ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Formulation and Evaluation of Ramipril SR Matrix Tablets by Using Tamrindus Kernal Mucilage as Release Retardent

P Sivannarayana[1]*, A Prameela Rani[2], and V Saikishore[3]

[1]Vishwabharathi College of pharmaceutical Sciences, perecherla, Guntur, A.P.
[2]University College of Pharmaceutical Sciences, Acharya Nagarjuna University, Guntur, A.P.
[3]Bapatla College of Pharmacy, Bapatla, Guntur (dt), A.P.

ABSTRACT

The aim of this work is to design sustained release matrix tablets of Ramipril using tamarind kernels mucilage and evaluate the effect of polymer on release pattern of the drug. Ramipril is an antihypertensive drug used in the treatment of hypertension. The biological half life of Ramipril is about 2-4 hr; therefore it requires multiple dosing to maintain therapeutic drug blood level. Ramipril sustained release matrix tablets were prepared by wet granulation method by using starch as granulating agent. The dissolution studies were carried out in 900ml phosphate buffer (pH 6.8) for 12 hours. The release mechanism was explored with zero order, first order, Higuchi equation and Korsmeyer's equation. It was found that the release of drug from matrix tablet decrease with the increasing of percentage of polymer.

Keywords: Sustained release, matrix tablet, tamarind kernels mucilage.

Corresponding author

ISSN: 0975-8585

INTRODUCTION

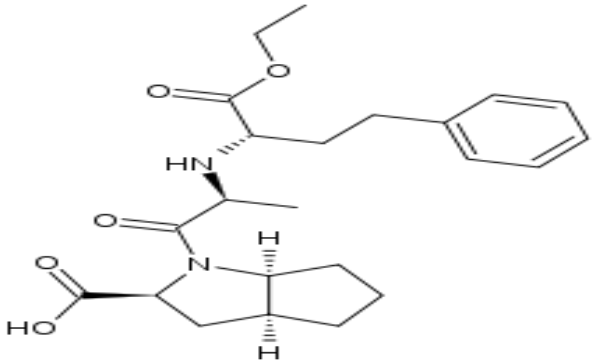
Oral drug administration has been the predominant route for drug delivery due to the ease of administration, patient convenience and flexibility in formulations. However, it is a well accepted fact today that drug absorption throughout the gastrointestinal tract is not uniform. Using currently utilized technology, oral drug delivery for 12 or even 24 hours is possible for many drugs that are absorbed uniformly from GI tract.

The design of oral controlled drug delivery system should be primarily aimed to achieve the more predictability and reproducibility to control the drug release, drug concentration in the target tissue and optimization of the therapeutic effect of a drug by controlling its release in the body with lower and less frequent dose.

The controlled release systems for oral use are mostly solid and based on dissolution or diffusion or a combination of both the mechanisms in the control of release rate of drug [1-4].

Sustained release dosage forms are designed to achieve a prolonged therapeutic action by continuous releasing medication over an extended period of time after administration of single dose. In order to achieve steady level of medication, biodegradable polymer may play a vital role due to their biodegradability [5].When hydrophilic matrices interact with aqueous media (water, buffers, physiological fluids etc.) both the polymer hydration and the dissolving of soluble components take place. Dissolution of the drug at tablet surface cause a burst effect in the release profile of the system. This is more or less pronounced depending on the drug solubility and the polymer hydration rate [6, 7].

Ramipril is an antihypertensive drug used in control of blood pressure. Ramipril belonging to ACE inhibitors group. Ramiprilat, the active metabolite of the Prodrug ramipril, is a potent and long acting angiotensin-converting enzyme (ACE) inhibitor. In plasma and tissue, ACE catalyses the conversion of angiotensin I to the vasoconstrictor angiotensin II and also the breakdown of the vasodilator bradykinin. The vasodilatation induced by Ramipril causes a reduction in blood pressure pre-load and after-load.



