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FORMULATION AND EVALUATION OF VALSARTAN CONTAINING SURFACE SOLID DISPERSIONS FOR THE DEVELOPMENT OF ORODISPERSIBLE TABLET

Pharma

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ABSTRACT

In this postulations we think about Surface Solid Dispersion and Oro dispersible tablet for upgrade of disintegration rate of valsartan. The medications having low solvency, the disintegration of these medications is rate constraining advance in their bioavailability in oral measurements frames. To defeat this number of innovations are accessible. Among them surface solid dispersion and oro dispersible tablets are two promising systems. Surface solid dispersion is a method for scattering at least one fixing on a water solvent transporter of to a great degree high surface territory to accomplish expanded bioavailability and disintegration rates of insoluble medications, and oro dispersible tablets are one of the novel oral medication conveyance framework that break down or scatter rapidly in almost no time after situation in month without water.

KEYWORDS

high blood pressure, hypertension, Polyplasdone XL.

INTRODUCTION

The purpose of this research is to get ready orodispersible tablets (ODTs) containing valsartan (VAL) by direct compression method. ODTs are comfortable for that ill person who rejected to take a tablet, such as geriatric, pediatric, mentally ill, disabled and uncooperative. ODT breaks rapidly to produce an early onset of action, improved bioavailability by pre-gastric absorption, decreasing the adverse effect, no need of water to swallow so it is highly convenient [1]. The US-FDA center for drug assessment and research defined in Orange book About ODT "A solid dosage form whose contain medicinal substances when take upon the tongue which disintegrates within sec [2]. Tablet is defined as solid unit pharmaceutical dosage form who keeps medicament with or without suitable excipients & made either by compression or molding[3, 4]. Solid dispersion is defined as a gathering of solid products which is composed of a hydrophobic drug dispersed in at least one hydrophilic carrier, resulting increase surface area and, increase drug solubility and dissolution rate. Solid dispersion classification based on the method of preparation binary solid dispersion, ternary solid dispersion, and surface solid dispersion[5]. Drugs is safe and tolerable, excellent solubility, half life 6 to 7h, log P=1-2, stability throughout the gastrointestinal tract and high potency. VAL is an intensely better antihypertensive and antagonizing.VAL is available in the dose 40, 80, 160, and 320 mg, all doses have been found to be safe, tolerable and to prevent the blood pressure. Drug is sold world wild approximately $6.053 billion.VAL ODTs marketed under the brand name Diovan [6]. The dispersible polymer is used in Diovan in crospovidone, HPMC, MC. SSG is rapidly absorbing water, exist as a very fine white odourless, hygroscopic powder used as a disintegrant in Tablets it also used in food industry, density 1.56 g/cm^3, melting point does not melt, solubility almost insoluble in methylene chloride, It gives a opaque suspension with water, high permeable. (SSG application guideline)[7].

MATERIALS AND METHODS

Drug

Drug (valsartan) has been obtained as a gift sample from Unimark Pharmaceutical Limited, Ahemdabad & other excipients has been procured/purchased.

ANALYTICAL METHODOLOGY

Determination of λ max of Valsartan

UV Spectrophotometric studies

Precisely measured 10mg of valsartan was dissolve in 100ml of particular media to give a grouping of 100µg/ml. From this 3ml arrangement was pipette out into 10ml volumetric Flask. The volume was made up to 10ml with individual media (30µg/ml).

This arrangement was checked between 200-400nm. using phosphate buffer pH6.8 as blank. 250nm λ_{max} of valsartan was recorded.

Calibration

Preparation Of Standard Stock Solution

Take 10ml of methanol and dissolve Valsartan (100mg). volume prepared 100ml in volumetric flask with the help of phosphate buffer pH 6.8. 10ml was taken from this stock solution preparation and it diluted in 100ml volumetric flask which gives100µg/ml.

Preparation Of Calibration And Validation Samples

Calibration sample from this stock solution 5µg/ml, 10µg/ml, 15µg/ml, 20µg/ml, and 25µg/ml takes in volumetric flask.

Preparation Of Calibration Curve

Absorbance taken at 250nm with the help of Shimadzu UV- 1700 UV-Vis double beam spectrophotometer by phosphate buffer pH6.8. Then absorbance values of the calibration sample plot against their respective concentration find the calibration curve.

Validation Of Analytical Method

Linearity

Absorbance value of the calibration sample plot against their respective concentration to get calibration curve and linear regression was performed. Linearity was accessed by correlation coefficient determination (r^2).

Accuracy

Mean concentration value for each data of validation samples was calculated and %error (a measure of accuracy) for each concentration calculated with the formula, %error = (calculated mean concentration-actual concentration)/actual concentration*100.

Precision

Percentage relative standard deviation value was calculated (as a measure of precision) for each set of concentration by given formula, % RSD = standard deviation/calculated mean concentration*100.

