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FORMULATION AND DISSOLUTION STUDY OF VALSARTAN IMMEDIATE RELEASE TABLETS

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ABSTRACT

In the present study, design of oral immediate release tablets of Valsartan by direct compression technique was carried out. The main aim and objective of the work is to formulate immediate release tablets using different direct compression vehicles (DCV'S) in different ratios. The main motive is to compare the dissolution profile of these formulations and conclude the best formulation which release drug at a faster rate. To determine the best fit dissolution profile for the dosage forms. Valsartan tablets were formulated by using microcrystalline cellulose (diluent), potato starch, acacia (binder) and magnesium stearate (lubricant). The granules were compressed into tablets and were subjected to dissolution studies. The dissolution profile of the formulation F2 was found to have better dissolution rate compared to others. The Invitro dissolution studies of all the formulations were conducted and the results were obtained, it was concluded that formulation F2 was the best with fast release of drug compared to others.

KEY WORDS: Valsartan, direct compression vehicles (DCV'S), Acasia, MCC, Lactose, Sucrose, Fructose.

INTRODUCTION

An immediate release dosage form allows a manufacturer to extend market exclusivity, while offering patients a convenient dosage form or dosage regimen. Immediate release tablets are those tablets which are designed to disintegrate and release their medication with no special rate controlling features, such as special coatings and other techniques [1-3]. Immediate release and fast dispersing drug delivery system may offer a solution to these problems. Recently immediate release tablets have started gaining popularity and acceptance as a drug delivery system, mainly because they are easy to administer, has quick onset of action is economical and lead to better patient compliance [4]. They are also a tool for expanding markets, extending product life cycles and generating opportunities.

Direct compression is the preferred method for the preparation of tablets [5-7]. It offers several advantages [8,9]. Notable among them are (i) It is economical compared to wet granulation since it requires fewer unit operations (ii) More suitable for moisture and heat sensitive APIs since it eliminates wetting and drying steps (iii) Changes in dissolution profile are less likely to occur in tablets made by direct compression method on storage than in those made from granulations [4]. This is extremely important because the official compendium now requires dissolution specifications in most solid dosage forms. Disintegration or dissolution is the rate limiting step in absorption in the case of tablets of poorly soluble API prepared by wet granulation. The tablets prepared by direct compression disintegrate into API particles instead of granules that directly come into contact with dissolution fluid and exhibits comparatively faster dissolution. The direct compression process is mainly influenced by the properties of the excipients [10,11]. The physico mechanical properties of excipients that ensure a robust and successful process are good flowability, good compressibility, low or no moisture sensitivity, low lubricant sensitivity, and good machineability even in high-speed tabletting machinery with reduced dwell times [12-14].

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Direct compression excipients mainly include diluents, binders and disintegrants. Generally these are common materials that have been modified during the chemical manufacturing process, in such a way to improve compressibility and flowability of the material. It should have good compressibility. It should not show any physical or chemical change in its properties on aging. It should be colourless, odorless and tasteless. It should accept colourants uniformity [16]. It should be easily available and economical in cost.

MATERIALS AND METHODS

Valsartan, Micro crystalline cellulose, Acasia(Binder), Potato starch(super disintegrant), Lactose: sucrose(Diluent), Lactose: fructose(Diluent), Magnesium Stearate.

Equipments used

UV-Visible Spectrophotometer (Spectro- 2080 plus), Dissolution apparatus (veego), Tablet Compression machine (Cadmach) (12 stationary).

Methods

Preparation of standard stock solution

Standard drug solution of Valsartan was prepared by 50mg pure drug in 50ml methanol to obtain a concentration of 1000µg/ml of stock solution from which desired concentrations of solutions were prepared [11].

Determination of λ_{max}

10µg/ml solution of Valsartan was prepared and scanned in UV range of 200-400nm and spectrum was obtained. The λ_{max} was found to be at 209nm wavelength.

Preparation of calibration curve

From the stock solution, a series of dilutions from 2-10µg/ml were prepared. Absorbance of these solutions was measured at 209nm wavelength. A calibration curve was obtained by plotting graph between concentration and absorbance.

