WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 8, Issue 12, 1041-1047. Research Article ISSN 2277– 7105

FORMULATION AND EVALUATION OF SUSTAINED RELEASE MATRIX TABLETS OF LOSARTAN POTASSIUM

P. Purnima*, Dr. P. Arun, P. Shailendra, P. Bhavesh and D. Neelesh

Department of Pharmacy, Shri Ram Group of Institution, Iti Madhotal Jabalpur 482002.

Article Received on
31 August 2019,
Revised on 21 Sept. 2019,
Accepted on 11 Oct. 2019
DOI: 10.20959/wjpr201912-16055

***Corresponding Author**
P. Purnima
Department of Pharmacy, Shri Ram Group of Institution, Iti Madhotal Jabalpur 482002.

ABSTRACT

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drug via pharmaceutical products of different dosage form. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient acceptance, and cost effective manufacturing process. Pharmaceutical products designed for oral delivery are mainly immediate release type or conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption.

INTRODUCTION

It is a reasonable assumption that drug concentration at the site of action is related to drug plasma level and that, in the great majority of cases, the intensity of effect is some function of drug concentration at the target site. The objective of the most therapeutic regimens is to rapidly raise the plasma concentration to the required level and then to hold it constant for the desired duration of treatment. The extent to which this situation can be achieved depends on many factors, including the minimum effective concentration of the drug, the level at which side effects occur, the dose administered, the rate of drug release from the dosage form, the rate of elimination and the frequency of dosing. If the dose size and frequency of administration are correct, therapeutic 'steady state' levels of the drug can be achieved rapidly and maintained by the repetitive administration of conventional oral dosage forms.

Thus, various modified drug products have been developed to release the active drug from the product at a controlled rate. The term controlled release drug products was previously used to describe various types of oral extended-release dosage forms, including sustained release, sustained action, prolonged action, slow release, long action, and retarded release.

MATERIALS

Excipients Used

List of excipients with source

S.No	Name of Ingredients	Name of supplier
1	Losartan potassium	Fourrts India Pvt Ltd., Chennai.
2	HPMC K100M	Griffon laboratories Pvt. Ltd., Mumbai.
3	Xanthan Gum	Qualigens fine chemicals, Mumbai.
4	Ethyl cellulose	Qualigens fine chemicals, Mumbai.
5	MCC	Griffon laboratories Pvt. Ltd., Mumbai.
6	Starch	Qualigens fine chemicals, Mumbai.
7	Polyvinylpyrolidone	Qualigens fine chemicals, Mumbai.
8	Magnesium stearate	Qualigens fine chemicals, Mumbai.
9	Talc	Qualigens fine chemicals, Mumbai.
10	Hydrochloric acid	S d fine-chem limited, Mumbai.
11	Methanol	Qualigens fine chemicals, Mumbai.
12	Ethanol (95%)	S d fine-chem limited, Mumbai.
13	Acetonitrile	Qualigens fine chemicals, Mumbai.
14	Isopropyl alcohol	Qualigens fine chemicals, Mumbai.
15	Glacial acetic acid	S d fine-chem limited, Mumbai.
16	Acetone	Qualigens fine chemicals, Mumbai.
17	Sodium hydroxide	S d fine-chem limited, Mumbai.

Equipments used

List of equipments with model/make

S.No	Equipment	Model/ Make
1	Electronic balance	Shimadzu BL-220H, Japan.
2	Bulk density apparatus	Indolabs VTAP/MATIC-II.
3	Standard sieve (20 and 40#)	Jayant scientific, IND.
4	Hot air oven	Precision scientific Co., Chennai.
5	Sixteen punch tablet compression machine	Cadmach, Ahemdabad, India.
6	Friability apparatus	Veego scientific VFT-DV, Mumbai.
7	Hardness tester	Monsanto
8	Varnier caliper	MITUTOYO, Indolabs.
9	Humidity chamber	Labtech, Ambala.
10	USP dissolution test apparatus Type II	Veego scientific VDA-8DR, Mumbai.
11	UV spectrophotometer	Shimadzu-1700 PharmaspecUV-Visible spectrophotometer, Japan.
12	FTIR spectrophotometer	Parkin elmer-Pharmaspec-1.
13	Differential scanning calorimeter	Shimadzu DSC 60, Japan.

