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Research Article

Design and In-vitro Characterization of Lisinopril Retentive Floating Tablets

T. Jahnavi*, Bh. Sriswetha, D. Raghava, K. Nageswara Rao

Department of Pharmaceutical Technology, K.G.R.L College of Pharmacy, Bhimavaram-534201, Andhra Pradesh, India

Abstract
Lisinopril is a potent, competitive inhibitor of angiotensin-converting enzyme (ACE), the enzyme responsible for the conversion of angiotensin I (ATI) to angiotensin II (ATII). ATII regulates blood pressure and is a key component of the renin-angiotensin-aldosterone system (RAAS). Lisinopril may be used to treat hypertension and symptomatic congestive heart failure, to improve survival in certain individuals following myocardial infarction, and to prevent the progression of renal disease in hypertensive patients with diabetes mellitus and microalbuminuria or overt nephropathy. The object of the present work is preparing lisinopril gastro-retentive floating tablets. The gas-generating agent accrual was added in different concentrations with varying amounts of retardation polymers. HPMC K100M, Sodium alginate, and HPMC K200 were used as retarding polymers. The formulation blend was evaluated for various physicochemical properties and all the parameters were found to be within limits. The formulations F1-F9 were formulated and evaluated for various quality control parameters. All the formulations passed the tests and the results were within limits. From the dissolution data, it was evident that formulation F4 and F9 was found to be best with a maximum % drug release of 98.9% and 98.2% and a floating time of 12 hours.

Keywords: Lisinopril, gastro-retentive floating tablets

Article Info

Corresponding Author
T. Jahnavi
Department of Pharmaceutical Technology,
K.G.R.L College of Pharmacy,
Bhimavaram-534201, Andhra Pradesh, India

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Contents

1. Introduction

Lisinopril is highly soluble in water, sparingly soluble in methanol, and practically insoluble in ethanol. It would be more helpful to retain the drug in the stomach for a prolonged period so as to achieve maximum absorption and bioavailability. Lisinopril shows pH-dependent solubility. So, gastro retentive floating tablet is a

desirable approach to prolong the residence time of the dosage form in the stomach or upper gastrointestinal tract until the drug is completely released from the system. The aim of this study was to formulate and evaluate gastro retentive floating tablets of Lisinopril.

2. Methodology

Materials: Lisinopril, HPMC K100M, Sodium alginate, Sodium bicarbonate, Citric acid, Isopropyl alcohol, Magnesium stearate, Talc.

Analytical Method Development Preparation of 0.1 N Hydrochloric Acid (pH 1.2): 8.5 ml of concentrated hydrochloric acid was taken and diluted with distilled water up to 1000 ml.

Determination of λ_{max} of Lisinopril in 0.1N HCL:

Procedure:

Working standard: 50mg of Lisinopril was weighed and dissolved in 50ml 0.1N HCL and then made up to a volume of 50ml with 0.1N HCL it giving 1000µg/ml ppm concentrated stock solution. **Dilution 1** From the working standard solution 1ml was diluted to 10ml with 0.1NHcl it will give 100µg/ml concentrated solution. This solution was scanned at the range of 200-400nm wavelength light corresponding scan spectrum curve was noted. The corresponding wavelength having the highest absorbance is noted as λ_{max}

Construction of calibration curve of Lisinopril in 0.1N HCL:

Procedure:

Working standard:

50mg of Lisinopril was weighed and dissolved in 50ml 0.1N HCL and then made up to a volume of 50ml with 0.1N HCL it giving µg/ml concentrated stock solution.

Dilution 1

From the working standard solution 1ml was diluted to 10ml with 0.1NHcl it will give 100µg/ml concentrated solution. From dilution 1, take 0.5, 1, 1.5, 2, and 2.5ml of solution and dilute up to mark in a 10ml volumetric flask to obtain 5, 10, 15, 20, and 25µg/ml concentrated solutions. This solution's absorbance was noted at $\lambda_{max=2}$

Method of Preparation:

In this work, the direct compression method has been employed to prepare floating matrix tablets of Lisinopril with, HPMC K 100M, Sodium alginate, and HPMC K200M. All the ingredients were accurately weighed and passed through mesh # 40. Then granulation with Isopropyl alcohol and dry in a hot air oven. The above blend was lubricated with # 60 Sieve passed Magnesium stearate and talc. The final granules were compressed into tablets using 16 station tablet compression machines with an average hardness of 4.0kg/cm^2, by using an 8mm to 10mm die.

