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Research Article

FORMULATION AND EVALUATION OF SUSTAINED RELEASE VALSARTAN MATRIX TABLETS BY USING NATURAL POLYMERS

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ABSTRACT

The present study was aimed to develop antihypertensive sustained release matrix tables of valsartan Angiotensin II receptor antagonist, using natural polymers (guargum and pectin) as the matrix material in different proportion by direct compression method.the tablets were prepared by Guargum diffrent formulations FG_1,FG_2,FG_3(1:0.5,1:1,1:1.5) and same as with Pectin different formulations FP_4,FP_5,FP_6 (1:0.5,1:1,1:1.5) . The tablets were subjected to weight variation test, drug content, hardness, friability, and in vitro release studies.. In vitro dissolution studies indicate that among all the formulations FG3 (1:1.5) significantly reduced the rate of drug release compared to other formulations. The result of dissolution study indicate that the formulation prepared by guargum (1:1.5) ratio showed maximum drug release up to 23 hrs. Methematical treatment of the *in vitro drug* release data suggest that, optimized formulation FG_3 fitted in to zero order and Peppas release kinetic shows R2 value 0.982. Drug release from the matrix occurred by combination of two mechanism, diffusion and erosion of tablet. So when compared to Pectin the Guargum is the best polymer to control the release of Valsartan tablet.

Key words: Valsartan, Guargum, Pectin, Sustained Release, Matrix Tablet.

INTRODUCTION

The goal of designing sustained or controlled release drug delivery systems of Valsartan matrix tablets is to reduce the frequency of dosing or to increase the effectiveness of the drug by localization at the site of action, reducing the dose required, or providing controlled drug delivery.

Valsartan is an angiotensin II receptor antagonist class of drug used for the treatment of hypertension, myocardial infarction and congestive heart failure. It treats the hypertension by blocking the vasoconstrictor and aldosterone secreting effect of angiotensin II selectively by blocking the binding of angiotensin II and angiotensin1 receptor in many tissues. Valsartan drug was comes under BCS class III, low bioavaibility (approximately 20-25%), and shorter half-life (nearly 6 hours). The treatment of anti hypertension therapy need long duration and to maintain plasma concentration the constant drug release due to over come of toxic effects. so to design controlled delivery system of Valsartan for gradual release of drug in amounts sufficient to maintain therapeutic response for a specific period of time and to maintain dose frequency. In vitro disssolution study conducting diffrent mediums 0.1N Hcl for 2 hrs, 7.4 phosphate buffer up to 22hrs. The

selection of natural polymers than synthetic polymers as matrix system for sustained drug delivery is to obtain desired drug release, patient compliance,cost effectiveness and to enhance compatability with the drug. Hence in the present study an attempt has been made to develop sustained release matrix tablet of Valsartan using natural polymers. Matrix materials such as Guargum and Pectin are used in the formulation. The natur l polymer Guargum the concentration increase to delay the drug release up to certain extent. After the concentration increase the drug release will be constant so, we are optimize (1:3) ratio of the Guargum to fulfill our object.

Material and Methods

Valsartan was a gift sample from Aurabindo pharma pvt.ltd , Hyderabad .guargum was purchased from S.Kant.Healthcare ltd Vapi, Gujarat. pectin was purchased from Coax Bioremedies Pvt. Ltd., Hisar. Other ingredient lactose was obtained from Qualigens Fine Chemicals, Mumbai, magnesium stearate from S. D Fine Chem. Ltd., Mumbai and talc was obtained from Nice Chemicals Pvt. Ltd., Cochin. The other entire chemical used was of high analytical grade.

Preparation of matrix tablet

Initially,valsartan tablets with different concentration of hydrophilic polymer were prepared by direct compression technique. Required quantities of all ingredients were weighed individually on electronic balance (citizen India). All ingredients were first sieved through sieve #44 and mixed for 5 min by adding lactose then blended with talc and magnesium stearate for lubrication which were then compressed on rotatiry tablet compression machine using circular 6.5mm tooling set (cadmech Ahmadabad India).

