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Research Article

# FORMULATION AND EVALUATION OF EFFERVESCENT TABLET OF VALSARTAN

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**Abstract**

The oral dosage forms are the most popular way of taking medication despite having some disadvantages like slow absorption and thus onset of action is prolong. The tabletswere successfully prepared by direct compression method. The preparation process was simple, reliable, and inexpensive. The flow properties of all the prepared formulations were good as indicated by low angle of repose and low compressibility index. The housner's ratio of the all formulations is less than 1.18 which indicates that good flow property. The good flow properties suggested that the powder produced were non aggregated. The same concentration of gas generating agent like Sodium bicarbonate and three different formulation contain three different polymers($F_1$-HPMC K15M, $F_2$ HPMCK100M,$F_3$CARBAPOL934 P) were found to affect on the tablet evaluation parameters like in vitro drug release.FTIR of Valsartan with excipients shown good compatibility and finely FTIR of optimized formulation showed no changes in the functional group of Valsartan. In vitro drug release of effervescent tablet of valsartan shown that the formulation $F_1$ was found to be the best formulation as it releases 83.49 %.

**Keywords:** Valsartan, Effervescent Tablet .HPMC K 15 M, HPMC K 100 M, CARBAPOL 934 P.

## Introduction

The oral dosage forms are the most popular way of taking medication despite having some disadvantages like slow absorption and thus onset of action is prolong. This can be overcome by administrating the drug in liquid from but, many APIs have limited level of stability in liquid form. So, effervescent tablets acts as an alternative dosage form. The tablet is added into a glass of water just before administration and the drug solution or dispersion is to be drunk immediately. [1] The tablet is quickly broken apart by internal liberation of $CO_2$ in water due to interaction between tartaric acid and citric acid with alkali metal carbonates or bicarbonates in presence of water. Effervescent Tablets Due to liberation in $CO_2$gas, the dissolution of API in water as well as taste masking effect is enhanced. The advantages of effervescent tablets compared with other oral dosage forms includes an opportunity for formulator to improve taste, a more gentle action on patient's stomach and marketing aspects.[2]A reason for selection of Effervescent tablets of Valsartan is angiotensin receptor blocker which reduces hypertension and is not available in the form of effervescent formulation with complete stability profile.Valsartan is poorly water soluble hence it will not degrade in stomach or acidic environment and easily cross cell membrane and shows biological action. Valsartan is also very economic drug as compare to other antihypertensive drug so cost factor will reduce by developing valsartan formulation.Other formulations of Valsartan tablets are available but it is new in effervescent form so hypertensive patient can get advantage from this formulation. More consistent response with accurate dosing.[3]

## MATERIALS AND METHODS

Valsartan is purchased from Novartis Pharmaceutical Corporation Ltd and description on API receipt shown 98.99% purity and its purity was confirmed in AGCOP college of Pharmacy by titrimetric assay method using titrant 0.1 N sodium hydroxide.HPMC K 15M,HPMC K100M,CARBAPOL 934 P, Sodium bicarbonate, Citric acid, PVP K30,

Magnesium sulphate, Talc, Aerosil MCC,are also used.

## METHODOLOGY

Effervescent tablets of valsartan (dose 420 mg) were prepared by direct compression method, employing sodium bicarbonate and citric acid, as gas generating agents. HPMC K 15 M,HPMC K100M, CARBAPOL 934 P and PVP K 30 were used in formulation. The compositions of the formulations are given in the Table 1. Weighed quantities of all the ingredients as given in the Table No-1.The all ingredients mixed properly with lubricant magnesium stearate,gliadanttalc and aerosil. The compression carried out on a KBr press (Model M-15, Techno search instrument) using a 13 mm flat punches.

## EVALUATION OF POWDER

### Angle of Repose

In general, the higher is the angle of repose poor is the flow ability of powder. The angle of repose of the granules was determined by using funnel method suggested by Neumann. The accurately weighed granules were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the granules. The granules were allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated by using the equation.Average values are given in Table .no.2

Blend $\tan\theta = h/r$.

therefore, $\theta = \tan^{-1}(h/r)$ Where, $\theta$ = Angle of repose = Height of the pile,

r = Radius of the cone made by powder.

