WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 13, Issue 1, 1163-1171. Research Article ISSN 2277–7105

FORMULATION AND IN VITRO EVALUATION OF FLOATING TABLETS OF LOSARTAN POTASSIUM

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Article Received on
03 November 2023,

Revised on 24 Nov. 2023,
Accepted on 14 Dec. 2023

DOI: 10.20959/wjpr20241-30706

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ABSTRACT

The preformulation parameters like organoleptic properties, angle of repose, bulk density, tapped density, Hausner's ratio, carr's index and compressibility index of pure drug was evaluvated and complied with the pharmacopoeial specifications. FTIR studies showed there was no interaction between drug and polymer. Gastro retentive floating matrix tablets of Losartan potassium were successfully prepared with hydrophilic polymers like HPMC K4M, HPMC K15M., HPMC 100M. The formulated batches were evaluated for physicochemical parameters, floating properties and dissolution profiles. From the evaluation results, it was observed that the tablets contain the higher viscosity HPMC showed long floating lag time when compared to tablets prepared with lower viscosity HPMC. The physical properties like hardness, weight variation and friability of majority of the batches complied with the pharmacopoeial specifications. The drug content of all tablets was in the range of 95 – 100%. *In vitro* dissolution study of all the formulations was done in 0.1 N HCL. The release rate was faster with lower viscosity grades of HPMC, probably owing to less polymer entanglement and less gel strength and also to the larger effective molecular diffusion area at lower viscosity as compared with higher viscosity grades of HPMC. The tablets containing HPMC K4M (F2) showed satisfactory results with short floating lag time (69 sec) total buoyancy time more than 12 h, cumulative % drug release (99.33) and controlled drug release up to 12 h. So F2 was taken for studies. The accelerated stability was carried for F2 formulation and shown no much change in physical parameters and cumulative % drug release. Hence formulation F2 conformed as stable. Hence it was concluded that formulation F2 choosen as optimum formulation. However *In vivo* studies and development of suitable packaging materialare made for future continuation of this experimental work.

KEYWORDS: Evaluation, Dosage form, Drug release, Viscosity, Invivo studies.

INTRODUCTION

The oral route currently represents the most predominant and preferable route of drug delivery. Unlike majority of parenteral dosage forms, it allows ease of administration by the patient and it's the natural, and therefore a highly convenient way for substances to be introduced into the human body. Oral drug delivery systems have progressed from conventional immediate release to site-specific delivery over a period of time. Every patient would always like to have an ideal drug delivery system possessing the two main properties that are single dose or less frequent dosing for the whole duration of treatment and the dosage form must release active drug directly at the site of action. Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage forms.

1. The oral dosage form has survived due to
2. Relatively simple and inexpensive to make
3. Convenient for the patient
4. Technology is easy to adapt to changing needs of the drug substance
5. Simplifies the regulatory approval process.

Pharmaceutical products designed for oral delivery are mainly conventional drug delivery systems, which are designed for immediate release of drug for rapid/immediate absorption.

Limitations of the Conventional Drug Delivery System

1. Drugs with short half-life require frequent administration, which increases chances of missing the dose of drug leading to poor patient compliance.
2. A typical peak-valley plasma concentration-time profile is obtained which makes attainment of steady state condition difficult.
3. The unavoidable fluctuations in the drug concentration may lead to under medication or overmedication as the steady state concentration values fall or rise beyond the therapeutic range.
4. The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever overdosing occurs.

In order to overcome the drawbacks of conventional drug delivery systems, several technical advancements have led to the development of controlled drug delivery system that could

revolutionize method of medication and provide a numberof therapeutic benefits.

Over the years, as the expense and complications involved in marketing new drug entities have increased with concomitant recognition of the therapeutic advantages of controlled drug delivery, greater attention has been focused on the development of modified release dosage forms. Modified release systems have been developed to improve the pharmacokinetic profiles of active pharmaceutical ingredients (APIs) and patient compliance, as well as reducing side effects. Oral modified release delivery systems are most commonly used for 1) delayed release (e.g., by using an enteric coating); 2) extended release (e.g., zero-order, first-order, biphasic release, etc.); 3) programmed release (e.g., pulsatile, triggered, etc.) and 4) site specific or timed release (e.g., for colonic delivery or gastric retention). Extended, sustained or prolonged release drug delivery systems are terms used synonymously to describe this group of controlled drug delivery devices, with predictability and reproducibility in the drug release kinetics. Delayed release dosage forms are distinguished from the ones mentioned above as they exhibit a pronounced lag time before the drug is released. Oral extended release dosage forms offer the opportunity to provide constant or nearly constant drug plasma levels over an extended period of time following administration. Extended release DDS include single-unit, such as tablets or capsules, and multiple-unit dosage forms, such as mini tablets, pellets, beads or granules, either as coated (reservoir) or matrix devices. Controlled release systems designed to maintain plasma levels in therapeutic range and thus minimize the effects of such problems. Furthermore; controlled release systems reduce the dosing frequency, thereby improving patient compliance and therapeutic efficacy.