3. Results and discussion

Pre compression Evaluation Parameters of Lisinopril

Floating Formulation Blend: The powder blends were prepared by mixing various ingredients mentioned and used for the characterization of various flow properties of the powder.

Bulk density: The bulk density of all the formulations was found to be in the range of 0.522 to 0.401(gm/cm3) showing that the powder has good flow properties.

Tapped density: The tapped density of all the formulations was found to be in the range of 0.581 to 0.460 showing the powder has good flow properties.

Compressibility index: The compressibility index of all the formulations was found to be ranging between. 18.09 to 12.36 which shows that the powder has good flow properties.

Hausner ratio:

All the formulations have shown the Hausner ratio ranging between 1.25 to 1.05 indicating the powder has good flow properties.

Angle of repose: All the formulations have shown the Angle of repose values ranging between 31.11 to 22.17 indicating the powder has good flow properties.

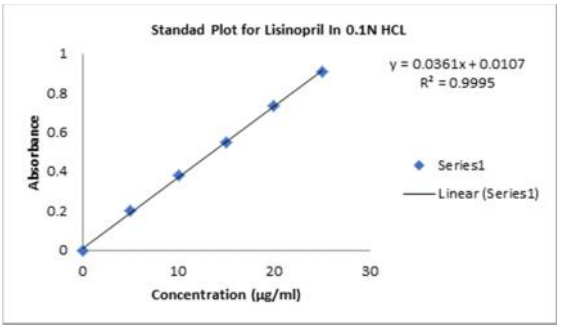

Fig.1: Standard calibration curve of Lisinopril in 0.1N HCl at λmax =221nm

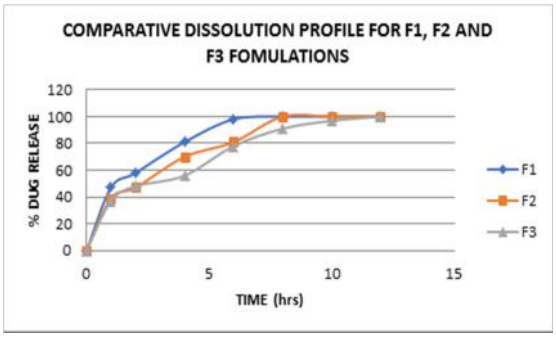

Fig.2: comparative dissolution profile for F1, F2, and F3 formulations

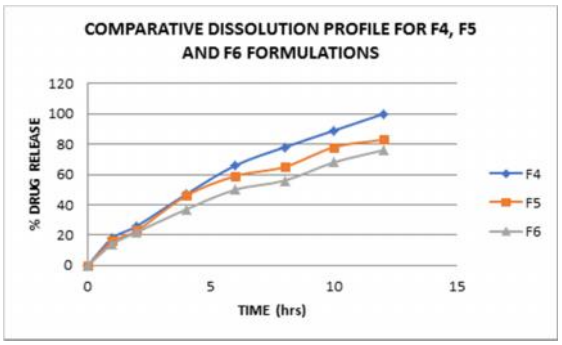

Fig.3: comparative dissolution profile for F4, F5, and F6 formulations

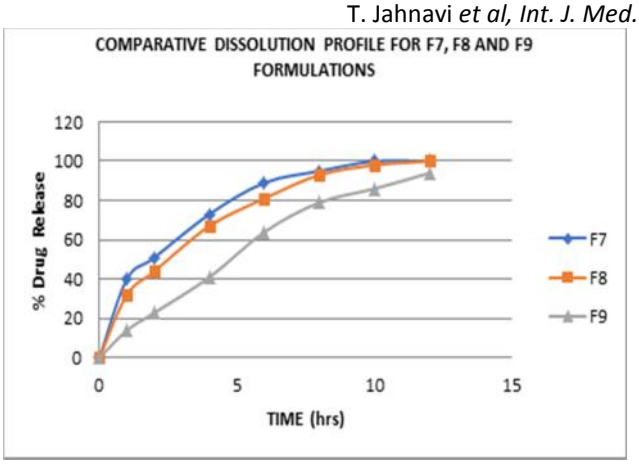

Figure-4: comparative dissolution profile for F7, F8, and F9 formulations

Post-Compression Evaluation Parameters of Lisinopril Floating Tablets:

Appearance:

The tablets were observed visually and did not show any effect such as capping, chipping, and lamination.

Physical characteristics:

The physical characteristics of Lisinopril floating tablets (F1 to F9) such as weight variation, thickness, hardness, friability, and drug content were determined and results of the formulations (F1 to F9) were found to be within the limits specified in official books.

(a) Thickness

Thickness and diameter specifications may be set on an individual product basis. Excessive variation in the tablet thickness can result in problems with packaging as well as consumer acceptance. There is no marked variation in the thickness of tablets within each formulation indicating uniform behavior of powders throughout the compression process. The thickness of the tablets of all formulations was found to be within the range of 5.3 to 5.9mm.

(b)Hardness:

