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FORMULATION AND EVALUATION OF IMMEDIATE RELEASE TABLETS OF VALSARTAN BY USING MILLET STARCH AS DISINTEGRANT

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ABSTRACT

The immediate release tablet of antihypertensive drug Valsartan were prepared and evaluated to increase solubility and bioavailability of low soluble drug. Immediate release tablet of valsartan prepared by using polymer such as Millet starch (9%), Millet starch (12%), Sodium starch glycolate, L-HPC, Pregelatinized starch by using direct compression technique. The immediate release tablets were evaluated for physicochemical parameter like thickness, hardness, weight variation, friability and *in-vitro* drug release. The *in-vitro* drug release studies were found that optimized formulation F4 show immediate drug release within 10 minutes up to 98.64%. From the above study it was concluded that all formulations F1-F9 in that F4 formulation was optimized for further *in vivo* studies.

Keywords: Valsartan, immediate release tablet, Millet starch, Sodium starch glycolate.

INTRODUCTION

Millets are cereals from the Poaceae grass family and are considered one of the oldest cultivated crops. Generally, pearl millet (*Pennisetum glaucum*) and finger millet (*Eleusine coracana*) are known as the two major millets used for food and feed. Pearl millet is believed to have originated from sub-Saharan Africa, and finger millet from the sub-humid uplands of East Africa [1]. The two account for most of the world's millet production and trade [2]. The majority of the recent research and agricultural programmes, which are routed towards the development of millets, have been dedicated to pearl and finger millets. Dube et al. [3] believe that the urge to route for millet and sorghum instead of maize and other major crops in recent years is derived from the fact that these grains are ecologically well-matched with semi-arid areas because of their ability to tolerate drought. They are considered tough crops in terms of growth requirements as they withstand harsh climatic factors such as unpredictable climate and nutrient-depleted soils [4].

Globally, pearl millet is an important grain and is considered the sixth highest producing crop, after maize, wheat, rice, barley, and sorghum [5]. It is also considered one of the crops that can provide good nutrition and income to small-scale farmers [6] and thus, contributes to livelihoods and the availability of food. Despite its value and contribution, pearl millet does not receive the attention it deserves as a crop that has an important role to play in food security. Perhaps the disregard can be attributed to it being termed a crop for poor farmers in marginal agricultural areas affected by socio-ecological conditions [1]. According to several researchers, millets can be an important source of essential nutrients such as amino acids, and mineral and trace elements [7]. Obviously, wide variations should be evident in the nutritional composition of pearl and finger millets [2]. Shweta, [7] reported that pearl millet contains higher energy compared to cereal grains such as rice and wheat, and is considered a significant source of thiamine, niacin, and riboflavin as stated by [6]. Moreover, the content of minerals such as calcium, iron and phosphorus in pearl millet is like those found in other cereals [7].

Starches of millets

Starch is made up of 2 primary molecular components: amylopectin and amylose. Depending on the type of fractionation, an intermediary structural component may be provided. Amylose is linear having several branches, α-(1-6) linkage, dispersed throughout the linear backbone, α-(1-4) linkage, while amylopectin has a significantly larger number of branches. The molecular structure of starch components is linked to their production, physical granular structures, functioning and possible application. [8]

Millet starch composition

Millets, like other grains, contains 51 to 79 per cent starch. The starch content of pearl and finger millets ranges from 71 to 81 per cent and 51 to 69 per cent, respectively. Millet starches typically comprise between 70 to 80 per cent amylopectin and 20 to 30 per cent amylose. The inclusion of additional elements as impurities in starch granules has a substantial impact on their functioning. Millet starches, for example, are mostly composed of polar phospholipids (89 per cent), with rest composed of nonpolar lipids, primarily triglycerides. Because of their cohesive nature and hydrophobic interactions, these lipids form complex with the amylose component of starch and may impair the flow ability and swelling capacity of starch. Protein has both hydrophobic and hydrophilic bonds, which influence its oil and water binding capabilities. The fibres are known to decrease uptake of oil, which may impair oil binding ability. Polyphenols' influence on millet starch functioning has yet to be documented. However, the effect of adding polyphenols from external sources, such as vanillic acid, gallic acid andquercetin to starch and their influence on many physicochemical aspects have been extensively studied. For example, with the addition of pomegranate peel extract, themaximum viscosity of wheat starch increases. In addition, black tea extract was shown to be more efficient than green tea extract in decreasing the cold paste viscosity of wheat, rice, maize and potato starch, [8]

Oral route is most common route of administration of drug because of its systemic effect, patient compliance, less expensive to manufacture. Tablet provides high precision dosing. In most of the cases immediate on set of action is required as compare to conventional therapy. To achieve the rapid onset of action and eliminate the drawbacks of conventional therapy immediate release dosage form is now a day's popular oral dosage form. Basic approach used in development is the use of superdisintegrants which provide rapid disintegration of tablet after administration [9]. This research work is concerned with the formulation and evaluation of immediate release tablet of Valsartan in order to provide immediate relief from hypertension.