Manufacturing steps for direct compression

Direct compression involves comparatively few steps:

- Milling of drug and excipients
- Mixing of drug and excipients
- Tablet compression

DISSOLUTION STUDIES

Dissolution parameters:

Medium: 6.8 pH phosphate buffer, Volume: 900ml, Apparatus: USP type II (paddle type), Speed: 50 rpm, Temperature: 37 ± 0.5°C, Sampling intervals: 10, 20, 30 ,……90 mins.

Invitro drug release

Invitro drug release was studied using USP type II (paddle type) in 900 ml 6.8 pH phosphate buffer at 37 ± 0.5°C 50rpm.Five ml of sample was withdrawn for every 10min and was replaced with an equal volume of fresh medium. Collected samples were analyzed at 209nm using same as blank on UV spectrophotometer. Dissolution study was conducted for all formulations F1, F2, F3, F4, F5. Results are shown in Table-3.

Table 1. Calibration Data for Analysis of Valsartan

Concentration (µg/ml)	Absorbance
0	0
2	0.089
4	0.150
6	0.226
8	0.303
10	0.339

Table 2. Composition of Formulations

S.NO	INGREDIENTS	F1	F2	F3	F4	F5
1	Valsartan	80mg	80mg	80mg	80mg	80mg
2	Microcrystalline cellulose	-	80mg	80mg	40mg	40mg
3	Potato starch	22mg	22mg	22mg	22mg	22mg
4	Acacia	4.4mg	4.4mg	4.4mg	4.4mg	4.4mg
5	Talc	4.4mg	4.4mg	4.4mg	4.4mg	4.4mg
6	Magnesiun stearate	4.4mg	4.4mg	4.4mg	4.4mg	4.4mg
7	DCV(Diluent)	104.8mg Lactose:sucrose= 1:1	24.8mg Lactose:sucrose=1:1	24.8mg Lactose:fructose=1:1	64.8mg Lactose:sucrose =1:0.5	64.8mg Lactose:fructose=1:0.5

RESULTS AND DISCUSSIONS

Table 3. Data showing dissolution profile of all formulations

Time (min)	%Drug Released				
	F1	F2	F3	F4	F5
0	0	0	0	0	0
10	19.7	19.2	20.2	21.7	14.3
20	31.6	37.2	29.3	30.3	24.6
30	42.7	49.6	42	41	32
40	50.7	61.3	49.8	52.2	41.7
50	58.2	73.1	61.1	60.8	49.7
60	62	81.1	70.7	71.1	55.1
70	65.3	87.4	81	84.2	64.7
80	69.5	93.2	89.8	91	74.2
90	70.9	**99**	91.8	94.1	85.8