Drug products that provide “extended” or “sustained” drug release appeared as a major class of dosage form. Many terms as sustained-release, sustained-action, prolonged- action, controlled-release, extended-release, timed-release, and long- acting have been used to describe product types and features. For the most part, theseterms are used to describe orally administered dosage forms, whereas the term rate- controlled delivery is applied to certain types of drug delivery systems in which the rate of drug delivery is controlled by features of the device rather than by physiological or environmental conditions as gastrointestinal pH or drug transit time through the gastro intestinal tract (GIT).

This term has come into general use to describe dosage forms having drug release features based on time, course, and/or location which are designed to accomplish therapeutic or convenience objectives not offered by conventional or immediate-release forms.

Extended-release dosage form is one that allows a reduction in dosing frequency to that presented by a conventional dosage form.

Dosage form is designed to release the drug from the dosage form at a time after administration. The delay may be time- based or based on the influence of environmental conditions, as gastrointestinal pH.

METERIALS AND METHODS

MATERIALS: API Losartan, HPMC K4M, HPMC K15M, HPMCK100M, Lactose, Talc, Magnesium Stearate and Sodium bicarbonate. All materials should be formulation grade.

METHODS

Formulation of floating matrix tablets of Losartan potassium

The key ingredients included in the formulation are: Hydrophilic polymers: HPMC K4M, HPMC K15M, and HPMC K100M, Sodium carbonate, Lactose, Talc, Magnesium Stearate. Accurately weighed quantities of polymer and lactose were taken in a mortar and mixed geometrically to this required quantity of Losartan was added and mixed with the pestle. Accurately weighed quantity of sodium bicarbonate was then mixed with the drug blend. The powder blend was then lubricatedwith magnesium stearate and talc mixed for about 3 minutes. Finally this mixture was compressed on a 16-station rotary tablet machine using 10-mm standard flat-face punches.

Table 1: Composition of floating matrix tablets of Losartan potassium.

Ingredients (mg)	FORMULATION					
	F1	F2	F3	F4	F5	F6
Losartan pot.	50	50	50	50	50	50
HPMCK4M	75	100	125	-	-	-
HPMC K100M	-	-	-	75	100	125
$NaHCO_3$	50	50	50	50	50	50
Lactose	172	147	122	172	147	122
Mg. Stearate	1.5	1.5	1.5	1.5	1.5	1.5
Talc	1.5	1.5	1.5	1.5	1.5	1.5
Total wt (mg)	300	300	300	300	300	300

RESULTS AND DISCUSSIONS

Solubility analysis

Losartan potassium samples are examined and it was found to be soluble in water and phosphate buffer pH 1.2, 6.8 and 7.4.

Melting point of drug

The melting point of Losartan potassium was determined by capillary method, melting point of Losartan potassium was found to be 184°C. Melting point compared with USP standards that showed that drug was pure.

Loss of Drying

It was determined as per procedure given in methodology. The results were as follows

Table 2: Observations for loss on drying.

Test	Loss on drying	Observation
Loss on drying	Not more than 0.5%	0.42%

Drug powder characterization

Angle of repose

Table 3: Determinations of Angle of repose.

Material	Angle of repose
Losartan potassium Raw Material	24°55"

Flow properties

The method to determine the flow properties are given in methodology.

Table 4: Flow properties of pure drug.

Material	Bulk density	Tapped density	Carr's index (%)	Hausner's ratio (%)
Losartan potassium	0.346±0.04	0.390±0.07	15.51±0.01	1.18±0.06

EVALUVATION OF PRECONPRESSION PARAMETERS

Table 5: Precompression parameters.