FORMULATION DEVELOPMENT

Method of preparation and characterization of powder blend

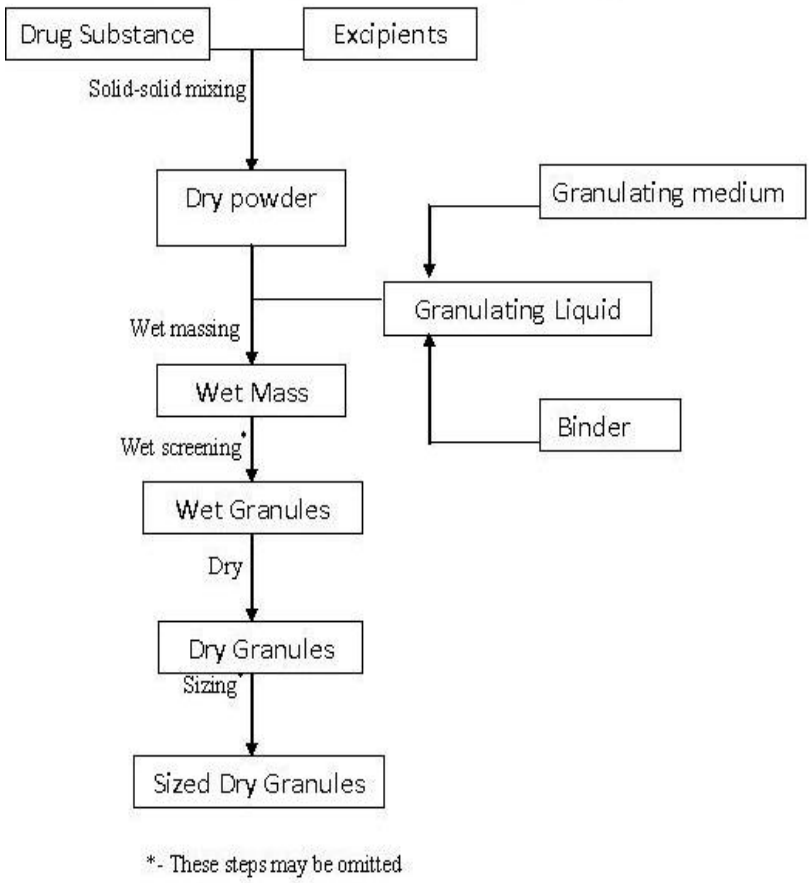
Table: Composition of Losartan potassium SR Matrix tablet.

Ingredients*	F1	F2	F3	F4	F5	F6	F7	F8	F9
Losartan potassium	50	50	50	50	50	50	50	50	50
HPMC K100M	50	75	100	-	-	-	-	-	-
Ethyl cellulose	-	-	-	50	75	100	-	-	-
Xanthin gum	-	-	-	-	-	-	50	75	100
MCC	125	100	75	125	100	75	125	100	75
PVP	20	20	20	20	20	20	20	20	20
Iso propyl alcohol	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Talc	3	3	3	3	3	3	3	3	3
Magnesium stearate	2	2	2	2	2	2	2	2	2
Total weight	250	250	250	250	250	250	250	250	250

*All the quantities are expressed as mg per tablet.

Preparation of granules. ***(****Lachman L., et al., 1991)***

The granules were prepared by wet granulation method. This method involved use of appropriately selected tablet additives which would act as binders for the mixtures of drug and other tablet excipients.



Compatibility testing of drug with polymer (*IP, 2007; Aulton M.E., 2002)*

The proper design and formulation of a dosage form requires consideration of the physical, chemical and biological characteristics of all drug substances and excipients to be used in the fabricating the product. Each polymer used in the formulations was blended with the drug levels that are realistic with respect to the final dosage form. Each polymer was thoroughly blended with drug to increase drug- polymer molecular contacts to accelerate the reactions if possible.

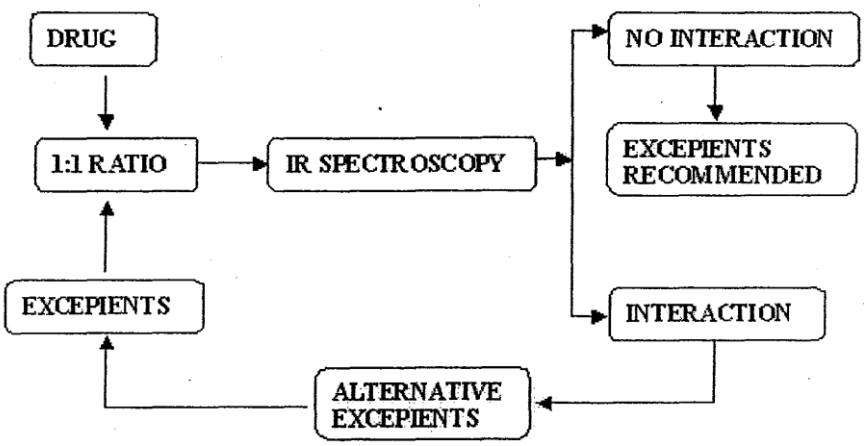


Figure: Schematic representation of compatibility studies.