A difference in tablet hardness reflects the difference in tablet density and porosity. The hardness of tablets was found to be in the range of 5.9 Kg/cm2 to 6.3 Kg/cm2

(c) Percentage friability

Percentage friability of all formulations was found to be in the range of 0.48% to 0.68%. This indicates good handling properties of the prepared tablets.

(d) Weight variation

The average weight of the tablet is 300mg. The pharmacopoeia limit for percentage deviation is ±5%. The weights of all tablets were ranged from 299mg to 301mg.

(e) Drug content

All the floating tablet formulations shown good uniformity in drug content and they contain 99.67 to 100.21% of Lisinopril which is within the specified limit.

Inference:

- The variation in weight was within the limit
- The thickness of the tablets was found to be between 5.34-5.91 mm.
- The hardness for different formulations was found to be between 5.9 to 6.3 kg/cm^2, indicating satisfactory mechanical strength
- The friability was <1.0% W/W for all the formulations, which is an indication of good mechanical resistance of the tablet.
- The drug content was found to be within limits of 98 to 102 %.
- The FLT was found to be within limits of < 2 min.
- The formulations having matrix integrity and TFT upto10-12 hrs.

In-vitro buoyancy studies: To provide in vitro buoyancy, an effervescent approach was selected. Sodium bicarbonate was added as a gas-generating agent. As the dissolution medium (0.1N HCl) imbibed into the tablet matrix, the interaction of acidic fluid with sodium bicarbonate resulted in the generation of CO_2. The generated gas was entrapped and protected within the polymer thus decreasing the density of the tablet. As the density of the tablet falls below 1, the tablet becomes buoyant. The system should float in a few minutes after contact with gastric fluid to prevent the dosage form from transiting into the small intestine together with food. All the formulations (F1 to F9) showed a floating lagtime of <81 sec.

Table-1: Formulations table of GRFT

Ingredients	HPMC K100M alone			HPMC K100M + Sodium Alginate			HPMC K200M alone		
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Intra granular									
Lisinopril	10	10	10	10	10	10	10	10	10
HPMC K100M	20	40	60	20	40	60	-	-	-
Sodium Alginate	-	-	-	10	10	10	-	-	-
HPMC K200M	-	-	-	-	-	-	20	40	60
Avicel PH101	128	108	88	118	98	78	128	108	88
Sodium Bicarbonate	30	30	30	30	30	30	30	30	30
Citric Acid	6	6	6	6	6	6	6	6	6
Isopropyl alcohol	*q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	*q.s.	q.s.	q.s.
Extra granular									
Magnesium Stearate	3	3	3	3	3	3	3	3	3