MATERIALS AND METHODS

Preparation of Calibration Curve

10mg of Valsartan was weighed accurately in a digital weighing balance and transferred into a dry 10ml volumetric flask. 10ml of phosphate buffer P^H 6.8 was added to dissolve the drug. The solution was taken into 100ml volumetric flask and made up to the mark with pH 6.8 phosphate buffer. From this (100µg /ml) solution, solutions of 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1 ml were transferred into 10ml volumetric flasks and their volume was made up to 10ml. The concentrations of these are 1, 2, 3, 4, 5, 6, 7, 8, 9, 10µg /ml respectively. The absorbance of each of these solutions was measured in a Shimadzu double bean UV-spectrophotometer, in photometric mode, using phosphate buffer P^H 6.8 as a reference blank. The procedure was carried out at the absorbance maxima obtained from the spectrum.

The λ max was found to be at 250nm in SHIMADZU UV-1800 spectrophotometer.

Solubility Studies

The solubility study was used to find out the suitable oil, surfactant and co-surfactant that possess good solubilizing capacity for valsartan. The solubility of Valsartan in various oils (Capmul MCM, Capryol 90, Castor oil, Captex 355, Vitamin E TPGS) (shown in table 14), surfactants (Kolliphor HS 15, Kolliphor RH 40, Gelucire 44/14, labrasol, Lauroglycol), and co-surfactants (Peg 400, Peg 600, Propylene glycol) (shown in table 16) were determined by mixing excess amount of Valsartan (approximately 600mg) with 2 ml of each of the individual components. The drug was added to a 5-ml capacity stoppered glass vial and mixed for 10min with each component using a vortex mixer. The mixture vials were then kept at 37±1^{0}C in an isothermal shaker for 72h until homogeneity. The homogenate samples were then centrifuged at 18,000rpm for 30min at 4^{0}C. The supernatant was removed by pipetting and the drug concentration was determined by UV at 250nm. Concentration of dissolved drug was determined spectrophotometrically.

Formulation Development

API and Formulation Characterization:

The following tests were done for API and all formulations. Bulk density, Tapped density, Compressibility index, Hausner ratio and Particle size distribution. [10]

Formulation Development by Direct Compression:

Step 1: Weighing and Blending- the active ingredients, filler, disintegration agents, are weighed and mixed

Step 2: Drugs, mannitol and MCC were mixed thoroughly, super disintegrants were incorporated in the powder mix along with magnesium stearate, weighed individually and punched into tablets using Cadmach single punch tabletting machine.

Table 1: Formulation details of F1-F9

Ingredients (gm)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Valsartan	40	40	40	40	40	40	40	40	40
Microcrystalline cellulose	49	46	49	46	49	46	43	46	42
Mannitol	51	51	51	51	51	48	50	51	50
Millet starch (9%)	2	5	--	--	--	--	--	--	--
Millet starch (12%)	--	--	2	5	--	--	--	--	--
Sodium starch glycolate	--	--	--	--	2	8	--	--	--

L-HPC	--	--	--	--	--	--	9	--	--
Pregelatinized starch	--	--	--	--	--	--	--	5	10
Aerosil	2	2	2	2	2	2	2	2	2
Aspartame	4	4	4	4	4	4	4	4	4
Magnesium stearate	2	2	2	2	2	2	2	2	2
Strawberry flavour	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Average weight (mg)	150	150	150	150	150	150	150	150	150

Evaluation of tablets

The formulations were evaluated for hardness, weight variation, thickness, friability, disintegration time, disintegration time in oral cavity, *in vitro* dispersion time, wetting time and water absorption ratio, content uniformity, and *in vitro* dissolution study [11].

In vitro Dissolution studies

The *in vitro* dissolution study was carried out in USP dissolution test apparatus Type 2 (paddle). Samples were withdrawn at 1, 2, 4, 6, 8, and 10 minutes time intervals by replacing with same dissolution medium and the dissolution of the drug was expressed as percentage drug dissolved by using following formula.

Drug Excipients Compatibility Studies

The drug Excipients compatibility studies were carried out by Fourier Transmission Infrared Spectroscopy (FTIR) method and Differential Scanning Colorimetry (DSC) method.

Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry (DSC) studies were carried out using DSC 60, having TA60 software, Shimadzu, Japan. The DSC thermograms were recorded for pure drug, HPMC E15, Maltodextrin, Drug and HPMC mixture and optimized formulation. Accurately weighed samples were placed on aluminium plate, sealed with aluminium lids and heated at a constant rate of 5ºC /min, over a temperature range of 0 to 250ºC.

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectra for pure drug, physical mixture and optimized formulations were recorded using a Fourier transform Infrared spectrophotometer. The analysis was carried out in Shimadzu-IR Affinity 1 Spectrophotometer. The IR spectrum of the samples was prepared using KBr (spectroscopic grade) disks by means of hydraulic pellet press at pressure of seven to ten tons.

Stability studies

The stability study of the formulated fast-dissolving films was carried out under different conditions according to ICH guidelines. The film was packed in the aluminium foil and stored in a stability chamber for stability studies. Accelerated Stability studies were carried out at 40 ^{0}C / 75 % RH for the best formulations for 2 months. The patches were characterized for the drug content and other parameters during the stability study period.

RESULTS AND DISCUSSION

Fast Dissolving Tablet is a new drug delivery system with several advantages and clinical benefits such as ease of administration for patients who are mentally ill, disabled and uncooperative, rapid disintegration and dissolution with increased bioavailability, no necessity of water or chewing and ability to provide advantages of liquid medication in the form of solid preparation. In the present study, attempt was made to prepare such a tablet of various drugs by using addition of super disintegrants technique. The drug was selected for this study from the categories: Anti hypertensive Valsartan on the basis of low drug dose and necessity of immediate action.

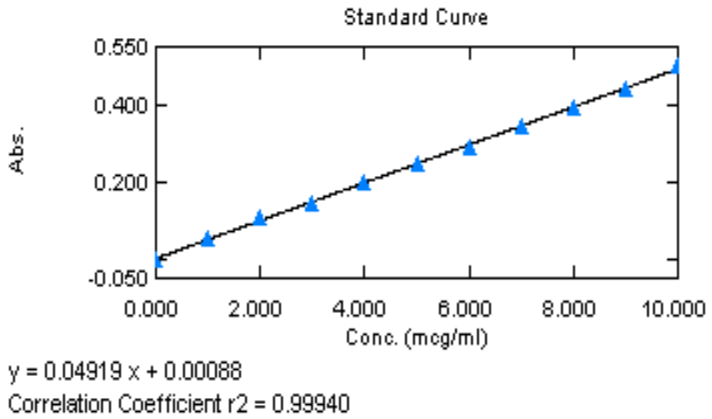

Fig 1: Calibration Curve of Valsartan in P^H 6.8 Phosphate buffer

The linearity (calibration) curves were plotted for Valsartan using different concentrations ranges from 1-120µg/ml. The absorbance graphs are shown in Fig 1. Perfect linearity was observed in all cases shown by the R^2 (correlation coefficient) value indicating the absorbance varies

proportionally with concentrations in the selected range obeying Beer-Lambert's law.

Solubility studies

The Valsartan drug solubility of pure drug was found to be 34.91 mg/ml. the solubility of the Valsartan drug was tested in different oils phases (Capmul MCM, Capryol -90, castor oil, Vitamin E TPGS, Captex 355) and maximum solubility was determined in capmul MCM C8 55.62 mg/ml (shown in Table 2), and was selected as oily phase for SEDDS formulation.

Table 2: Solubility of Valsartan in Different Oils

S.NO	OILS	SOLUBILITY
1	CAPMUL MCM	55.62
2	CAPRYOL-90	52.89
3	CASTOR OIL	48.67
4	VITAMIN E TPGS	42.33
5	CAPTEX 355	42.09

API Characterization

The physical characteristics of selected API such as bulk density, tapped density, Hausner ratio, compressibility index, and partial size distribution are given in Table 3. The bulk density of all the drugs were found in the range of 0.48 - 0.52 g/ml and tapped density was 0.54 - 0.60 g/ml (Table 3). The Hausner's ratio was found in the range of 1.14 - 1.15 (Table No. 10), indicating the drugs under study have poor flow properties because Hausner's ratio less than 1.25 indicates better flow property. The compressibility index was found in the range of 12.6 % -13.6 % (Table 3). The values below 15% indicates a powder having good flow characteristics, whereas above 25% indicates poor flow ability.

