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Research Article

Formulation and Development of Sustained Release Tablets of Valsartan Sodium

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ABSTRACT

The objective of the present study was to develop a sustained release tablets of Valsartan Sodium an anti hypertensive drug. The sustained release tablets were prepared by wet granulation and formulated using different drug and polymer ratios, formulations such as F1 to F9. Polymers like Hydroxypropyl methylcellulose (HPMC), Ethyl Cellulose (EC) and Kollidon were used. Compatibility of the drug with various excipients was studies. The compressed tablets were evaluated and showed compliance with Pharmacopoeial limits. The optimized formulation (F4) on the basis of acceptable tablet properties and in vitro drug release. The resulting formulation produced tablets with optimum hardness, weight uniformity and friability. All tablets exhibited gradual and near completion sustained release for Valsartan Sodium, and 96.45% released at the end of 12h. The results of dissolution studies indicated that formulation F4 the most successful of the study, exhibited drug release pattern very close to theoretical release profile.

Keywords: Valsartan Sodium, Hydroxy Propyl Methyl Cellulose, Ethyl Cellulose, Kollidon.

INTRODUCTION

Sustained release dosage forms are designed to complement the pharmaceutical activity of the medicament in order to achieve better selectivity and longer duration of action. Sustained release preparations are helpful to reduce the dosage frequency and side effects of drugs and improve patient's convenience. Sustained release matrix tablet is relatively easy to fabricate by incorporating drug molecules in slowly disintegrating or inert porous materials. The most commonly used method of modulating the drug release is to include it in a matrix system[1,2].

Valsartan Sodium is a potent, highly specific ACE Inhibitor with antihypertensive activity. It is readily absorbed from the gastrointestinal tract with oral bioavailability of about 46% and a plasma elimination half-life ranging from 3 to 3.5 hours[3,4].

The novel system of drug delivery offer a means of improving the therapeutic effectiveness of incorporated drugs by providing sustained, controlled delivery and / or targeting the drug to desired site. The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve promptly and then maintain the desired drug concentration. There is a continuously growing interest in the pharmaceutical industry for sustained release oral drug delivery systems. There is also a high interest for design a dosage formulation that allows high drug loading, particularly for actives with high water solubility. Oral route has been the most popular and successfully used for sustained delivery of drugs because of convenience and ease of administration, greater flexibility in dosage form design and ease of production and low cost of such a system.

The sustained release systems for oral use are mostly solid and based on dissolution, diffusion or a combination of both mechanisms in the control of release of drugs. In this type of dosage forms, a sufficient amount of drug is initially made available to the body to cause a desired pharmacological response.

MATERIALS

Valsartan Sodium was obtained from Dr Reddys laboratories, Hyderabad. HPMC was received as gift sample from Oxford Laboratories, Mumbai. Kollidon was gifted by Indian Research Products, Chennai. Ethyl cellulose was obtained as gift sample from Oxford Laboratories, Mumbai. Talc, Magnesium sterate, Lactose, Micro crystalline cellusose was obtained from S.D. Fine Chem. Ltd, Mumbai, India.

Preparation and Characterization of Granules
The granules were prepared by wet granulation method and were evaluated for their bulk density, tapped density, compressibility index, angle of repose and Hausner ratio.

Compressibility index = $[\rho_t-\rho_b/\rho_t] \times 100$
Hausner ratio = ρ_t/ρ_b

Where ρ_t = tapped density
ρ_b = initial bulk density of tablet blend.
Angle of repose θ of tablet blend measures the resistance to particle flow and was determined by fixed funnel method[5].

Formulation of Sustained Release Tablets
After evaluation of granules the sustained release matrix tablets were formulated by compressing the granules. The tablets were formulated such that each tablet contains 50 mg of Valsartan Sodium and total weight of 350 mg, containing 20% (w/w) of the drug.

Compatibility Testing of Drug with Polymer Fourier Transforms Infra-Red (*FTIR*) Spectroscopy
FTIR study was carried out to check compatibility of drug with polymers. Infrared spectrum of Valsartan Sodium and other Polymers was determined on fourier transform infrared spectrophotometer using KBr dispersion method[6].

Evaluation of Sustained Release Tablets
The prepared sustained release tablets were evaluated for uniformity of weight hardness and friability[7,8].