Preparation of standard graph of Losartan potassium

Preparation of solutions

Preparation of 0.1N hydrochloric acid

0.1N HCl was prepared according to I.P. 1996. A quantity of 8.5 ml of HCl was diluted with fresh distilled water to produce 1000 ml.

Preparation of stock solution of Losartan potassium

Accurately weighed 20 mg of Losartan potassium was dissolved in little quantity of distilled water and volume was adjusted to 100 ml with the same to prepare standard solution.

Procedure

From the stock solution, aliquots of 1, 2, 3, 4, 5, 6, 7, 8 ml were transferred to 100 ml volumetric flasks and final volume was made to 100 ml with 0.01N HCl. Absorbance values of these solutions were measured against blank (0.01N HCl) at 205.5nm using Shimadzu-1700 UV spectrophotometer.

Quantification of Drug

Accurately weighed 20 mg of Losartan potassium was dissolved in little quantity of distilled waterand volume was adjusted to 100 ml with the same to prepare standared solution. From the above solution, aliquots of 5 ml were transferred to 100 ml volumetric flasks and final volume was made to 100 ml with 0.01N HCl. Absorbance values of these solutions were measured against blank (0.01N HCl) at 205.5 nm using Shimadzu-1700 UV spectrophotometer.

RESULT AND DISCUSSION

Preformulation Parameters

Physicochemical parameters of drug

Organoleptic properties

Odourless, white or almost white crystalline powder.

Melting point

Melting point values of Losartan potassium sample was found to be in range of 185^{0}C to 189^{0}C. The reported melting point range for Losartan potassium is 183.5^{0}C to 184^{0}C. Hence, experimental values are in good agreement with official values.

SOLUBILITY STUDY

Table: The solubility of Losartan potassium in various solvents.

Name of solvent	Inference
Distilled water	Freely soluble
Methanol	Very soluble
Iso propyl alcohol	Soluble
Acetonitrile	Sparingly soluble
Acetone	Slightly soluble
Chloroform	Slightly soluble
0.1N HCl	Slightly soluble
0.01N HCl	Soluble
Phosphate buffer(pH6.8)	Soluble

ANALYTICAL METHODS

λ max Determination

The absorption maximum for Losartan potassium was found to be 205.5 nm.

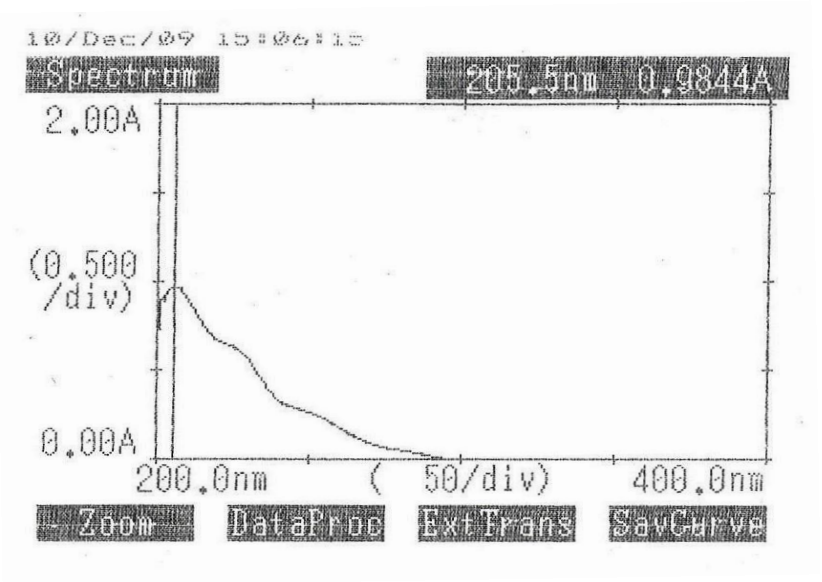


Figure: λ max observed for Losartan potassium in 0.1N HCl.