Fig. 1. Steps involved in Direct Compression Method

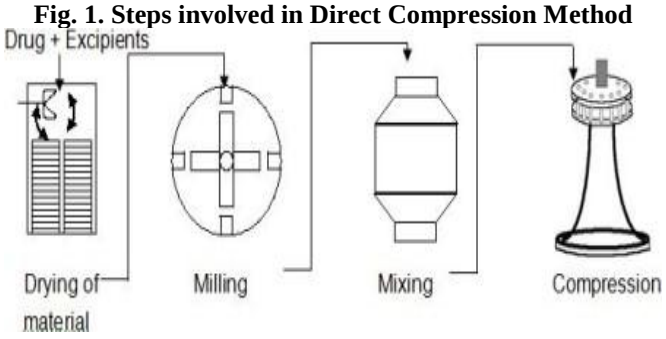


Fig.2. Spectra of Valastran in methanol

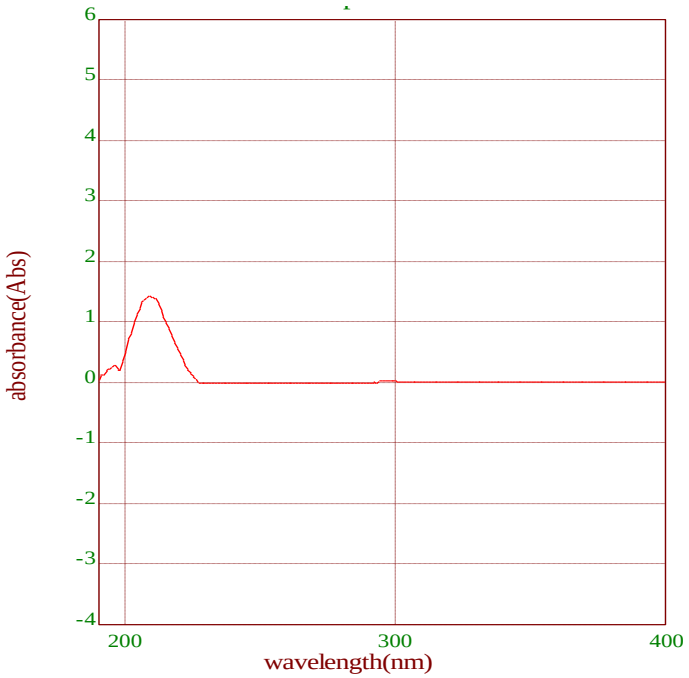


Fig. 3. Calibration curve of Valsartan

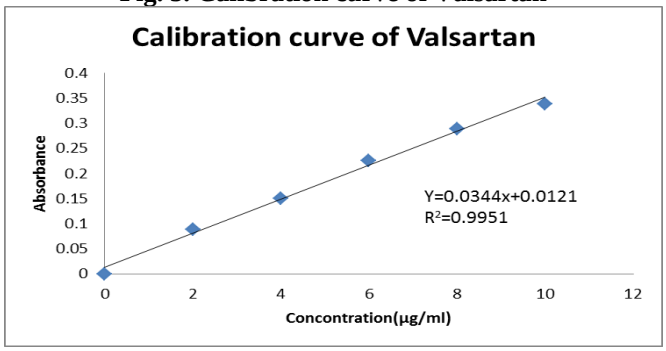


Fig. 4. Dissolution profile of F1

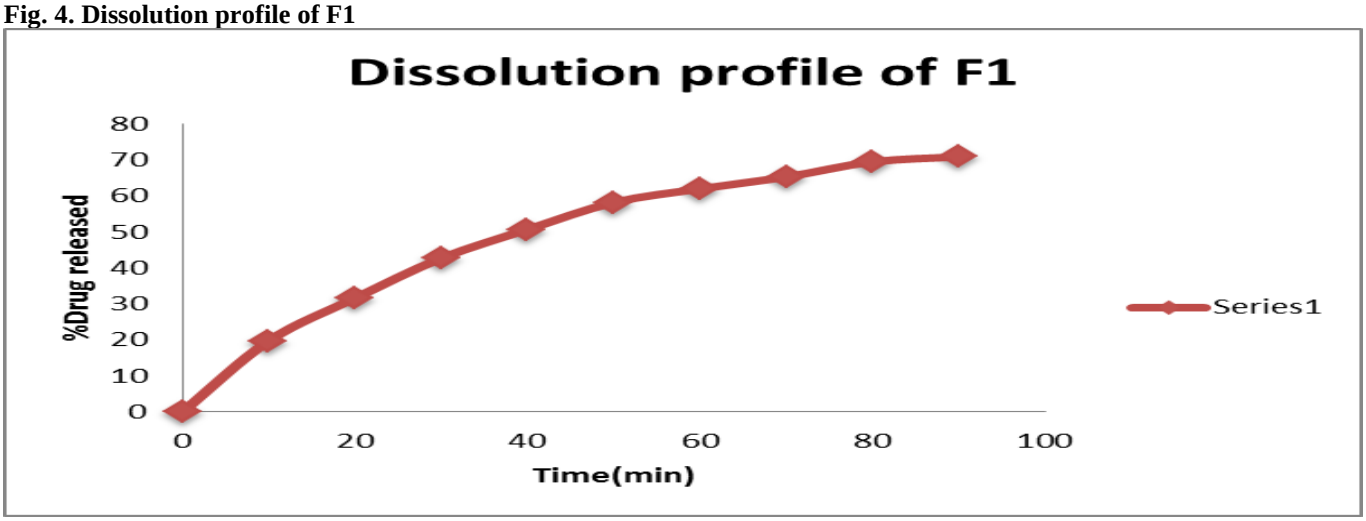


Fig. 5. Dissolution profile of F2

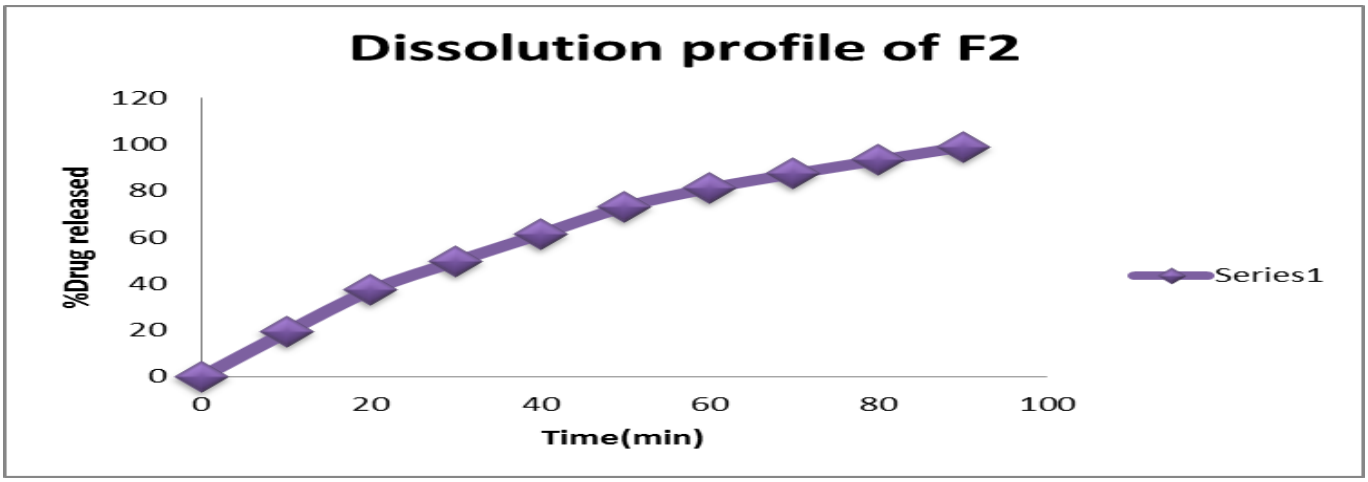


Fig 6. Dissolution profile of F3

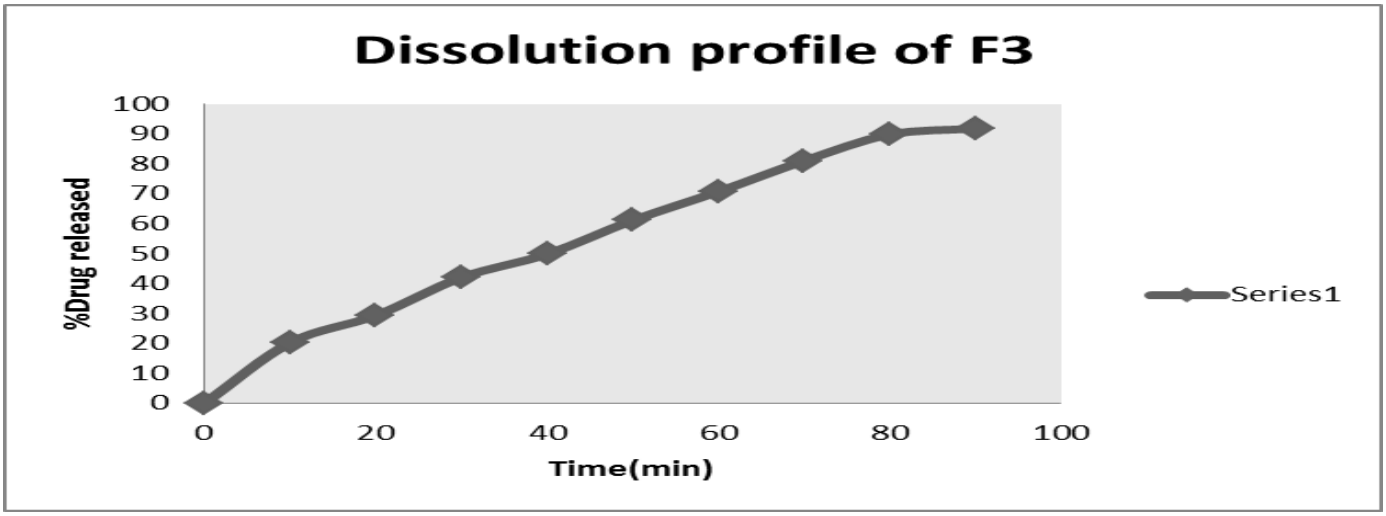