***In-Vitro* Dissolution Studies**
The *in vitro* dissolution was carried out using USP Dissolution testing apparatus type-II. The tablets were placed in pH 6.8 phosphate buffers for next 12 hours, then the apparatus was run at 37ºC ± 0.5ºC and a rotating speed of 50 rpm in a 900 ml dissolution medium. The 5 ml aliquots were withdrawn at intervals of 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10 hours and replacement was done each time with equal amounts of fresh dissolution medium maintained at same temperature. Each 5 ml aliquot was filtered through Whatman filter paper (No. 41). 5 ml of sample with pH 6.8 phosphate buffers for 12 hours and absorbance was measured at 205.5 nm using a Shimadzu-1700 UV spectrophotometer[9].

Table 1: Composition of Valsartan Sodium SR matrix tablet

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
VS	160	160	160	160	160	160	160	160	160
HPMC	40	80	120	-	-	-	-	-	-
KOLLIDON	-	-	-	40	80	120	-	-	-
EC	-	-	-	-	-	-	40	80	120
PVP	8	8	8	8	8	8	8	8	8
MCC	137.2	97.2	57.2	137.2	97.2	57.2	137.2	97.2	57.2
MS	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6
TALC	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2
Total	350	350	350	350	350	350	350	350	350

Table 2: Physico-chemical characterization of Valsartan Sodium SR matrix tablets

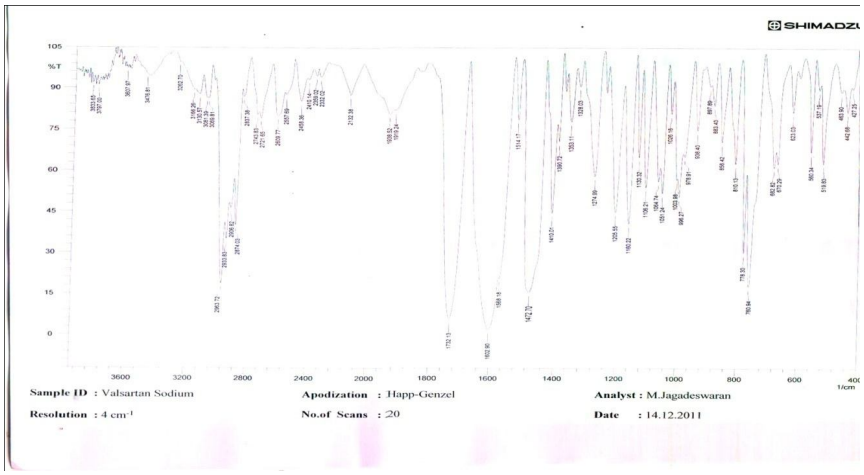
F Code	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Weight variation (%)
F1	3.22	5.50	0.36	119.8±1.48
F2	3.37	5.50	0.39	120.4±0.54
F3	3.14	5.58	0.12	118.6±0.41
F4	3.20	5.66	0.41	118.8±1.64
F5	3.08	4.25	0.54	120.6±1.14
F6	3.33	4.08	0.58	119.2±0.83
F7	3.13	4.12	0.34	117.2±0.12
F8	3.21	5.42	0.46	118.9±0.23
F9	3.25	5.31	0.51	119.3±0.39

RESULTS AND DISCUSSION
The prepared sustained release tablets were evaluated for thickness, weight variation, hardness, friability, drug content, in vitro drug dissolution studies and stability studies. The granules prepared for compression of sustained release tablets were

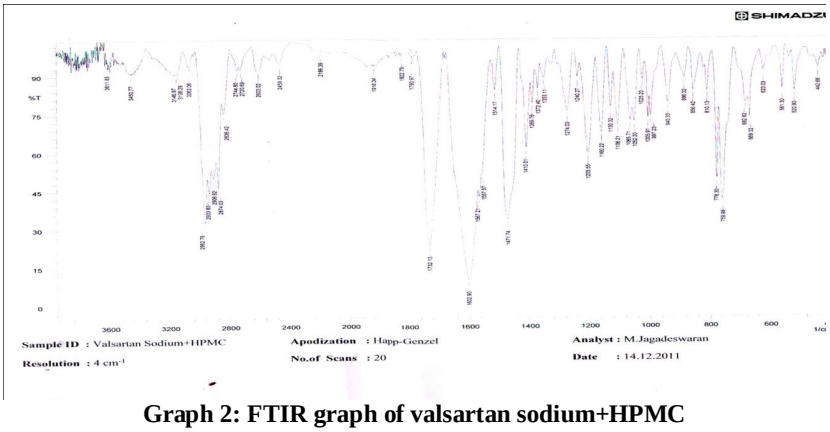
evaluated for their flow properties. Angle of repose was in the range of 25.49 to 31.23 which indicates excellent flow of granules for all formulations. The bulk density of the granules was in the range of 0.214 to 0.362 g/ml, which indicates that the powder was not bulky. The Carr's index was found to be in the range of 14.74 to 18.32, the Hausner's ratio was found to be in the range of 1.17 to 1.19, indicating compressibility of the tablet blend is good. These values indicate that the prepared granules exhibited good flow properties.