Table 3: Physical Characteristics of API

S. No.	Properties	Valsartan
1	Bulk density (g/ml)	0.520
2	Tapped density (g/ml)	0.602
3	Compressibility index	13.6
4	Hausner's ratio	1.15
5	Angle of repose	28.7^{o}

Table 4: Particle size determination of API

S. No.	Sieve size (µ)	Sieve No.	Cumulative % oversize Valsartan
1	1.18 mm	14	0.22
2	710	22	1.37
3	500	30	2.09
4	355	44	1.28
5	250	60	2.73
6	180	85	25.41
9	Collector		116.9

Table 5: Physical characteristics of product of Formulation No. F1 – F9

Parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9
Bulk density (g/ml)	0.39± 0.02	0.41± 0.03	0.38± 0.04	0.49± 0.02	0.51± 0.01	0.49± 0.03	0.39± 0.01	0.49± 0.04	0.53± 0.01
Tapped density (g/ml)	0.45± 0.01	0.47± 0.02	0.45± 0.02	0.58± 0.03	0.60± 0.02	0.57± 0.02	0.48± 0.04	0.58± 0.01	0.59± 0.05
Compressibility Index (%)	13.3± 1.32	15.7± 1.22	15.5± 1.43	14.43± 1.43	15.04± 1.45	13.76±1. 65	19.11± 1.54	14.21± 1.54	13.98± 1.65
Hausner's ratio	1.15± 0.54	1.18± 0.65	1.18± 0.76	1.17± 0.87	1.17± 0.65	1.16± 0.85	1.17± 0.98	1.17± 0.65	1.18± 0.54
Angle of repose	26.7± 1.43	29.4± 1.43	28.7± 1.43	27.3± 1.54	28.5± 1.32	27.9± 1.54	31.2± 1.32	26.5± 1.65	28.4± 1.54

Table 6: Particle size distribution of Product Formulation No. F1 – F9

Sieve Size	Sieve No	F1	F2	F3	F4	F5	F6	F7	F8	F9
1.18 mm	14	0.23	0.46	1.26	0.95	0.36	0.24	0.54	0.98	0.42
710 µm	22	1.65	1.96	3.40	1.58	2.69	2.07	2.53	3.11	2.98
500 µm	30	2.23	1.36	4.79	3.11	3.80	3.65	1.42	2.56	3.13
355 µm	44	1.54	2.65	8.32	4.38	6.23	5.70	3.46	3.21	5.22
250 µm	60	3.15	2.78	11.14	5.82	7.36	8.49	6.11	5.72	7.52
180 µm	85	20.65	31.53	23.58	12.23	10.36	13.69	23.42	25.43	14.53
Collector / pan		108.17	113.42	93.28	113.89	115.74	109.21	113.42	109.05	116.2

Evaluation of Tablets

The tablet parameters observed are given in Table No. 14. The tablets were compressed at the specified weight (Table 7). The weights of tablets were within ± 3% which falls within the acceptable weight variation range of ± 7.5% as per USP. Hence all formulations passed the weight variation test. Hardness of all formulations was in the range of 3.1 – 3.6 Kg/cm^2 (Table 7). The hardness of all formulations was kept constant within the above mentioned range by adjusting the compression load in order to compare the disintegration time between the formulations prepared using different excipients. Friability values of none of the formulations exceeded 0.68% (Table 7). The results of friability indicate that the tablets were mechanically stable and could handle the rigors of transportation and handling. Thickness of all formulations was between 3.42 – 3.76 mm indicating fairly acceptable tabletting.

Disintegration time is very important parameter of FDT, the internal structure of tablet that is pore size distribution, water penetration into tablet and swelling of disintegrant substance are suggested to be the mechanism of disintegration. The disintegration time of Formulation No.F1-F6 was satisfactory because it disintegrate within 1 min (Table 7). An ideal FDT should disintegrate within a minute. The disintegration time of tablets of Formulation No.F1 – F9 were found to be good because none of tablet disintegrate greater than 29 sec. But the Formulation No.F2 gives best disintegrating time i.e. 16.24± 2.13Sec (Table 7). Percentage drug content (Assay) of Formulation No. F1 – F9 were found to be 93% w/w (Table 7) which is within the acceptable limits as per individual monograph of selected drugs. *In vitro* dispersion time was measured by the time taken to undergo uniform dispersion as per the British Pharmacopoeia. The dispersion time of Formulations No.F1 – F9 were given in Table 7. The rapid dispersion was observed in the Formulation No.F2 indicating direct information regarding the disintegrating nature of Millet starch effect of mannitol and Microcrystalline cellulose combination and the aqueous solvent. Wetting time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tongue. Some individuals have the tendency to chew or crush the tablet after keeping in the oral cavity. This is the reason why the disintegration time in oral cavity and the wetting values do not coincide. Even though the disintegration time in oral cavity and the wetting time values do not generally coincide, wetting time is still considered very valuable parameters to assess the disintegration time of the tablet. The wetting time of Formulation No.F1 – F9 were found in the range of 37 - 87 sec and 34-79 sec (Table 7). This may be due to ability of swelling and also water absorption capacity. Water absorption ratio is closely related to inner structure of tablets. The water absorption ratio values of Formulation No. F1 – F9 were to found 12.4-16.1%.