### Bulk Density

Accurately weighed 20 g granules were allowed to flow in fine stream into a graduated cylinder and final volume was noted. The bulk density is obtained by dividing the weight of the sample in grams by final volume in cm3. Average values are given in Table .no.2

$$\varrho b = M / Vb,$$

Where$\varrho b$ = Bulk density = Weight of the powder,Vb = Bulk volume.

### Tapped Density

20 gm granules were allowed to flow in fine stream into a graduated cylinder 0f mechanical tapping device. The measuring cylinder was tapped for 100 times and final tapped volume noted. The tapped density was obtained by dividing the weight of sample by final tapped volume. Average values are shown in Table .no.2

$$\varrho t = M / Vt,$$

Where, $\varrho t$= Tapped density,M = Weight of the powder,Vt =Tapped volume.

**Table no 1. Composition of Effervescent tablets of Valsartan**

| | | | |
|---|---|---|---|
| Valsartan | 10 | 10 | 10 |
| HPMC K 15 M | 100 | --- | --- |
| HPMC K 100 M | --- | 100 | --- |
| Carbapol 934 P | --- | --- | 100 |
| MicrocrystallineCellouse | 100 | 100 | 100 |
| Sodium bicarbonate | 120 | 120 | 120 |
| Citric acid | 60 | 60 | 60 |
| PVP K 30 | 10 | 10 | 10 |
| Magnesium sulphate | 10 | 10 | 10 |
| Talc | 5 | 5 | 5 |
| Aerosil | 5 | 5 | 5 |

**Carr's compressibility index**

Carr has developed an indirect method of measuring powder flow from bulk densities. The percentage compressibility of a powder was a direct measure of the potential powder arch or bridge strength and stability. Average values are given in Table .no.2. [4]

$$\text{Compressibility index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}}$$

**Hausner's Ratio**

It is essential to determine the compressibility strength of powder. Hausner's ratio is simple method to evaluate stability of powder column and to estimate flow properties. Average values are shown in table no.2. [5]

Hausner's ratio = Tapped density /Bulk density

**EVALUATION OF TABLETS**

**Thickness and diameter**

Thickness and diameter of tablets were important for uniformity of tablet size. As there was no much variation in thickness of tablets in each formulation, it shows that powder blends were consistent in particle size and uniform behavior during compression process. Thickness and diameter were measured using vernier caliper. Average values are shown in Tableno.3. [6]

**Hardness**

The hardness was measured in terms of kg/cm2. The resistance of tablets to shipping orbreakage, under conditions of storage, transportation, and handling before usage depends on its hardness. For each formulation, the hardness of five tablets was checked using the Monsanto hardness tester. Average values of tablet hardness are given in Table no.3. [7]

**Friability of Tablet**

Friability is the measure of tablet strength. Roche friabilator was used for testing the friability using the following procedure. Twenty tablets were weighed accurately and placed in the drum that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 min the tablets were weighed and the percentage loss in tablet weight was determined. The results are reported in Table no.3

$$\% \text{ Loss} = \frac{\text{Initial weight of tablets} - \text{Final weight of tablets}}{\text{Initial wt. of tablets}}$$

**Uniformity of Weight**

This test helps to ensure uniformity of dosage forms. It is a simple way to assess variation in drug dose thus; it helps in quality control procedure during tablet production. The test was performed on 20 tablets. Each tablet was weighed individually using an electronic balance. The average weight was calculated and individual tablet weight was compared with the average value and the deviation was recorded. The results are reported in Table no.3. 8

**Dissolution rate study**

The dissolution rate study of valsartan tablets was studied by using Dynamica Halo DB – 20 8 station dissolution apparatus, which contains 900ml of phosphate buffer pH 7.4 and paddles rotates at 50rpm. The temperature was maintained at 37± 0.5˚c throughout the experiment. 2ml of dissolution media were withdrawn through a filter (0.45µ) at regular time intervals. Samples are diluted and assayedfor valsartan at 250nm. The withdrawn samplewas filledwith fresh fluid.The results are reported in Table no.3

**Uniformity of Weight:**

The average weight of tablets was in the rage of 397 to 439 mg. All the tablets passed weight variation test, as there was no deviation of the tablet weights from the average weight beyond the pharmacopoeial standard. The results are reported in Table no.3. 9

**RESULT AND DISCUSSION**

**Drug Authentication**

The sample of Valsartan was evaluated for their physical characteristics, viz, hardness, thickness, friability, and wt. variation, drug content and effervescent properties.