Formulation of valsartan sustained release tablets

S. No	Ingredients	FG_1 (mg)	FG_2 (mg)	FG_3 (mg)	FP_4 (mg)	FP_5 (mg)	FP_6 (mg)
1	Valsartan	30	30	30	30	30	30
2	Guargum	15	30	45	-----	-----	-----
3	Pectin	-----	-----	-----	15	30	45
4	Lactose	102	87	72	102	87	72
5	Mg stearate	2%	2%	2%	2%	2%	2%
6	Talc	2%	2%	2%	2%	2%	2%
	Total tablet weight	150	150	150	150	150	150

FG: valsartan with guargum ; FP: valsartan with pectin

Evaluation of tablets

Weight variation test

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance (Citizen, India), and the test was performed according to the official method.

Hardness and friability

For each formulation, the hardness and friability of 6 tablets were determined using the Hardness tester (Monsanto, India) and the friabilator (Roche Friabilator India), respectively.

In Vitro release studies

Release of the prepared tablets was determined up to 24 hour using U.S.P type II paddle type dissolution rate test apparatus (VEEGO, India). 900 ml of 0.1 N HCl(pH 1.2) was used as dissolution medium for first 2 hrs and (pH 7.4) phosphate buffer for up to 24 hrs the test of the period as dissolution medium. The paddle was adjusted at 75 rpm and the temperature of 37±0.5ºC was maintained throughout the experiment. Samples of 5 ml were withdrawn at known time intervals and were replaced with same volume of fresh dissolution media after each withdrawal. The samples were analyzed for drug contents by measuring absorbances at 251 nm using UV-VIS double beam spectrophotometer thermo scientific, India.

Drug content

Three tablets were selected randomly from each batch, powdered separately and then taken into three volumetric flasks of 100 ml. In each flask 100 ml of phosphate buffer pH

7.4 was poured and kept for 24 hrs. After filtering the solution and making suitable dilutions, the absorbance of the filtrate was measured at 251nm using UV-VIS double beam spectrophotometer thermo scientific, India. From this absorbance, drug content was determined. Drug content was determined according to the following formula

Drug content = (Actual drug content / theoretical drug content) X100

Swelling index

Measurement of the swelling index was carried out to gain an insight into the phenomenon of polymer hydration and to evaluate the extent of media penetration within the tablets. The swelling index was determined by equilibrium weight gain method the study was carried out in the USP dissolution apparatus type 1. The tablets were accurately weighed, placed in dissolution basket, immersed in phosphate buffer (pH 7.4) and maintained at 37±0.5^{0}c in the dissolution vessel. At regular intervals of 2, 4, 6, 8, 10 up to 24 hrs.The weighted basket matrix system was withdrawn from the dissolution vessel, lightly blotted with the tissue paper to remove excess test liquid and re-weighed. The swelling index (SI) of each tablet was calculated according to the following equation.

$$S.I. = \{(Wt-W0) / W0\} \times 100$$

Where, W0 = initial weight, Wt = final weight

Releasekinetics

In order to examine the release mechanism of drug sample from the prepared matrix tablets of the optimized formulation (FG_3), the results of the dissolution study was examined in accordance to the kinetic models such as zero-order, first order, Higuchi equation, Korsemeyer–Peppas equation and Hixson–Crowell equation.

Stability study

Stability of a drug can be defined as the time from the date of manufacture and the packaging of the formulation, until its chemical or biological activity is not less than a predetermined level of labeled potency and its physical characteristics have not changed appreciably or deleteriously. The selected formulations were packed in yellow-color PVDC/ALU, Blister. They were then stored at 40^{0}c / 75 % RH for 3 months and evaluated**.**

RESULTS AND DISCUSSION

The tablets of different formulation were evaluated for hardness, weight variation, friability and drug content. The result of tablets of formulation FG_1 to FP_6 where weight variation ranging from 1.25±0.22 to 1.29±0.22, hardness were maintained 5.5kg/cm^2, friability 0.78% to 0.8%, drug content values ranging from 93% to 98%. The results of tablets are concluded that all the parameters are within the acceptance range.