Table 7: Evaluation of Formulation No.F1-F9

Evaluation	F1	F2	F3	F4	F5	F6	F7	F8	F9
Weight variation (mg)	150±2.12	150±1.43	151±1.56	150±2.54	150±1.23	149±2.57	150±2.67	151±1.66	150±2.33
Thickness (mm)	3.53± 0.08	3.49± 0.04	3.51± 0.04	3.53± 0.02	3.76± 0.03	3.63± 0.02	3.57± 0.06	3.62± 0.05	3.57± 0.05
Friability (%)	0.60	0.48	0.64	0.57	0.62	0.51	0.63	0.56	0.51
Hardness (Kg/cm^2)	3.3± 0.2	3.6± 0.2	3.1± 0.4	3.4± 0.2	3.6± 0.4	3.3± 0.3	3.5± 0.4	3.4± 0.3	3.6± 0.3
Disintegration time (sec)	26± 1.15	17± 2.1	32± 1.16	23± 2.15	41± 2.27	30± 1.19	50± 2.41	57± 3.16	49± 2.18
Dispersion time(sec)	33± 2.18	22± 1.15	38± 2.47	28± 1.21	49± 3.25	38± 1.90	61± 2.10	68± 4.15	59± 2.31±
Content uniformity (%)	96.1± 0.8	99.1± 1.3	93.2± 1.6	97.4± 2.1	94.3± 2.4	96.1± 1.31	95.1± 1.31	94.3± 1.1	95.5± 1.9
Water absorption ratio	13.1± 1.7	12.4± 1.8	13.1± 0.8	14.3± 1.7	13.9± 1.7	15.1± 0.6	14.8± 1.3	16.1± 1.7	15.2± 1.1
Assay (%w/w)	98.1	99.3	97.3	98.1	96.9	97.1	93.2	94.3	95.2
Wetting time	42.1± 1.61	37.3± 1.37	47.1± 1.01	39.1± 1.62	59.1± 1.89	52.7± 1.09	74.6± 3.10	81.5± 3.25	68.3± 2.15

In vitro Dissolution study

The dissolution study on Formulation No.F1 – F9 were carried out using USP dissolution apparatus II (paddle). The Formulation No .F1, F2, F3, F4, F5 , F6, F7, F8, F9 shows 74.32±2.43, 98.64±2.54, 67.56±3.65, 94.59±4.76, 58.10±3.65, 85.13±2.7, 70.27±2.87, 66.21±4.32 and 79.72±2.76 in 10 min respectively. The rapid *in vitro* dissolution was found in the Formulations containing Millet starch 9% (F2) and Millet starch 12% (F4). High dissolution resulted due to faster breakdown and rapid dispersion of tablet; it may be due to rapid diffusion or the porous nature of the tablet. The dissolution graphs are shown in Fig 2. The percent drug release of Formulation No. F4 correlates with drug content. By this study, an important conclusion can be drawn that Addition of super disintegration technique has improved the dissolution profile of the water soluble drugs besides expediting the disintegration time.