Formulation code	Angle of repose (degree± SD)	BD (gm/ml±SD)	TD (gm/ml±SD)	Carr's index (%± SD)	Hausner's ratio (%± SD)
F1	24.11±0.04	0.316±0.01	0.366±0.02	14.64±0.06	1.07±0.05
F2	23.06±0.01	0.325±0.03	0.388±0.04	15.22±0.07	1.08±0.04
F3	26.03±0.03	0.338±0.06	0.382±0.01	13.64±0.04	1.12±0.02
F4	25.01±0.07	0.348±0.04	0.392±0.07	16.56±0.01	1.18±0.06
F5	22.96±0.09	0.297±0.03	0.321±0.03	13.11±0.03	1.15±0.03
F6	25.72±0.06	0.261±0.01	0.335±0.01	15.26±0.01	1.14±0.01

Evaluation of physical parameters of floating matrix tablets of Losartan potassium

Table 6: Physical parameters of floating matrix tablets of Losartan potassium.

Batch No	Tablet Thickness (mm)	Weight Variation(mg)	Hardness Kg/cm^2	Drug content (%)	Friability (%)	Lag time (sec)	Total floating time (sec)
F1	3.53±0.05	351±7.2	4.1±0.4	98.77±1.2	0.45	66	>12
F2	3.52±0.07	351±8.3	4.2±0.3	97.5±0.98	0.44	69	>12
F3	3.54±0.06	353±7.1	4.05±0.6	96.5±0.43	0.37	71	>12
F4	3.52±0.03	353±9.4	4.01±0.4	93.4±1.43	0.52	81	>12
F5	3.53±0.08	352±7.8	4.01±0.2	86.7±0.56	0.53	74	>12
F6	3.53±0.04	351±9.4	4.2±0.2	99.8±1.43	0.28	71	>12

SWELLING STUDIES

Table 7: Percent swelling of formulations.

Time (hr)	F1	F2	F3	F4	F5	F6
1	15.42	21.84	23.54	16.98	22.88	22.46
2	19.97	34.34	37.66	22.48	35.74	36.43
3	42.18	52.34	56.64	48.35	53.69	54.67
4	60.23	71.27	75.65	69.18	72.35	78.75
6	79.88	84.75	88.79	81.84	90.43	99.37
8	68.27	79.29	80.28	79.58	82.68	88.15
10	61.16	72.37	76.86	76.01	76.94	82.63
12	59.36	68.49	71.37	70.98	73.28	78.56

IN VITRO DRUG RELEASE STUDY

Table 8: Cumulative Percentage drug release of formulations.

S. No	Time (hrs)	F1	F2	F3
1	0	0	0	0
2	1	21.22	19.97	18.50
3	2	33.13	29.13	26.70
4	4	50.56	47.00	40.36
5	6	73.18	64.46	62.83
6	8	99.91	73.61	75.07
7	12	-	99.33	92.88

S. No	Time (hrs)	F4	F5	F6
1	0	0	0	0
2	1	17.98	15.17	14.83
3	2	29.98	24.41	20.57
4	4	47.55	41.41	36.70
5	6	63.52	55.66	50.41
6	8	76.57	69.32	61.12
7	12	95.84	85.33	83.81

7.9 STABILITY STUDIES

In the present study, stability studies were carried out on formulation F2. The tablets were stored at 40 ± 2^0 C 75 ± 5 % RH for a duration of three months. The selected formulation was evaluated for stability studies.

The formulationwere stored at 40°C at 75%RH for 3 months and analysed for their physical parameters, drug content and friability after 3rd month the data were showed in table no 29.

Table 9: Physical parameters studies.

	Drug content (%)	Hardness(kg/cm^2)	Friability (%)
After 1 month	99.33±0.17	4.1±0.3	0.45
After 2 months	99.12±0.15	4.0±0.42	0.46
After 3 months	99.12±0.15	4.0±0.42	0.46

From the above tables (table no 29 & 30) it was observed there is no much change in its physical properties and % drug release. Hence formulation (F2) conformed stable.