TAMARIND KERNELS MUCILAGE

The tamarind kernels mucilage can be obtained from the seeds of Tamarindus indica.

Isolation of Tamarind seed polysaccharide [8]

The seeds of Tamarindus indica were washed thoroughly with water to remove the adhering materials. Then, the reddish testa of the seeds was removed by heating seeds in sand in the ratio of 1:4 (Seed: Sand). The testa was removed. The seeds were crushed lightly. The crushed seeds of Tamarindus indica were soaked in water separately for 24 h and then boiled for 1 h and kept aside for 2 h for the release of mucilage into water. The soaked seeds were taken and squeezed in a muslin bag to remove marc from the filtrate. Then, equal quantity of acetone was added to precipitate the mucilage. The mucilage was separated. The separated mucilage was dried at temperature 50°C, powdered and passed through sieve number 80. The dried mucilage was powdered and stored in airtight container at room temperature.

Characterization of selected polysaccharide [9-11]

Identification tests for gum:

In freshly prepared corallin soda, the sample was mounted, covered with a cover slip and after a few seconds it was irrigated with 25% sodium carbonate solution. Identification tests for gums as recommended by FAO (1991) were carried out.

Determination of purity of gum:

To determine the purity of gum tests for alkaloids, carbohydrates, flavonoids, steroids, terpins, saponins, tannins and phenols were carried out.

Organoleptic Evaluation:

The Organoleptic evaluation refers to the evaluation of colour, odour, shape, taste and special features which include touch and texture. The majority of information on the identity, purity and quality of the material can be drawn from these observations. The values are shown in the table (1).

Physicochemical characterization of mucilage [12]

The physicochemical properties of mucilage like true density, bulk density, swelling index, angle of repose, compressibility index, Hausner's ratio, solubility, pH, melting point were studied. The solubility parameter is shown in table (2).

Tapped density (g/cc)	: 0.781 ± 0.02
Bulk density (g/cc)	: 0.651 ± 0.04
Angle of repose (^{0})	: 29.50 ± 0.12

Compressibility index (%)	: 16.64 ± 0.04
Hausner's ratio	: 1.02 ± 0.09
pH	: 6.81 ± 0.21
Melting point	: 240 -260
Swelling index (%)	: 1700 ± 0.56

Table-1: Organoleptic properties of tamarind kernel gum

Parameter	Tamarind seed polysaccharide
Colour	Cream
Odour	Odour less
Taste	Taste less
Shape	Irregular
Touch& Texture	Hard and rough

Table-2: solubility profile of tamarind kernel gum

Solvent	Solubility behaviour
Cold water	Sparingly soluble
Warm water	Quickly soluble forming a viscous colloidal solution
Ethanol	Insoluble
Methanol	Insoluble
Acetone	Insoluble
Ether	Insoluble

MATERIALS AND METHODS

Materials

Ramipril was gifted from natco pharma ltd. Hyderabad, The tamarindus seeds are obtained from natural source. Microcrystalline cellulose, starch were purchased from SDfine chemicals, Mumbai, India and all other chemicals of analytical grade.

Preparation of Ramipril sustained release matrix tablets

Ramipril sustained release matrix tablets can be prepared by wet granulation method. In this method the drug pass through the sieve no: 40 and retention on sieve no: 60 is taken for the formulation. The polymers were weighed in require quantities. The drug should mix with polymer solution (granulating agent). Then finally the drug polymer mixture is dried and compressed as tablets. The Ramipril sustained release matrix tablets were prepared as per formula showed in the table (3).