Compatibility Testing of Drug with Polymer Fourier Transforms Infra-Red (*FTIR*) Spectroscopy

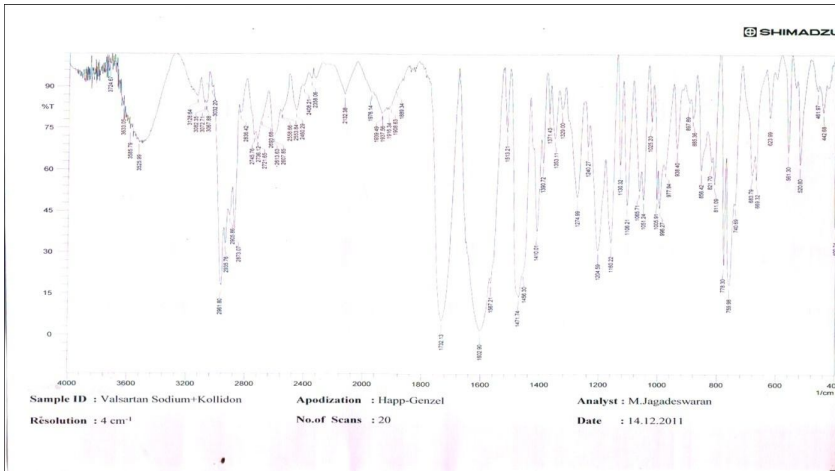
Major functional groups present in Valsartan Sodium show characteristic peaks in IR spectrum. Figure 1 shows peaks observed at different wave numbers and the functional group associated with these peaks for drug and drug with different polymer. The major peaks are identical to functional group of Valsartan Sodium. Hence, it was confirmed that there was no incompatibility between drug and various polymers.



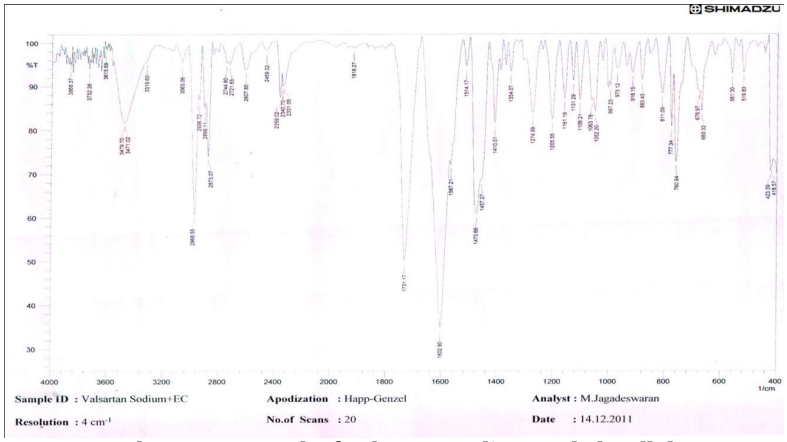
Graph 1: FTIR graph of valsartan sodium



Graph 2: FTIR graph of valsartan sodium+HPMC



Graph 3: FTIR graph of valsartan sodium+Kollidon



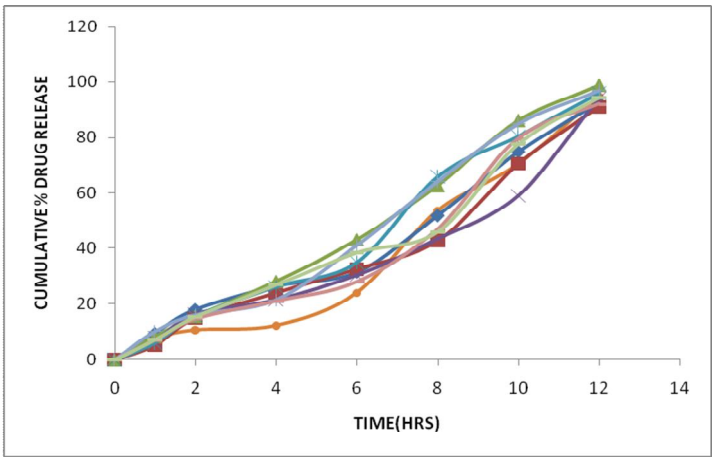
Graph 4: FTIR graph of valsartan sodium+Ethyl Cellulose