**Melting Point**:-

The melting point of valsartan was in the range of 116°C.

**Loss on Drying-**

Loss on drying of sample was not more than 0.7 percent

**Determination of λ max-**

10 µg/ml solution of valsartan was prepared and scanned in UV range of 200-400nm and spectrum was obtained. The λmax was found to be at 250nm wave length where absorbance was maximum at this wavelength. Hence this is considered as absorbance maxima (λmax).

**Calibration curve of Valsartan in Methanol-**

The absorbance values at different concentration obtained by double beam spectrophotometer (Dynamica Halo DB – 20) are given in Table .4 Using absorbance and concentration data the calibration curve was plotted as shown in Fig1.. The graph of absorbance vs. concentration was appeared to be linear in the concentration range of 2–20 µg/ml at 250 nm. Obeying Beer-Lambert's law in the range of 2–20 µg /ml.

**Table no 2. Granule Properties of all the batches**

| Batch Code | Bulk density (g/cm3) | Tapped density (g/cm3) | Carr's index (Ic) | Hausner's Ratio (Hr) | Angle of repose (θ) |
|---|---|---|---|---|---|
| $F_1$ | 0.50 | 0.62 | 19.35 | 0.12 | 21.48 |
| $F_2$ | 0.51 | 0.64 | 20.31 | 0.13 | 26.74 |
| $F_3$ | 0.49 | 0.60 | 18.33 | 1.22 | 24.14 |

**Table no 3. Tablet properties of Valsartan effervescent tablet**

| Batch Code | Average weight (mg) | Thickness (mm) | Diameter (mm) | Hardness (Kg/cm2) | Friability (%) |
|---|---|---|---|---|---|
| $F_1$ | 420 | 2.16 | 13.13 | 4.1 | 0.237 |
| $F_2$ | 417 | 2.07 | 13.11 | 4.6 | 0.311 |
| $F_3$ | 419 | 2.2 | 13 | 4.3 | 0.297 |

**Table no 4. Calibration Curve of Valsartan in Methanol**

| Sr. no. | Concentration(µg/ml ) | Absorbance 250nm |
|---|---|---|
| 1 | 0 | 0 |
| 2 | 2 | 0.086 |
| 3 | 4 | 0.155 |
| 4 | 6 | 0.221 |
| 5 | 8 | 0.300 |
| 6 | 10 | 0.334 |
| 7 | 12 | 0.433 |