SUMMARY AND CONCLUSION

The preformulation parameters like organoleptic properties, angle of repose, bulk density, tapped density, Hausner's ratio, carr's index and compressibility index of pure drug was evaluvated and complied with the pharmacopoeial specifications. FTIR studies showed there was no interaction between drug and polymer. Gastro retentive floating matrix tablets of Losartan potassium were successfully prepared with hydrophilic polymers like HPMC K4M, HPMC K15M., HPMC 100M. The formulated batches were evaluated for physicochemical parameters, floating properties and dissolution profiles. From the evaluation results, itwas observed that the tablets contain the higher viscosity HPMC showed long floating lag time when compared to tablets prepared with lower viscosity HPMC. The physical properties like hardness, weight variation and friability of majority of the batches complied with the pharmacopoeial specifications. The drug content of all tablets was in the range of 95 – 100%. *In vitro* dissolution study of all the formulations was done in 0.1 N HCL. Therelease rate was faster with lower viscosity grades of HPMC, probably owing to less polymer entanglement and less gel strength and also to the larger effective molecular diffusion area at lower viscosity as compared with higher viscosity grades of HPMC. The tablets containing HPMC K4M (F2) showed satisfactory results with short floating lag time (69 sec) total buoyancy time more than 12 h, cumulative % drug release (99.33) and controlled drug release up to 12 h. So F2 was taken for studies. The accelerated stability was carried for F2 formulation and

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BIBLIOGRAPHY

1. Amit, K., Nayak, R.M., Biswarup, D. Gastroretentive drug delivery systems, a review, Asian Journal of Pharmaceutical and Clinical Research, 2010; 3(1): 2-10.
2. Anand, P., Moin, M., Dushyant, S., Vishnu, P. development and In Vivo floating behavior of Verapamil HCL intragastric floating tablets, AAPS PharmSciTech, 2009; 10(1): 310-315.
3. Caldwell, L.J.L., Gardner., Colin, R., Cargill., Robyn, C. drug delivery device which can be retained in the stomach for a controlled period of time. Merck & Co., Inc., 1988a; (Rahway, NJ), United States.
4. Caldwell, L.J.L., KS), Gardner, Colin R. (Lawrence, KS), Cargill, Robyn C. (Lawrence, KS), Drug delivery device which can be retained in the stomach for a controlled period of time. Merck & Co., 1988b; Inc. (Rahway, NJ), United States.
5. Chang, R.K., Hsiao, C., Eudragit R.L., Pseudolatices R. S. Properties and Performance in Pharmaceutical Coating as a Controlled Release Membrane for Theophylline Pellets. Drug Dev. Ind. Pharm, 1989; 15: 187-196.
6. Chang, R.k., Peng, Y., Trivedhi., N., shukla, R. C., Sheskey, P.J., Quinn, M. E. Hand book of Pharmaceutical excipient, 2009; 6th ed: 385-395.
7. Chien, Y.W. Novel drug delivery systems. 2nd ed (NY):Marcel Decker, INC, 1992.
8. Chung, Y.L., Gordon, L.A., Rosemary, R.B., Fleshier, D., Carole, Y., Jennifer B.D. comparison of gstro intestinal pH in dogs and humans: Implications in the use of the beagle dog as a model for oral absorption in humans. J. Pharm. Sci., 1986; 75: 271-274.
9. Patel, D.M., Patel, N.M., Pandya, N.N., Jogani, P.D. Gastroretentive drug delivery system of carbamazepine: formulation optimization using simplex lattice design: a technical note. AAPS PharmSciTech, 2007a; 8(11): 50-57.
10. Davis, S.S., Stockwell, A.F., Taylor, M.J., Hardy, J.G., Whalley, D.R., Wilson, C.G., Bechgaard, H., Christensen, F.N., The effect of density on the gastric emptying of single- and multiple-unit dosage forms. Pharm. Res, 1986; 3: 208-213.
11. Elkhesen, Seham, A., Yassin, Alaa Eldeen, B., Alsuwaeh, Saleh, Alkhaled, Fayza, A., Invitro and inviovo evaluation of floating controlled release dosage forms of Verapamil

hydrochloride. Pharmazeutische, 2004; 66(11): 1364-1372.

12. Hoffman, A., Stepensky, D., Lavy, E., Eyal, S., Klausner, E., Friedman. Pharmacokinetic and pharmacodynamic aspects of gastro retentive dosage forms, Int. J.Pharm, 2004; 277: 141-153.
13. Hoffman, A., stepensky, D., Lavy, E., Eyal, S., Klausner, E., Friedman, M., pharmacokinetic and pahrmacodyanamic aspects of gastro retentive dosage forms. Int J Pharm, 2004; 277: 141-153.
14. Ichikawa, M., Watanabe, S., Miyake, Y. A New multiple-unit oral floating dosage system. Preparation and in-vitro evaluation of floating and sustained-release characteristics. J Pharma Sci, 1991; 80(11): 1062-066.
15. Ichikawa, M. K., Watanabe, S., Miyake, Y. Granule remaining in stomach. Eisai Co., Ltd, 1989; 711-720.