Evaluation of Valsartan Sodium sustained release tablets

The Valsartan Sodium sustained release tablets were off-white, smooth, and flat shaped in appearance. The results of physicochemical characterizations are shown in Table 2. The thickness of sustained release tablets was measured was ranged between 3.22 and 3.25 mm. The weight variation for different formulations (F1 to F9) was found to be 119.8±1.48% to 119.3±0.39%, showing satisfactory results as per Indian Pharmacopoeia (IP) limit. The hardness of the sustained release tablets was measured by Monsanto hardness tester and was controlled between 5.50 and 5.31. The friability was below 1% for all the formulations, which is an indication of good mechanical resistance of the tablet.

***In-Vitro* dissolution studies**

In vitro dissolution studies of all the formulations of sustained release tablets of Valsartan Sodium were carried out in pH 6.8 phosphate buffers for 12 hrs. The study was performed for 12 hours, and percentage drug release was calculated at 1 hours time intervals. The results of *in vitro* dissolution studies of all formulations were shown in Figure 5.



Graph. 5: Cumulative % Drug Release Vs Time (hrs)

Stability study

The stability study results obtained were shown in Table 4. The Valsartan Sodium sustained release tablets did not show any significant change in physicochemical parameters and other tests. Thus, it was found that the sustained release tablets of Valsartan Sodium formulation (F4) were stable under these storage conditions for at least 3 months[10].

CONCLUSION

The aim of the study was to formulate SR tablets of Valsartan Sodium various hydrophilic and hydrophobic polymers on in vitro release rate from sustained release tablets of Valsartan Sodium. Different types of polymers like HPMC, Ethyl cellulose and Kollidon were studied. Formulation F4 showed sustained drug release for 12 hours so it was selected as the best formulation among all the nine formulations. The Valsartan Sodium sustained release tablets were stable at 40ºC/75% RH up to 3 months.

REFERENCES

1. Basak SC, Jayakumar RBM and Lucas MK, Formulation and release behavior of sustained release Ambroxol hydrochloride HPMC matrix tablet, Indian Journal of Pharmaceutical Sciences. 2006; 68(5):594-597.
2. Dandagi PM, Mastiholimat VS, Patil MB, Manvi FV, Gagad AP, and Sharma R. Development and evaluation of Theophylline and Salbutamol sulphate sustained release matrix tablets, Indian Journal of Pharmaceutical Sciences. 2005; 67(5):598-602.
3. Shruti C, Gayathri VP and Sanjay KM. Release modulating hydrophilic matrix systems of losartan potassium: Optimization of formulation using stastical experimental design, Science direct, 2006.
4. Chopra S, Patil GV and Motwani SK. Response surface methodology for optimization of Losartan potassium controlled release tablets, Science direct. 2006;1(5):15-19.
5. Lachman L, Lieberman HA and Kanig JL. The theory and practice of industrial pharmacy. 3rd edn., Varghese Publishing House, Mumbai, 1991;67-71:183-184, 320.
6. Aulton ME. Eds, Pharmaceutics: The science of dosage form design, 2nd edn., Churchill Livingstone, New York, 2002;487-488:492-495.
7. Anonymous, The Indian Pharmacopoeia. Volume- I, II, III. The Controller of publication, New Delhi, 2007;1319-1320.
8. Banker, G.S. and Rhodes, C.T. Eds. Modern Pharmaceutics. 3rd edn., Marcel Dekker, Inc. New York, 1996, 668-669.
9. Yeole PG, Galgatte UC, Babla IB and Nakhat PD. Design and evaluation of Xanthan gum-based sustained release matrix tablets of Diclofenac Sodium, Indian Journal of Pharmaceutical Sciences. 2006;185-189.
10. Manavatan R and Ramasamy S. Physical Pharmaceutics, 1st edn. Vignesh Publisher, Chennai. 1995;288-299.