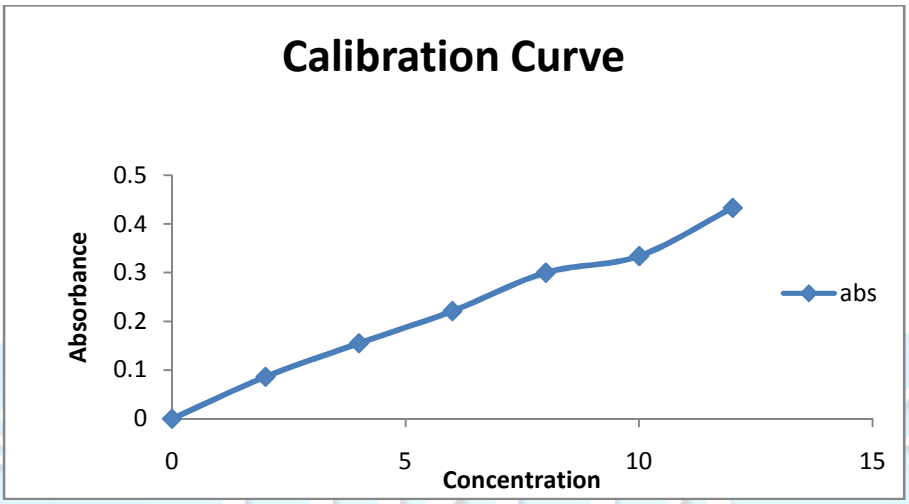


**Fig no.1.Calibration curve of valsartan**

**Table no 5.Various constants for calibration curve**

| Parameters | Value for calibration curve methanol |
|---|---|
| Slope | 0.034 |
| Intercept | 0.010 |
| $R^2$ | 0.996 |

**Table no 6. Relation between average tablet weight and % deviation allowed**

| Avg. wt. of tablet | % Deviation allowed |
|---|---|
| 80 mg or < 80mg | 10 |
| > 80mg to < 250 mg | 7.5 |
| > 250mg or more | 5 |

## DISSOLUTION STUDIES

**Table no 7. Dissolution data of batches $F_1$ to $F_3$**

| TIME (Min) | Cumulative % drug release | | |
|---|---|---|---|
| | **$F_1$** | **$F_2$** | **$F_3$** |
| 0 | 0 | 0 | 0 |
| 2 | 24.35 | 5.76 | 2.31 |
| 4 | 44.86 | 7.10 | 20.64 |
| 6 | 59.03 | 13.76 | 55.48 |
| 8 | 69.26 | 28.93 | 66.23 |
| 10 | 83.49 | 44.93 | 80.71 |