Fig.7. Dissolution profile of F4

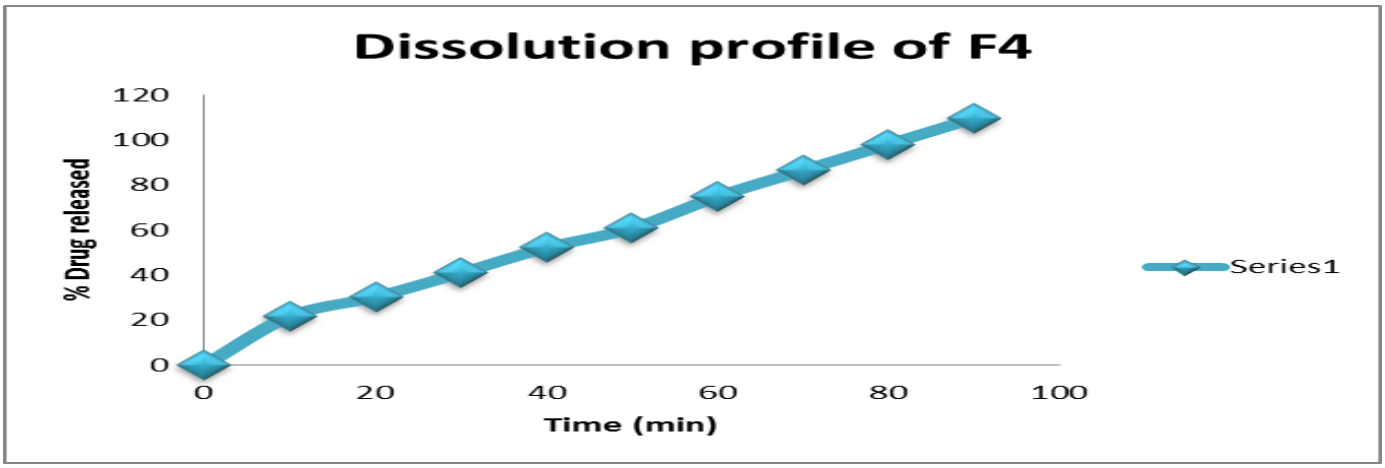


Fig.8. Dissolution profile of F5

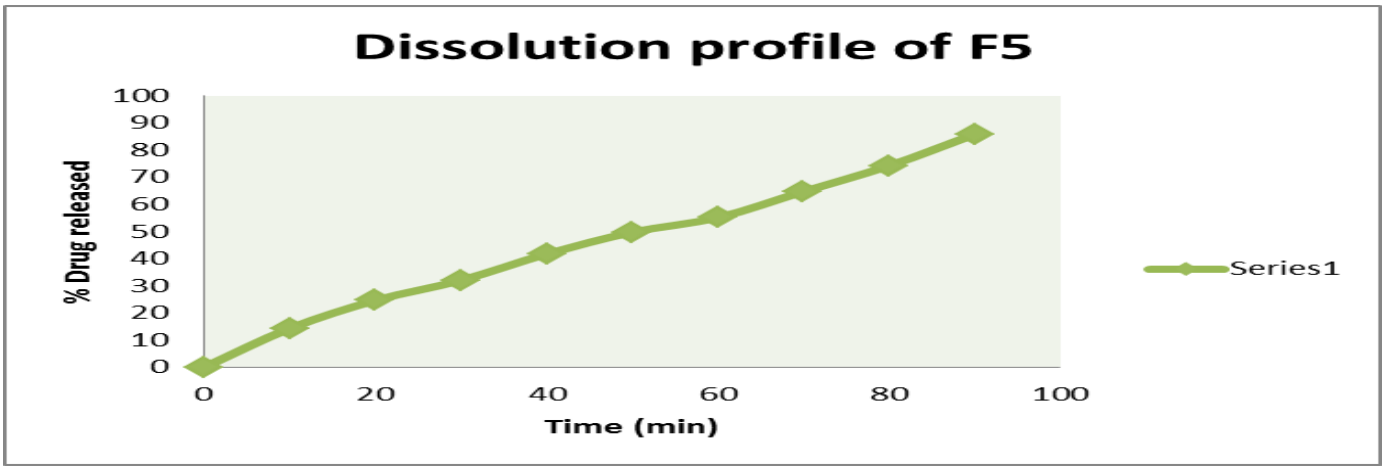
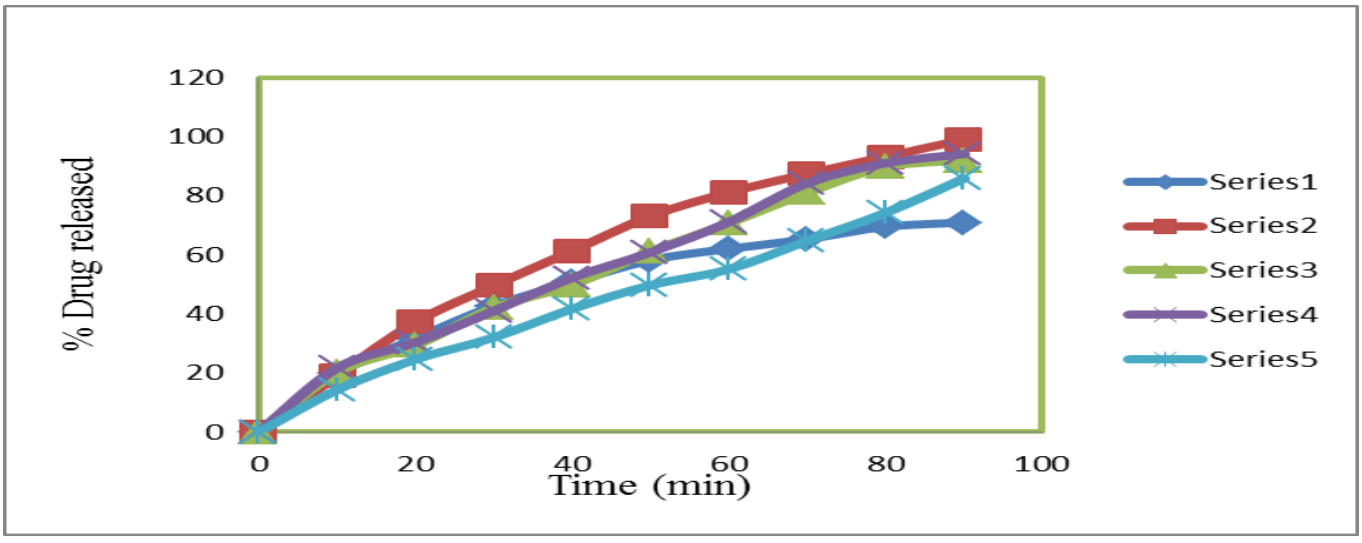


Fig 9. Comparison of invitro drug release of all formulations



DISCUSION & CONCLUSION

Valsartan tablets were formulated by using Microcrystalline cellulose (diluent), Potato Starch, Acacia (binder) and Magnesium Stearate (lubricant). The granules were compressed into tablets and were subjected to dissolution studies. The dissolution profile of the all the formulations was given in Table -3 and Fig no -4-9. Among all the formulations formulation F2 was found to have better dissolution rate compared to others Fig-9. The Invitro dissolution studies of all the formulations were conducted and the data was obtained. From the results obtained it was concluded that formulation F2 was the best with fast release of drug compared to others.

From the dissolution data of all the formulations developed, solubility or dissolution of Valsartan was increased by using drug and polymer(MCC) in 1:1 ratio and Diluent as Lactose:Sucrose in 1:1ratio(F2). Therefore it can be concluded that formulation of drug with high concentration of disintegrating polymer enhances the dissolution, Moreover the Diluent of lactose-sucrose also enhances dissolution compared to lactose-fructose. Further the ratio of lactose and sucrose of 1:1 has better dissolution ability rather than 1:0.5 ratio.

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