Drug Excipients Interaction Study

The interaction studies of various excipients with valsartan reported in the previous project (Devendra Singh 2015).

Preparation Of Blend

All Ingredient Mention In Following Table. 1.1

Table 1.1 Ingredients Used In Tablets Formulation

	Amount		
Compounds	**F1**	**F2**	**F3**
Valsartan	80	80	80
Mannitol	35	30	20
Polyplasdone XL	5	10	20
Sodium saccharine	4	4	4

Magnesium stearate	22	22	22
Flavor	2	2	2
Sodiumstarchglycolate	2	2	2

Evaluation Of Blend

Angle Of Repose

A powder funnel was adjusted with tripod stand and clamp in such a manner that lower part was 8cm above the surface. 3 gm of powder taken and opening of funnel was (4mm) blocked with thumb powder put into the funnel. Subsequently, the thumb removed and powder permit to flow opening and fall on surface. The height and diameter of the heap takes. The angle of repose was determine according to the formula, Tan θ = h/r where, h = height of pile, θ = angle of repose, r = radius of the base heap.

Drug's Bulk Density:

3gm compound pour into 10ml graduate measuring cylinder and its volume takes as it was. Bulk density measure according to formula, Bulk density =Mass/Bulk volume.

Tapped Density:

Placing 3gm of powder into 10ml graduated measuring cylinder and start mechanical tapping apparatus. The drawn volume was measured and calculated as Formula, Tapped density = Mass/Tapped volume**.**

Compressibility Index:

This value was determined as formula, Carr's index= (Tapped density –Bulk density)./Tapped density

Hausner's Ratio:

It is determine according to formula Hausner's ratio =Tapped density./Bulk density.

% moisture content of drug:

Moisture analyzer balance determine the % moisture content.

FORMULATION OF VALSARTAN ODT's

General Method Of Manufacturing

The tablets ready by DCM**.** All materials weight and passed through300um (#50) sieve, the drug and excipients without lubricant first mixed for 15 minutes with mortar pestle After the addition of magnesium stearate, the mixing procedure continued for 5 minutes. The blend was directly compressed into core tablet using 6mm circular biconcave punch on single station tablet punching machine. 80mg valsartan (tablet weight is 150mg).

Method of formulation of SSD.

Surface robust dispersion solvent evaporation technique use ratios of active compound and carrier 1:1, 1:4, 1:8 drug first dissolved in dimethylformamide after it the carrier is dispersed in this solution. Evaporate the solution until the solvent evaporated. After it collected the mass and kept in desiccators for further use.

Evaluation Of ODT Tablets Of Valsartan

Assay:

6 tablets of VAL were crushed and weight powder equivalent to 80mg drug in 100ml of volumetric flask. Add 70 ml of phosphate buffer to dissolve on vortex. For 20min., make the volume up to 100ml with phosphate buffer and filter the solution. The mid concentration of calibration curve selected (15µg/ml) then the absorbance at 250nm.

Drug amount determine with the help of the intercept and slope from the calibration curve; finally, amount of drug in 150mg of powder was determined by following equation.

Amount in 150mg = concentration of sample ×dilution factor× volume of original sample.

Where dilution factor was 6.66.

Thickness:

The 10 tablets select randomly for every formulation and width of TAB measure with the help of vernier calipers.

Hardness:

10 Tablets were picked randomly, placed in monsanto hardness tester individually and hardness of tablets takes. Average hardness value consider to average ± (min/max)

Friability:

20 tablets choose at random and collectively weight. Tablets keeps in friabilator and revolved at 25 rpm for 4 minutes. Dust removed from tablet and tablets reweighed for % weight loss calculation.

Weight Variation:

we weight of 20 tablets individually with the help of weighing machine, and take the avg weight it compare with the individual tablet weights.

Condition of dissolution test was as follows (IP.2018)

Apparatus : Type 1 Indian pharmacopoeia (Paddle type)
Analytical method : UV -spectroscopy (250 nm)
Dissolution media : 900ml phosphate buffer
Speed and time : 100 rpm 30min
Temperature : 37ºC ± 0.5ºC
Sample amount : 5ml with replacement
Sampling time : 5 min, 10min, 15min, 20min, 25min, 30min.

RESULT AND DISCUSSION

Analytical Method Development

Calibration Of Pure Drug

The pure drug absorbance with their respective concentration is mentioned in table 1.2.