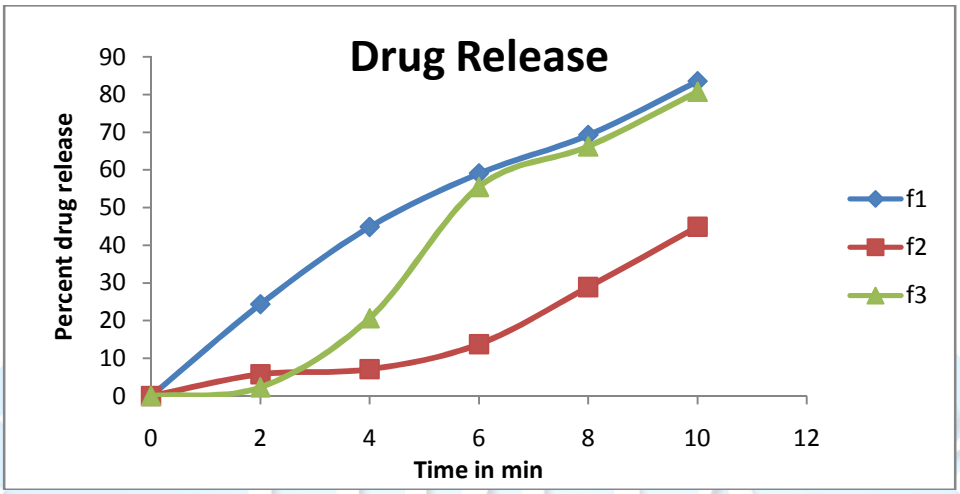


**Fig no.2.Drug release Profile of Valsartan tablets f1,f2,f3**

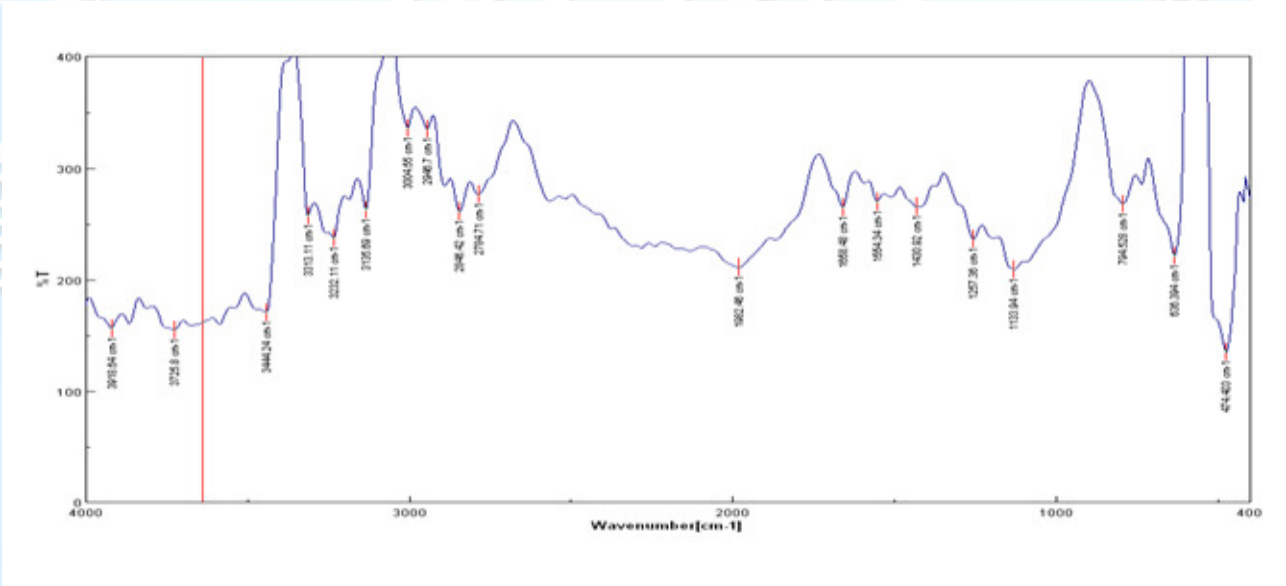


**Fig no.3. FTIR of API of Valsartan**

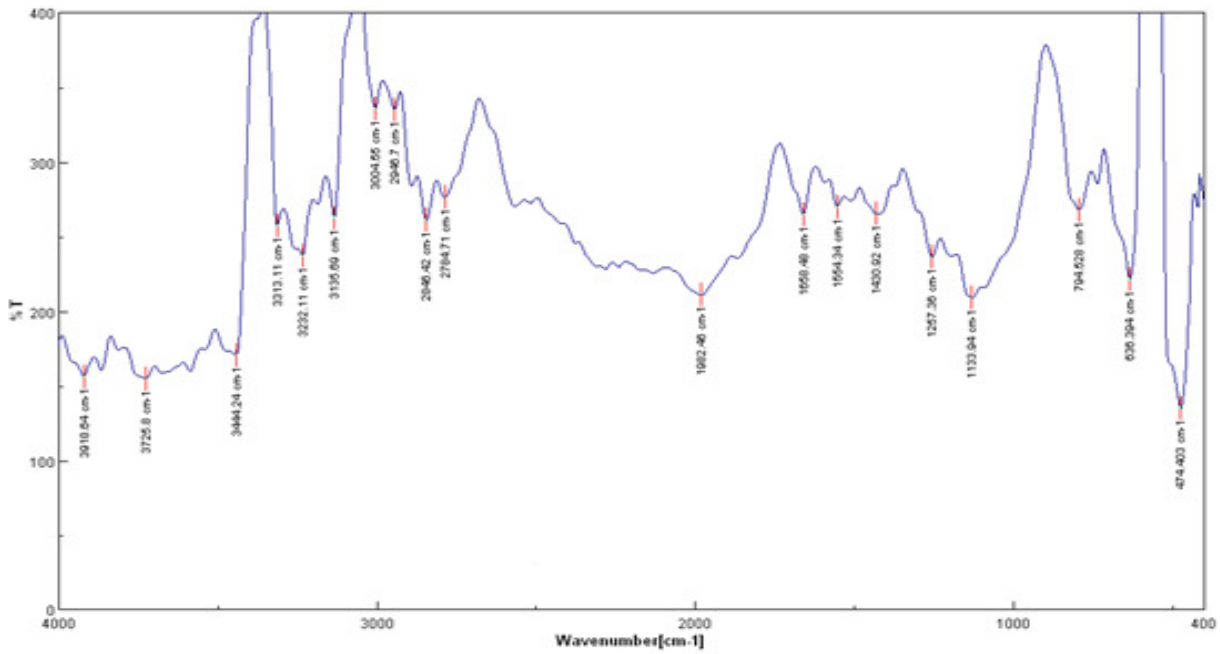


**Fig no.4. FTIR of Valsartan with HPMC K 100, Microcrystalline Cellulose, Citric acid, PVP K 30 mixed for 5 Days shown no changes in functional group of Valsartan.**