Talc	3	3	3	3	3	3	3	3	3
Average Weight	200	200	200	200	200	200	200	200	200

Table-2: Pre-compression studies of Lisinopril Floating tablets

Formulation Code	Pre-compression studies				
	Angle of repose (^{o})	Bulk density (g/cc)	Tapped density (g/cc)	Carr's Index (%)	Hausner's Ratio
F1	22.17±0.15	0.515±0.015	0.522±0.008	13.15±1.04	1.10±0.07
F2	31.11±0.11	0.471±0.011	0.476±0.012	16.23±0.23	1.21±0.11
F3	25.71±0.13	0.505±0.005	0.527±0.015	14.26±0.65	1.15±0.31
F4	23.31±0.13	0.522±0.023	0.519±0.022	12.36±0.26	1.09±0.23
F5	28.27±0.15	0.496±0.065	0.499±0.053	17.42±0.96	1.12±0.08
F6	24.67±0.12	0.481±0.022	0.511±0.024	18.09±0.52	1.07±0.13
F7	22.32±0.13	0.500±0.025	0.581±0.016	13.12±0.61	1.16±0.21
F8	27.37±0.15	0.441±0.062	0.510±0.022	13.27±0.23	1.25±0.36
F9	23.17±0.13	0.401±0.003	0.462±0.014	13.10±0.17	1.5±0.12

Table-3: Post-Compression Studies

Formulation Code	Average weight	Thickness	%Friability	% Drug Content	Hardness (Kg/cm^2)	Floating lag time (sec)	Total floating time
F1	300.4±0.6	5.82±0.34	0.59	99.98±0.18	5.9±0.26	20 ± 0.51	Up to 10
F2	300.2±0.4	5.91±0.23	0.68	100.21±0.20	6.2±0.25	40 ± 0.21	Up to 12
F3	299.6±0.4	5.84±0.10	0.58	99.67±0.12	6.3±0.21	80 ± 0.61	Up to 12
F4	300.0±0.3	5.88±0.10	0.59	100.32±0.14	5.9±0.23	20 ± 0.71	Up to 12
F5	300.6±0.3	5.87±0.21	0.62	100.65±0.18	6.3±0.13	30 ± 0.81	Up to 12
F6	300.9±0.3	5.34±0.14	0.59	99.89±0.22	6.1±0.20	35 ±0.51	Up to 12
F7	300.2±0.1	5.72±0.10	0.48	100.32±0.10	6.1±0.23	24 ± 0.31	Up to 12
F8	300.7±0.3	5.83±0.18	0.52	100.43±0.12	6.3±0.10	20 ± 0.81	Up to 12
F9	300.9±0.3	5.43±0.12	0.58	99.92±0.18	6.1±0.20	36 ± 0.71	Up to 12

Table-4: Drug release data of Lisinopril floating matrix tablets

Time (hrs)	% Drug released								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	0	0	0	**0**	0	0	0	0	**0**
1	47	39	37	**18**	16	14	40	32	**14**
2	58	47	48	**26**	23	22	51	44	**23**
4	81	70	56	**47**	46	37	73	67	**41**
6	98	81	78	**66**	59	50	89	81	**64**
8	100	100	91	**78**	65	56	95	93	**79**
10	100	100	97	**89**	78	68	100	98	**86**
12	100	100	100	**100**	83	76	100	100	**94**

4. Conclusion

The object of the present work is preparing Lisinopril gastro-retentive floating tablets. The gas-generating agent sodium bicarbonate was added in different concentrations with varying amounts of retardation polymers. HPMCK 100M, Sodium alginate, and HPMC K200M were used as retarding polymers. The formulation blend was evaluated for various physicochemical properties and all the parameters were found to be within limits. The formulations F1-F9 were formulated and evaluated for various quality control parameters. All the formulations passed the tests and the results were within limits. From the dissolution data, it was evident that formulation F4 and F9 was found to be best with a maximum % drug release of 98.9% and 98.2% and a floating time of 12 hours.

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