Drug release studies were found to be increase in concentration of polymers, Guargum there was an increase in time drug release. From the optimization studies it was concluded that with increase in concentration of Guargum, there was an increase in time of release of drug was observed in FG_3 (1:1.5) the drug release was up to 23 hrs. But increased concentration of Pectin does not seem to influence the release profile of drug when compared to Guargum as same concentration of Pectin FP_6 (1:1.5) the drug release was up to 9 hrs. Finally the control release of Valsartan failed to extend the release of drug with Pectin. Therefore formulation FG_3 was selected to fulfil our object. Drug release data and comparison of drug release curve of formulation are shown in graph respectively.

Measurement of the swelling index was carried out to gain an insight into the phenomenon of polymer hydration and to evaluate the extent of media penetration within the tablets. Formulation FG_3 was showed 195.73±0.79 % swelling index and result concluded that formulation FG_3 showed good swelling index property.

Release kinetic was showed that *in vitro* release curve fitted under zero order and Peppas model which show R2 value 0.982 is highest as compared to other models. The regression coefficient R2 value nearer to 1

indicated the model fitting of the release mechanism. R2 value and curve of different model are shows in table respectively

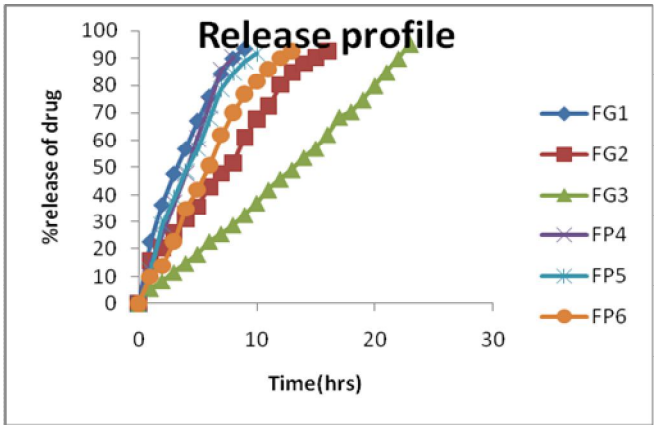
Stability studies were carried out at 40°c / 75 % RH for the selected formulation for the period of 3 months there was slightly acceptable changes was observed in physical and chemical parameter and slightly acceptable changes in drug release. FG_3 formulation was showed 98.46±0.16, 97.48±0.06 and 97.48±0.22 up to 24 hrs in 1 month, 2 month, and 3 month respectively. Result was concluded that formulation was stable under specific temperature and humidity condition.

Evaluation parameters

S.No	Parameter	FG_1	FG_2	FG_3	FP_4	FP_5	FP_6
1	Hardness(kg/cm²)	5.5	5.5	5.5	5.5	5.5	5.5
2	Weight variation(%)	1.25±0.22	1.28±0.22	1.30±0.22	1.25±0.22	1.27±0.22	1.29±0.22
3	Swelling index(%)	0.024	0.035	0.051	0.026	0.042	0.063
4	Drug content(%)	96	97.5	98	92.4	94	96.3

Coefficient values and drug release parameters

S. No	Formulation	Zero order	First order	Higuchi	Peppas	K_0	T_{50}	T_{90}
1	F_1	0.988	0.964	0.958	0.980	83.5	3	5
2	F_2	0.974	0.916	0.928	0.995	41.7	9	15.5
3	F_3	0.982	0.808	0.881	0.999	31.8	13	23
4	F_4	0.980	0.899	0.944	0.995	68.4	4	6
5	F_5	0.983	0.849	0.951	0.997	74.2	3.5	5
6	F_6	0.992	0.859	0.964	0.994	85.9	2.8	6



CONCLUSION

The approach of the present study was to make Valsartan sustained release matrix tablets by uing natural polymers with different ratios. Among all the six formulations, F_3 formulation with drug polymer (Guargum) ratio (1:1.5) for sustained release formulation of valsartan showing 23 hr drug release. By this our objective of sustained release of valsartan from matrix tablet has been fulfilled.

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