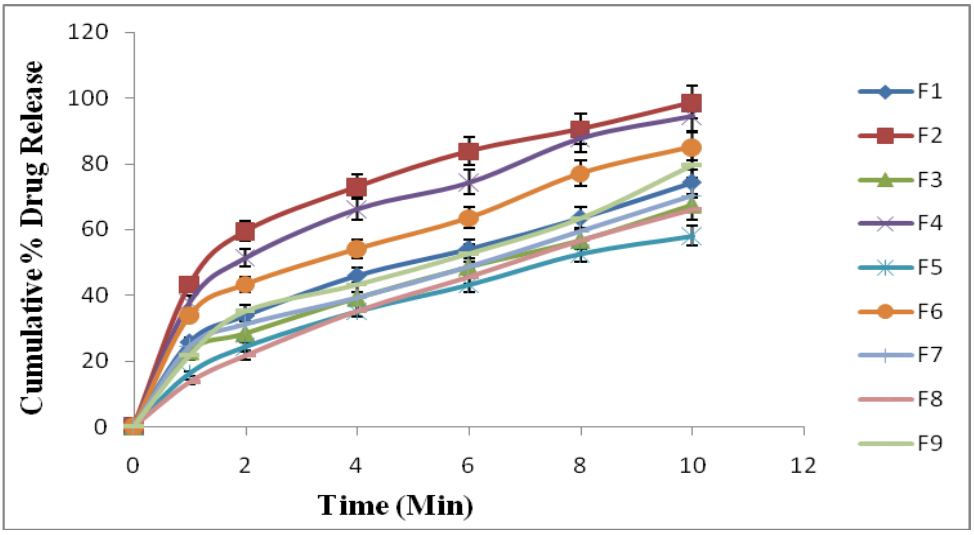

Fig 2: *in- vitro* Cumulative % Drug Release F1 – F9

Drug Excipient compatibility studies by FTIR

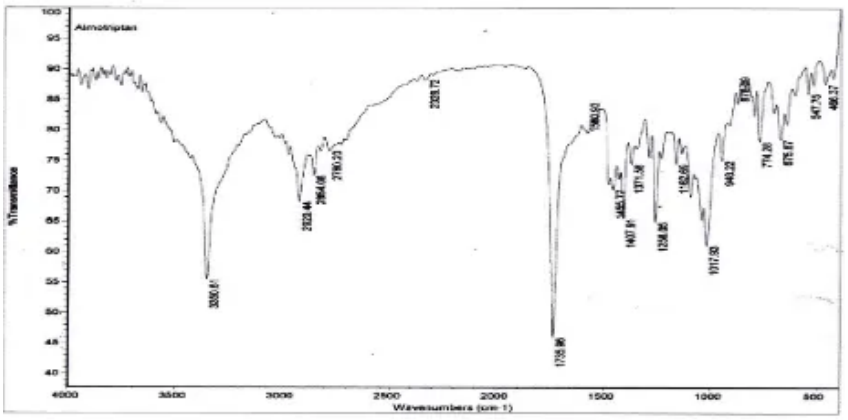

Fig 3: FTIR Spectra of Valsartan Pure Drug

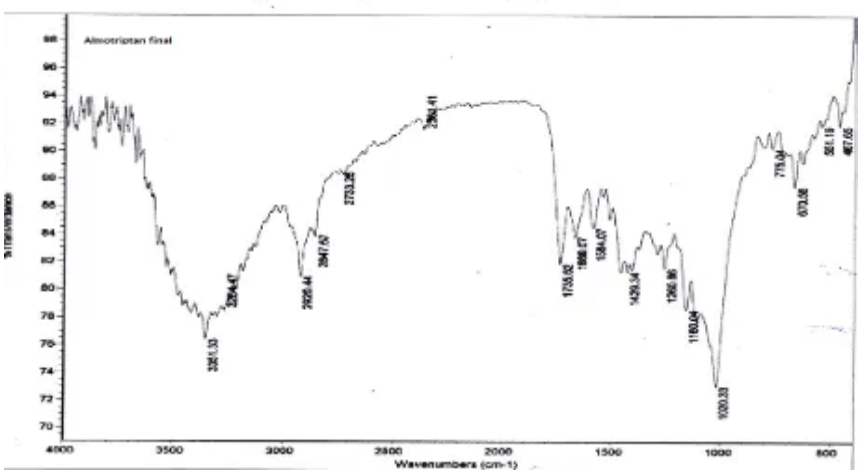

Fig 4: FTIR Spectra of Valsartan + Polymers

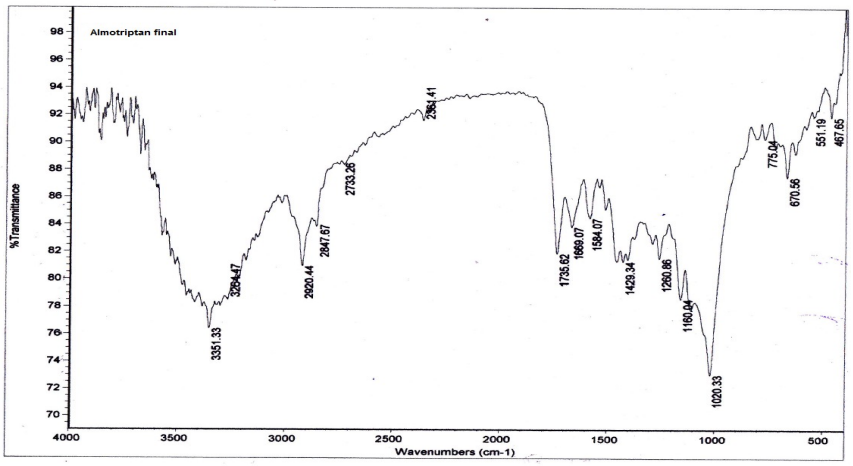

Fig 5: FTIR Spectra of Optimized Formulation (F4)