Table 1.2 Concentration And Absorbance Data Of Calibration Sample

Conc.(µg/ml)	Absorbance(nm)
5	0.329
10	0.584
15	0.815
20	1.025
25	1.236

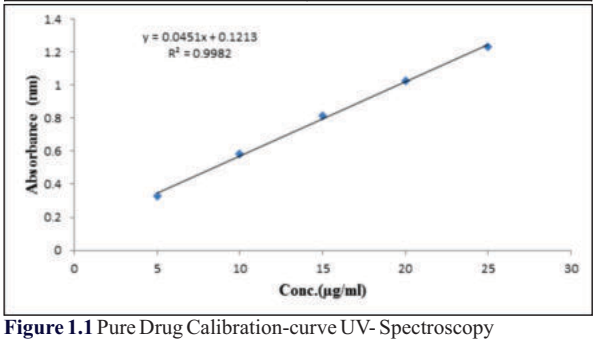

Figure 1.1 Pure Drug Calibration-curve UV- Spectroscopy

Calibration Data Of Drug With Excipients

The calibration data of drug with excipients is showed in above table 1.3

Table 1.3 Concentration And Absorbance Value Of The Calibration Sample

Conc.(µg/ml)	Absorbance (nm)
5	0.327
10	0.571
15	0.815
20	1.017
25	1.228

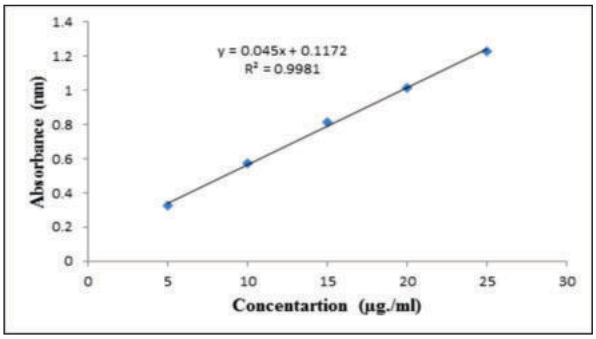

Figure 1.2 Pure Drug And Excipients Calibration-curve UV-Spectroscopy

Validation Of UV Analytical Technique

Linearity Range:

Value of correlation coefficient is determined r^2=0.998 in concentration range 5, 10, 15, 20, 25 (µg/ml) which indicated the linear relationship between absorbance and concentration. The spectrum for this method was 5-25(µg/ml)

Accuracy And Precision:

The exactness (measured by % error) and precision (measured by %RSD) for both intraday and interday studies, as mentioned below, were found+ within the acceptable range of 2%. Thus method was accurate as well as precise.

EVALUATION OF BLEND

The bulk density, hausner's ratio, angle of repose, tapped density, and carr's index given the following table 1.3.

Table 5.2 Evaluation Parameters And Values

Parameters	F1	F2	F3
Bulk-density	0.326g/c.c	0.337 g/c.c	0.375g/c.c
Tapped-density	0.356g/c.c	0.366 g/c.c	0.364g/c.c
Hausner's-ratio	1.096	1.076	1.046
Carr's-index	7.62	7.56	7.57
Particle size(µm)	21.70	21.11	21.57
Particle size(µm)	204.68	203.33	204.44

EVALUATION OF TABLETS

The formulation thickness, diameter, weight variation, hardness, percentage drug content and friability, were given within table 1.4

Table 1.4. Evaluation Of Tablet

Parameter	F1	F2	F3
Weight variation	150±11.25	150±11.25	150±11.25
Thickness	4.2	4.25	4.23
Diameter	8.3	8.3	8.3
Disintegration Time.(sec)	24.66	18	11.86
Hardness.(kg/cm^2)	33.15	3.27	3.32
Friability	0.7	0.7	0.5
% of drug content	97.28	97.67	98.34

Dissolution Test

The dissolution study of ODTs tablets using IP type 1(Paddle type) dissolution apparatus which shown in the table 1.5.

Table 1.5 All Formulations Percentage Drug Release With Time

% Drug release			
Time (min)	**F1**	**F2**	**F3**
0	0	0	0
5	36.39	39.25	41.43
10	46.56	49.57	52.43
15	55.30	58.56	63.53
20	66.87	70.33	74.60
25	79.05	81.36	87.56
30	90.03	93.33	97.56

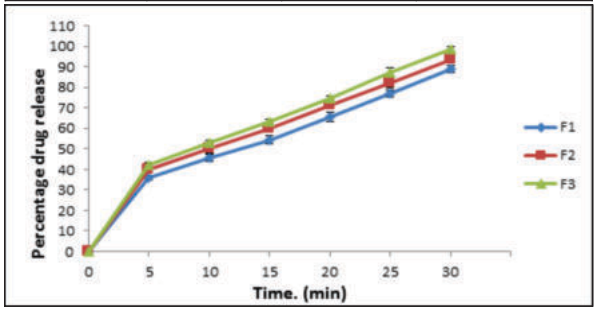

Figure 1.3 Graph Of Drug Release Profile Of Valsartan

The ODT's formulation of valsartan was given maximum release in the phosphate buffer, so this formulation could be used for further study.

CONCLUSION

ODTs formulations (F_1, F_2 and F_3) of Valsartan were directly compressed using Polyplasdone XL and SSG and it assess for hardness, friability, weight variation, thickness, content uniformity, disintegration, and in vitro drug release. Formulation F_3 had showed best release profile of 97% in 30 min. F_3 shall be used for further development studies.

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