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Table-3: Formula for the Preparation of Matrix Tablets of Ramipril:

s.no	Ingredients	Formulation batches			
		RF1(mg)	RF2(mg)	RF3(mg)	RF4(mg)
1	Ramipril	50	50	50	50
2	Tamarindus kernel powder	30	50	75	40
3	Microcrystalline cellulose	87.5	67.5	42.5	77.5
4	Starch	25	25	25	25
5	Magnesium stearate	2.5	2.5	2.5	2.5
6	Talc	5	5	5	5
7	Total weight (mg)	200	200	200	200

Evalution tests for Ramipril sustained release matrix tablets

Weight variation [13]:

The test is considered correct if not more than 2 tablets fall outside the range, if 20 tablets are taken for the test and not more than 1 tablet fall outside the range if only 10 tablets are taken for the test.

Hardness test [14]:

This is to force required to break a tablet in diametric compression. Hardness of the tablet is determined by Monsanto or Pfizer hardness tester. The hardness of 5 kg considered as suitable for handling the tablets.

Friability [14]:

This test performed to evaluate the ability to withstand abrasion in packing, handling and transporting. Initial weight of 20 tablets is taken and these are placed in the friabilator, rotating at 25 rpm for 4 min. the difference in the weight is noted and expressed as 1%. It should be preferably between 0.5 to 1.0%.

In-vitro Disintegration Test [15]:

The test was carried out on 6 tablets using Tablet disintegration tester ED-20 (Electrolab, Mumbai, India) distilled water at 37°C±2°C was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palable mass remaining in the apparatus was measured in seconds.

Dissolution test [13]:

The dissolution *test* for ramipril sr matrix tablets were done by USP paddle type apparatus using 900 ml of 6.8 pH of potassium dihydrogen orthophosphate buffer. The paddle speed was maintained at 100 rpm, and temperature of the medium was maintained at 370 c ±

ISSN: 0975-8585

0.5 0 c. the samples are withdrawn at an interval of 0.5,1,2,3,6,9,12 hours. The withdrawn samples are observed at UV spectrophotometer at λ max 290 nm. The percentage drug release values are shown in table (5).

Table-4: Evalution tests of tablets

S.no	Formulation batches	Hardness	Friability
1	RF1	4.7	0.11
2	RF2	5.7	0.09
3	RF3	6.2	0.04
4	RF4	5.2	0.06

Table-5: Dissolution studies of formulations

S.NO	FOR-BATCH	% DRUG RELEASE							
		0	0.5(hr)	1(hr)	2(hr)	3(hr)	6(hr)	9(hr)	12(hr)
1	RF1	0	27.4	38.10	54.2	58.4	67.7	76.7	86.8
2	RF2	0	26.03	36.1	44.2	53.2	63.3	72.2	83.5
3	RF3	0	25.7	35.29	43.7	48.7	58.8	70.0	77.8
4	RF4	0	26.89	36.42	45.9	54.3	65.5	75.6	84.5

Fig-2: Dissolution profile of formulated batches

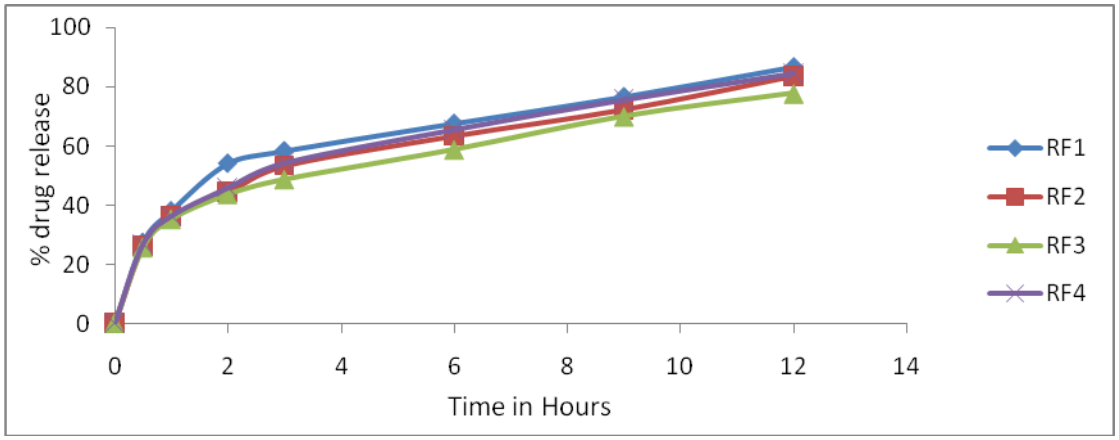

Fig -3: first order drug release pattern of Ramipril SR matrix tablet formulations