Interpretation of FTIR Data

The FTIR spectra of pure Valsartan displayed bands at 3450 cm^{-1} due to N-H stretch, at 1736 cm^{-1} due to C=O stretching, at 1651 cm^{-1} due to heterocyclic C=C stretching. The spectra also showed bands at 1370 cm^{-1} due to C-H bending. The FTIR spectrum of film containing Valsartan exhibited characteristic bands consistent with the molecular structure of Valsartan such as bands at 3456 cm^{-1} due to N-H stretch, at 1736 cm^{-1} due to C=O stretching, at 1650 cm^{-1} due to heterocyclic C=C stretching, at 1370 cm^{-1} due to C-H bending. Thus, the presence of characteristic absorption bands of Valsartan and the film containing Valsartan suggest that there is no interaction takes place between the drug and exc0ipients used in the formulation. Spectras are showed in Fig 3, 4, 5.

Drug Excipient compatibility studies by DSC

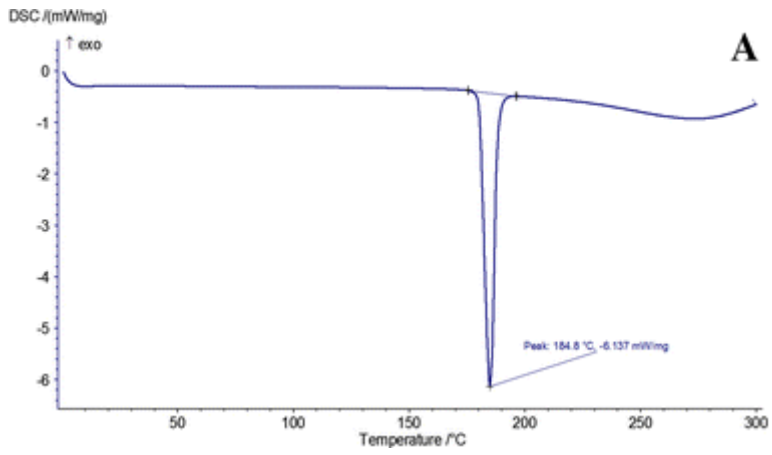

Fig 6: DSC thermogram of Valsartan Pure Drug

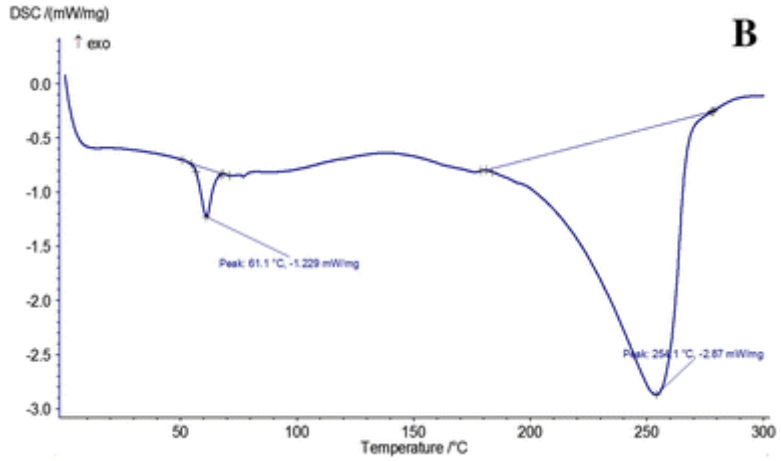

Fig 7: DSC thermogram of Valsartan Pure Drug ± Polymers

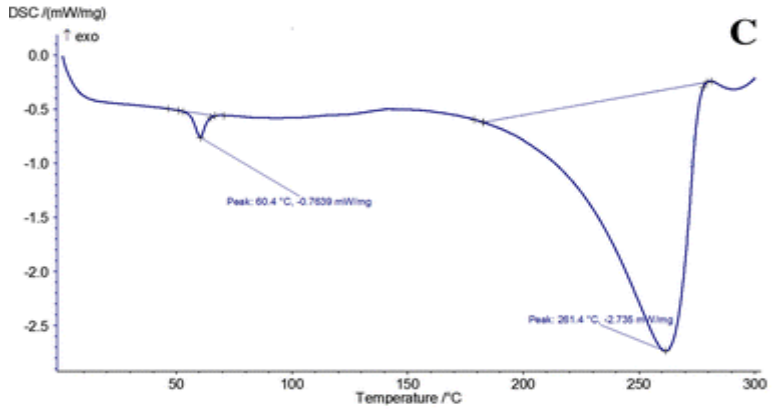

Fig 8: DSC thermogram of Optimized Formulation (F4)

DSC thermograms revealed that there is no considerable change observed in melting endotherm of pure drug (250) (fig 6) and drug in optimized formulation (276.36) (Fig 8). It indicates that there is no interaction takes place between drug and other excipients used in the formulation.

