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FORMULATION AND EVALUATION OF FAST-DISINTEGRATING SUBLINGUAL TABLET OF VALSARTAN FOR THE TREATMENT OF HYPERTENSION

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ABSTRACT:

Objective: The purpose of the investigation is to formulate fast disintegrating sublingual tablet of Valsartan which is used in the treatment of hypertension to achieve faster onset of action. **Materials:** Crospovidone(CP), Sodium starch glycolate(SSG), Microcrystalline cellulose(MCC), Magnesium stearate, Mannitol, and Talc. **Method:** Direct compression method used for the preparation of tablets. The influence of different concentrations of crospovidone and sodium starch glycolate was studied by 5 formulations batches (F1, F2, F3, F4 and F5). Here F1-F4 formulations contain different concentrations of superdisintegrants prepared whereas F5 is without superdisintegrants. **Result:** The hardness of F1 to F5 was ranges from 2.6 kg/cm^2 to 3.3 kg/cm^2. The friability of all the tablets was ranges from 0.83 % to 0.96 %. The wetting time of the tablets were found to be 41 to 81 seconds and disintegration time found to be 43 to 95 seconds. Drug release ranges from 78.70% to 99.47%.**Conclusion:** F4 formulation (with SSG) showed maximum drug release (99.47%) in half hour and concluded as best formulation.

Keywords: Fast disintegrating sublingual tablets, valsartan, solid dispersion

INTRODUCTION:

Fast disintegrating sublingual tablet are generally flat and small compared to other oral tablets. They are usually compressed with light force to keep them soft. The drug delivered by in this route produce fast systemic effect but the drug has good absorption properties. Sublingual tablets and film are formulated with bland excipients, which have property to not stimulate salivation. Salivation dissolves the drug content and may swallow instead of absorbed by sublingual mucosa. Drug stability increased because pH of the mouth is neutral relatively**.** After the tablets placed under the tongue (sublingual) the patient must take some very necessary precautions. They should avoid drinking, eating, talking and swallowing of saliva to keep the tablet and film in place. Bioavailability is high and fast onset of action is compare to oral route Fast absorption of drug due to high vascularisation in sublingual area. Low dose required so it reduces the side effects associated with high dose. The spread of drugs through the oral mucosa is considered an optimistic alternative for oral routes. Because of the sublingual rapid dissociation tablet, there can be a significant improvement in existing treatment options for specific patient groups, for example, children and the elderly.

MATERIALS: Valsartan, Crospovidone(CP), Sodium starch glycolate(SSG), Microcrystalline

cellulose(MCC), Magnesium stearate, Mannitol, and Talc.

➢ **Preformulation studies:**

- **Melting point of valsartan-** It was recorded by capillary method and was found to be 114-116^{O}.
- **Solubility of Valsartan in various solvents (Table 1)**
- **Calibration curve of Valsartan in phosphate buffer pH 6.8 (fig. 1)**

➢ **Composition of fast disintegrating sublingual tablet (Table 2)**

METHOD

The preparation of solid dispersion(Valsartan and beta-cyclodextrin) by kneading method **(Fig.2).** Fast disintegrating sublingual tablet were prepared by direct compression method.

RESULTS AND DISCUSSION

1. Pre-compression studies: The powder blends of all the six formulationswere studied for their granule properties such as Angle of repose, Bulk density, Tapped density, Compressibility index, and Hausner's ratio. **(Table 3)**

2. Post compression studies: All the formulated tablets were examined for evaluation parameters like thickness, friability, hardness, weight variations, content uniformity, wetting time, disintegration test **(Table 4)** and *in-vitro* drug release. (**Fig.3) (Table 5)**

Discussion: The Fast disintegratingSublingual Tablets of Valsartan were prepared by method of direct compression using superdisintegrants SSG (sodium starch glycolate) and CP with an aim to improve the disintegration simultaneously the release rate of the drug. The thickness of all the batches was ranges from 2.47mm to 2.53mm. The hardness of F1 to F5 was ranges from 2.6 kg/cm^2 to 3.3 kg/cm^2. The friability of all the tablets was ranges from 0.83 % to 0.96 %. The weight variations of all batches were found within the I.P. permissible limit of ± 7.5% is allowed for 250mg weight of tablet. The percent drug content uniformity was found to be 98.90% to 99.90%. The wetting time of the tablets were found to be 41 to 81 seconds and disintegration time found to be 43 to 95 seconds. Drug release ranges from 78.70% to 99.47%.

Table 1: Composition of fast disintegrating sublingual tablet

Ingredients (mg)	F1	F2	F3	F4	F5
Valsartan	40	40	40	40	40
SSG	10	15	-	-	-
CP			10	15	-
MCC	50	50	50	50	50
Magnesium stearate	5	5	5	5	5
Mannitol	91	86	91	86	101
Talc	4	4	4	4	4
Total	200	200	200	200	200

Table 2: Solubility of Valsartan in various solvent

Solvent	Solubility (mg/ml)
pH6.8 buffer	1.088
Ethanol	2.442
Methanol	2.970

Table 3: Results of pre-compression studies

Parameters	F1	F2	F3	F4	F5
Angle of Repose(θ)	27.44	25.69	26.32	24.75	29.80
Bulk density(gm/cm^3)	0.602	0.631	0.605	0.614	0.622
Tapped density (gm/cm^3)	0.687	0.714	0.702	0.722	0.709
Carr's index (%)	15.13	16.04	11.04	13.12	12.19
Hausner's ratio	1.17	1.15	1.18	1.09	1.12