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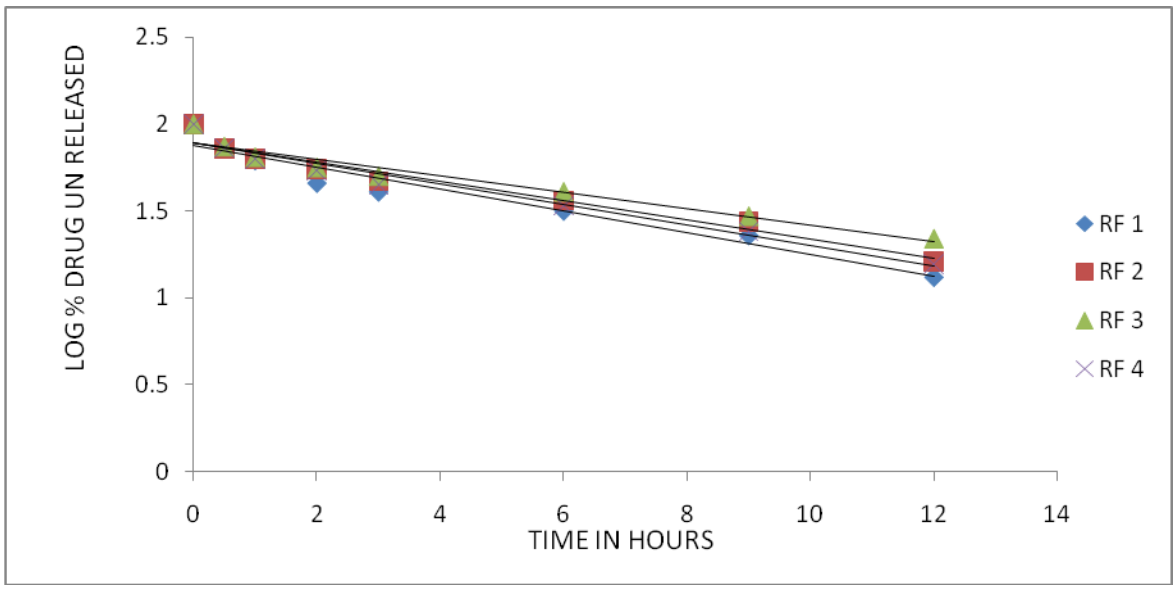
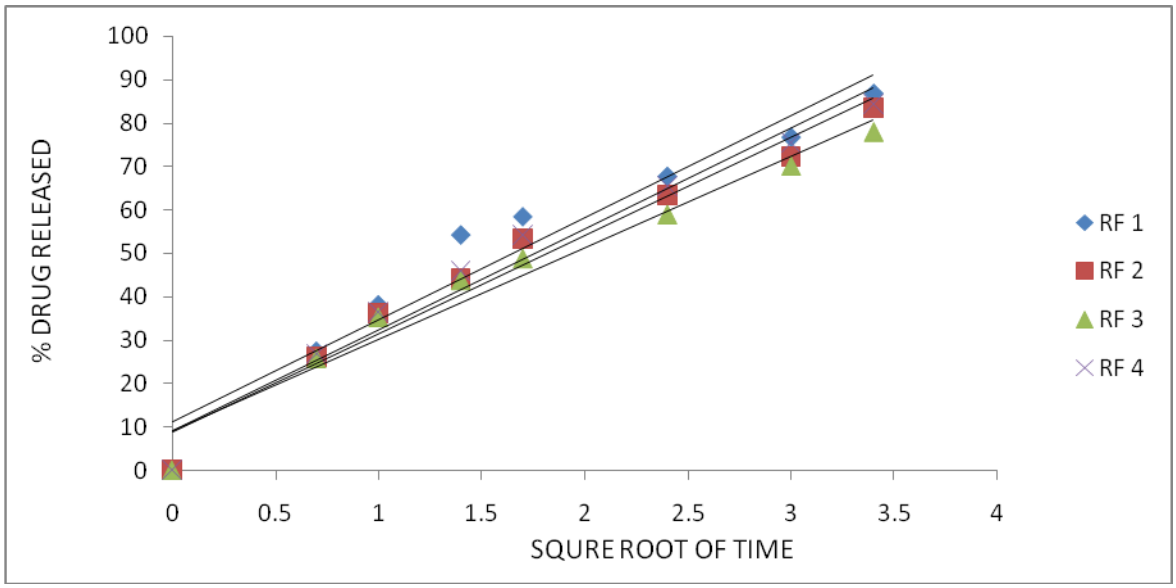