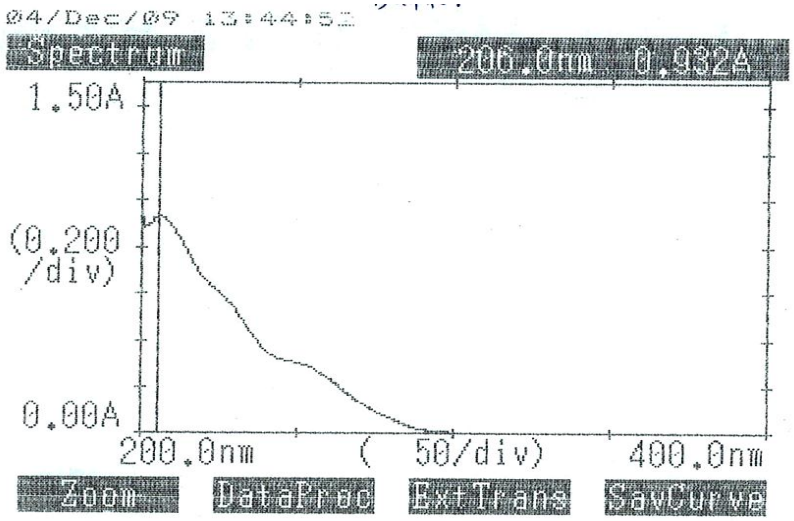


Figure 6.2: λ max observed for Losartan potassium in 0.1N HCl.

SUMMARY AND CONCLUSION

Oral ingestion has long been the most convenient and commonly employed route of drug delivery due to its ease of administration, high patient compliance, least sterility constraints and flexibility in the design of the dosage form. Developing oral controlled release tablets for highly water-soluble drugs with constant release rate has always been a challenge to the pharmaceutical technologist. Most of these highly water-soluble drugs, if not formulated properly, may readily release the drug at a faster rate and are likely to produce toxic concentration on oral administration. Hence, it is a challenging task to formulate a suitable dosage form for controlled delivery of highly water-soluble drugs.

Losartan potassium, was chosen as a drug having high solubility. Losartan potassium plays a major role in treating hypertension. It acts as an angiotensin antagonist. It's the drug with lower sideeffects so used widely. Because of its high solubility, short half-life and therapeutic use in such diseases, it is considered as an ideal drug candidate for the design of oral controlled release dosage form. It has been studied that a matrix tablet containing hydroxypropyl methyl cellulose K100M, ethyl cellulose and xanthan gum for oral controlled delivery of Losartan Potassium has been formulated with greater significance; hence it was decided to check the *in-vitro* drug-polymer study in formulating a sustained release tablet for Losartan Potassium.

REFERENCES

1. Agarwal R.K, Jain, Hemant K. and Singhai A.K. Estimation of Losartan potassium from tablets. Indian Drugs, 2000; 37(5): 26-30.
2. Bankar G.S. and Rhodes C.T. Eds. Modern Pharmaceutics. 3rd edn., Marcel Dekker, Inc. New York, 1996; 668-669.
3. Basak S.C, Jayakumar R.B.M and Lucas M.K. Formulation and release behaviour of sustained release Ambroxol hydrochloride HPMC matrix tablet. Indian Journal of Pharmaceutical Sciences, 2006; 68(5): 594-597.
4. Benson J.R, Nai Hong L. and William L. New polymer enables near Zero-Order release of drugs. Drug Delivery Technology, 2005; 5(2): 48-55.
5. Brahmankar D.M. and Jaiswal S.B. Biopharmaceutics and Pharmacokinetics A Treatise. 1st edn., Vallabh Prakashan, New Delhi, 1995; 35: 335.
6. Anton S, Kottai M.A, Wagh B.P. and Manavalan R. Formulation Development and Evaluation of Ondansetron Hydrochloride Sustained release Matrix tablets. Journal of Pharmaceutical Sciences and Research, 2009; 1(4): 48-54.
7. Aulton M.E. Eds. Pharmaceutics: The science of dosage form design. 2nd edn., Churchill Livingstone, New York, 2002; 487-488: 492-495.
8. Bandyopadhyay A.K. Novel drug delivery systems. 1st edn., Everest publishing house, Pune, 2008; 6-7.