Table 4: Results of post-compression studies

Parameters	F1	F2	F3	F4	F5
Thickness(mm)	2.53	2.51	2.50	2.49	2.47
Hardness(kg/cm^2)	3.1	2.9	2.6	2.8	3.3
Friability (%)	0.87	0.96	0.85	0.89	0.83
Weight variation(mg)	199.6	197.3	195.0	197.2	198.4
Wetting time(seconds)	62	50	55	41	84
Drug content (%)	98.57	98.90	99.70	99.73	99.68
Disintegration time	65	57	61	43	95

Table 5: *In-vitro* drug release

Time(min.)	F1	F2	F3	F4	F5
0	0	0	0	0	0
5	60.50	71.65	67.65	79.53	48.63
10	68.72	78.39	73.42	83.66	55.33
15	76.19	85.55	80.82	90.72	63.15
20	83.27	93.71	88.61	97.04	70.80
25	89.63	95.02	92.79	99.15	75.17
30	94.48	99.24	97.90	99.47	78.70

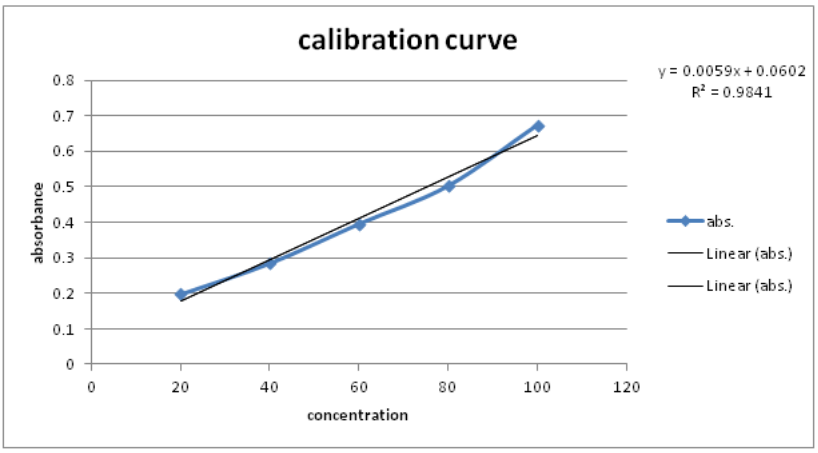

Fig.1 Calibration curve of Valsartan in phosphate buffer pH 6.8

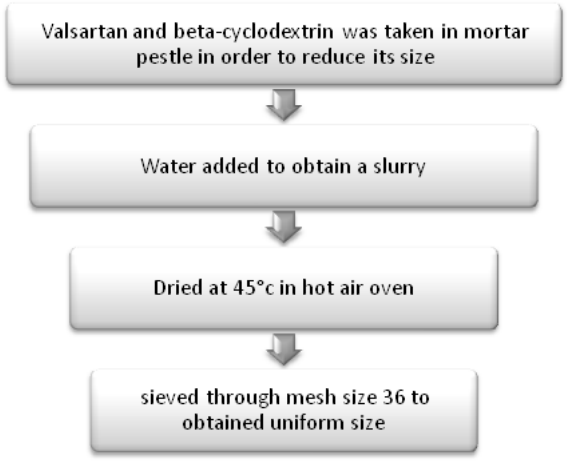

Fig.2 Kneading Method

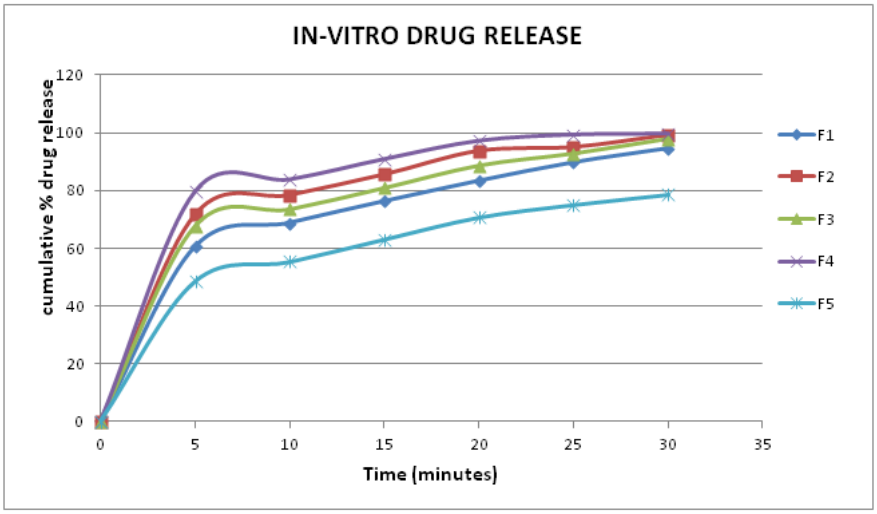

Fig.3 *In-vitro* drug release studies of Valsartan

CONCLUSION

F4 formulation (with SSG) showed maximum drug release (99.47) in half hour and concluded as best formulation. Fast disintegrating sublingual tablet using solid dispersion (Valsartan and beta-cyclodextrin) can increase solubility of drug (Valsartan) and prevent the drug from extensive first pass metabolism ultimately the bioavailability will get significantly enhanced.

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