Fig –4: Higuche profile of Ramipril SR matrix tablet formulations



Fig–5: Korsmeyer peppas profile of Ramipril SR matrix tablet formulations

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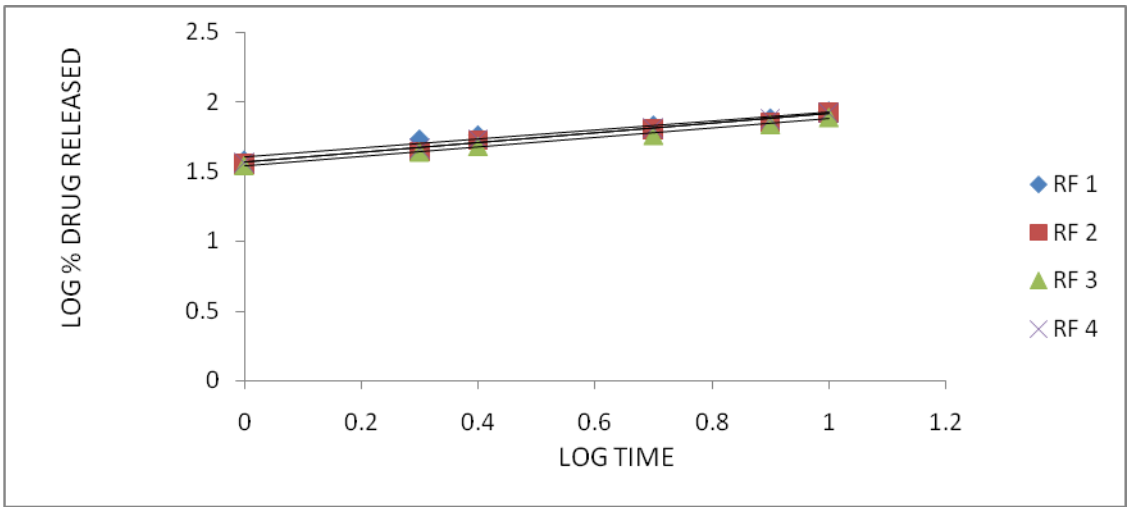

TABLE NO 6: THE DISSOLUTION KINETICS OF ALL RAMIPRIL SR MATRIX TABLETS

S.NO	FORMULATION BATCH	FIRST ORDER (R^2)	HIGUCHI (R^2)	PEPPAS (R^2)
1	RF 1	0.941	0.940	0.970
2	RF 2	0.954	0.965	0.982
3	RF 3	0.944	0.962	0.994
4	RF 4	0.960	0.967	0.990

RESULTS AND DISCUSSION

Drug content and physical evaluation of Ramipril matrix tablets was studied after preparing the matrix tablets, all the tablets of the proposed formulations were subjected to various evaluation tests such as hardness and friability, the results are shown in table(4).The release data obtained were treated according to zero-order (cumulative amount of drug release versus time), first order (log cumulative percentage of drug remaining versus time), Higuchi (cumulative percentage of drug release versus square root of time) and Korsmeyer-Peppas (log cumulative percentage of drug release versus log time) equation models.

