.74 seconds for tablet batches A – D. While the in-vitro disintegration time recorded ranged from 6.80 seconds (A_3) to 13.35 seconds (A1), batches B_1 to B_3 disintegrated in 10.88 and 19.23 seconds respectively. The B batches containing CCS and PEG 4000 had a longer disintegration time than batches A containing SSG and Mannitol. The fact is that, CCS mode of action is by rapid swelling, pronounced hydration capacity and wicking upon contact with water. This mechanism leads to gelling of CCS that makes its action a little bit longer than that of SSG which action is purely by rapid swelling. The C batches contained SSG, MN, and PEG disintegrated between 6.44 and 9.76 seconds. This DT range is far shorter and better than 11.5 -36.7 seconds obtained for D batches containing CCS, MN and PEG. From the above results, the combination of SSG, MN and PEG 4000 (C1 to C3) showed better disintegration results than the batches A, B, and D (Table 4).

Inclusion of PEG 4000 lowers tablet hardness as noticed in B1 – B3. Incorporation of MN along with PEG in C1 – C3 and D1 – D3 elevated tablet hardness to minimum acceptable values: C1 = 47.53 N, D1= 43.07 N. The FDTs produced with combination of MN and PEG (50:50) was softer than FDTs produced with MN and PEG respectively. They fulfilled the USP standard of DT < 30 seconds. From table 4, batches A1 – A3 yielded extreme hard tablets while C1 and D1 gave softer (average hard) tablets.

The presence of SSG/CCS, MN, PEG 4000, and aerosil, played positive role in lowering disintegration time by either facilitating tablet breakdown, and increasing wetting time. Summation of their contributing factor leads to the tremendous lower DT (Table 4).

In summary, based on tablet hardness and disintegration time in seconds, batches A1 (143.8 N, 13.35 s); A2 (107.8 N, 7.21 s); A3 (91.54 N, 6.80 s); C1 (47 .53 N, 6.44 s) and D1 (43.07 N, 11.50 s) could be recommended for pilot studies

Drug-Excipients Compatibility Studies

For the compatibility of the drug with various polymers, IR spectra of drug and formulation components were carried out. The IR spectra of the drug and all excipients were shown in figures 2 - 5. The characteristics absorption peaks of Valsartan were obtained at 3391.48, 2634.50, 1597.18, and 676.19. The peaks obtained in the spectra of each excipient correlate the peaks of drug spectrum.

CONCLUSION

It can be seen that batches A1 – A3 yielded hard tablets while C1 and D1 produced softer (average hard) tablets. The two categories fulfilled the USP standard of DT < 30 seconds. From the fact that C1 and D1 contained both MN and PEG 4000 in different proportion, PEG was responsible for lower tablet hardness, while both excipients played positive role in lowering disintegration time, C1 with average hardness and lower DT (47 .53 N, 6.44 s)will be adequate for FDT design for mouth disintegration on one hand, and A2 or A3 with hardness and DT :107.8 N, 7.21 s and 91.54 N, 6.80 s respectively could be best applied for the FDT intended to withstand rough handling transportation for commerce.

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