Stability studies for (F4) optimized formulation

F4 formulation was selected for stability studies on the basis of high cumulative % drug release and also results of *in vitro* disintegration time. Stability studies were conducted under different conditions according to ICH guidelines. From these results it was concluded that, formulations F4 is stable and retained their original properties with minor differences. The results of disintegration time, drug content and transparency are shown in the Table 8, which indicates no alteration after storage.

Table 8: Accelerated stability testing data of optimized formulation (F4) kept for Stability at 40 ºC /75 %RH

Retest Time For F4	Disintegration Time (sec)	Percent Drug Content/ Assay (%)	Transparency
1 Week	10.11±2.21	99.90	Transparent
2 Weeks	11.65±2.22	99.04	Transparent
1 Month	10.53±2.86	98.92	Transparent
2 Months	10.76±2.42	98.75	Transparent

CONCLUSION

The present study was aimed at developing immediate release tablet of Valsartan prepared by using polymer such as Millet starch (9%), Millet starch (12%), Sodium starch glycolate, L-HPC, Pregelatinized starch by using direct compression technique. The immediate release tablets were evaluated for physicochemical parameter like thickness, hardness, weight variation, friability and *in-vitro* drug release. The *in-vitro* drug release studies were found that optimized formulation F4 show immediate drug release within 10 minutes up to 98.64%.

REFERENCES

1. Dube T, Mlilo C, Moyo P, Ncube C, Phiri K. Will adaptation carry the future? Questioning the long-term capacity of smallholder farmers' adaptation strategies against climate change in Gwanda District. Zimbabwe J Hum Ecol. 2018;61(13):20-30.
2. Sharma KK, Ortiz R. Program for the application of genetic transformation for crop improvement in the semi-arid tropics. In Vitro Cell.Dev.Biol.-Plant. 2000;36(2):83-92. doi: 10.1007/s11627-000-0019-1.
3. Patel K, Gartaula H, Johnson D, Karthikeyan M. The interplay between household food security and wellbeing among small-scale farmers in the context of rapid agrarian change in India. Agric & Food Secur. 2015;4(1). doi: 10.1186/s40066-015-0036-2.
4. Anitha S, Govindaraj M, Kane-Potaka J. Balanced amino acid and higher micronutrients in millets complements legumes for improved human dietary nutrition. Cereal Chem. 2020;97(1):74-84. doi: 10.1002/cche.10227.
5. Shweta M. Pearl millet nutritional value and medicinal uses. IJARIIE-ISSN (O). 2015; 1(3);4396:2395.
6. Taylor JRN. In: Wrigley C, Corke H, Walker CE, editors. Millet: in encyclopaedia in grain science. Vol. 2. London: Elsevier; 2004. p. 253-61.
7. Adeola O, Orban JI. Chemical composition and nutrient digestibility of pearl millet (Pennisetum glaucum) fed to growing pigs. J Cereal Sci. 1995;22(2):177-84. doi: 10.1016/0733-5210(95)90048-9.
8. Srichuwong S, Jane JL. Physicochemical properties of starch affected by molecular composition and structures: a review. Food Sci Biotechnol. 2007;16:663-74.
9. Mahajan P, Bera MB, Panesar PS, Chauhan A. Millet starch: a review. Int J Biol Macromol. 2021;180(13):61-79. doi: 10.1016/j.ijbiomac.2021.03.063, PMID 33727186.
10. Jaimini M, Rawat S. A review on immediate release drug delivery system. Res J Pharm Chem Biol Sci. 2013;4(2):1721-30.
11. Masaki K, Ban K. Intra buccally disintegrating preparation and production thereof, US Patent No. 5466464; Nov 14, 1995. Heinemann, H, and Rothe, W; "Preparation of porous tablets," US Patent No. 3885026, May 20, 1975.
12. Makino T, Yamada M, Kikuta JI. Fast-dissolving tablets and its production, US Patent No. 5720974; Feb 24, 1998.