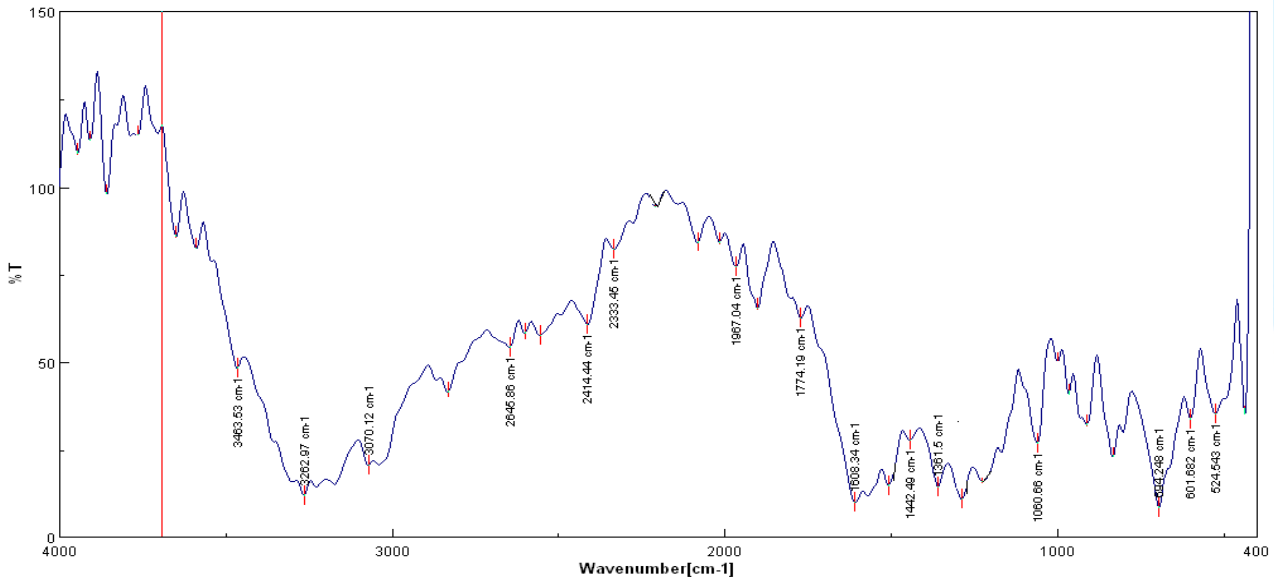


**Fig no.5.FTIR of Optimized Formulation optimized F2 formulation shows compatibility with exipients**

## CONCLUSION

It can be concluded from the present investigation that proper selection of polymers and drug is a prerequisite for designing and developing a Effervescent drug delivery system. The tablets were successfully prepared by direct compression method. The preparation process was simple, reliable, and inexpensive. The flow properties of all the prepared formulations were good as indicated by low angle of repose (<30) and low compressibility index (<16). The housner'sratio of the all formulations is less than 1.18 which indicates that good flow property. The good flow properties suggested that the powder produced were nonaggregated.

The same concentration of gas generating agent like Sodium bicarbonate andthreedifferent formulation containthreedifferent polymers($F_1$-HPMC K15M, $F_2$ HPMCK100M,$F_3$CARBAPOL934 P) were found to affect on the tablet evaluation parameters like in vitro drug release.FTIR of Valsartan with excipients shown good compatibility and finely FTIR of optimized formulation shown no changes in the functional group of Valsartan. In vitro drug release of effervescent tablet of valsartan shown that the formulation $F_1$ was found to be the best formulation as it releases 83.49 %.

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