The dissolution studies were carried out for the formulations RF1 to RF4 from the results, the formulations RF1, RF2, RF3& RF4 with polymer ratio 35, 50, 75, 40 respectively showed a good drug release profile and they reached the platue curve quickly.

The drug profile of RF3 show the good percentage drug release and it shows maximum percentage drug release at 12^{th} hour 83.5%.

CONCLUSION

From the above study we inferred that, the Tamarind kernel gum reduces the rate of release of Ramipril from tablet formulation.

The higher the molecular weight (or viscosity) of Tamarind kernel gum used, the greater the retardation of drug release. The release of Ramipril from Tamarind kernel gum matrix is almost diffusion / relaxation type of release.

Finally we concluded that the RF3 polymer drug ratio with higher concentration shows good retardant effect on the Ramipril tablet formulation and can be used for successful development of controlled release formulation of Ramipril.

REFERENCES

[1] Yie W Chien. Novel drug delivery systems, 2nd edition, revised and expanded, Marcel dekker, Inc., New York, Pg. no(a) 01-12, (b) 139-196,(c) 130-140.

[2] Joseph R Robinson, Vincent H Lee. Controlled drug delivery fundamentals and application, 2nd edition, revised and expanded, Marcelldekker, Inc., New York,Pg. no: (a) 08-13, (b) 373- 421.

[3] Ashok V Bhosale, Rahul V Talware, Sanjay D Swamy. Oral Novel Drug Delivery System, The Eastern Pharmacist, September 2000: 41- 43.

[4] Leon Lachman, Herbert A Lieberman. The theory and practice of Industrial Pharmacy. 3rd edition, Varghese publishing house., Bombay. Pg. no: 179-195, 430- 446, 317- 334.

[5] Chakraverty R. Preparation and evaluation of sustained release microsphere of norfloxacin using sodium alginate. International Journal Pharmaceutical Sciences and Research 2011; 3(1): 293-299.

[6] Huang X, Brazel CS. on the importance and mechanisms of burst release in controlled drug delivery- a review. J Control releas 2001; 73: 121-136.

[7] Madan F W. Rate Controlled Drug Delivery System. Int Pharm 1990; 24: 245- 261.

[8] Giriraj KT, Gowthamarajan K, Brahmaji G and Suresh B. J Scientific Ind Res 2002; 61: 529-532.

[9] Rosenthaler L. Eds, Bell G and Sons Ltd: London, 1930; 23 -155.

[10] Shah BS and Quadry JS. 3rd Edition, 1980; 16 - 24.

[11] Wallis TE. 3rd Edition, J.A. Churchill Ltd. London 1995; 111-115.

[12] Phani Kumar GK, Gangaraobattu, Kotha NS, Lova Raju. Isolation and Evaluation of Tamarind Seed Polysaccharide being used as a Polymer in Pharmaceutical Dosage Forms; RJPBCS 2011; 2(2):274-290.

[13] Indian Pharmacopoeia, 1996. 4th Ed, Ministry of Health and Family Welfare, Govt. of India. The controller of publications, New Delhi, A-54.

[14] Lachman L, A Lieberman and JL Kinig. The Theory and Practice of Industrial Pharmacy, Varghese Publishing House 1991: 67-68.

[15] Battue SK, MA Repay, S Maunder and MY Rio. Formulation and evaluation of rapidly disintegrating tablet Fenoverine tablets: Effect of superdisintegrants. Drug Dev Ind Pharm 2007; 33: 1225-1232.