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Design and Evaluation of Extended-Release Tablet Compositions Containing Oxaprozin: Integrating Concepts from Bioinformatics

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Abstract

The procured sample of Oxaprozin was tested for its identification. The manufacturer also was confirmed of quality and purity of sample. The sustained release tablets of Oxaprozin were prepared by wet granulation method, They were evaluated for weight variation, drug content, friability, hardness, and thickness for all batches (T-1 – T-10). The release of Oxaprozin from sustained release tablet of various formulations varied according to the ratio and degree of the polymer. In case of tablet of T1containing drug & HPMCK15M (quantity in mg). 200: 15: the release profile, was showing the release 102.69%. In case of tablets of T2 containing drug and HPMC K15M & HPMC K4M (in mg). 200:10:20 it was showing 100.25% release in 24 hours. In case of tablets of T3 containing drug polymer's (HPMCK15M, HPMCK4M in mg) 200: 15: 15: prepare to be seen in the effect of combination of polymers in release of drug but it was showing same release given 100.25% upto 24 hour. In case of tablets T4 containing drug and HPMC K15M & HPMCK 4M (in mg) 200: 10: 10 the release profile was showing drug release more than 100%. In case of tablets of T5 containing drug and HPMC K 4M & HPMC K15M PVP K30 (in mg) 200: 10: 10:10. Prepared the tablets. But it cannot maintain the release with in 100%. In case of tablets of T6 containing drug and HPMC K 15M (in Mg) 200: 5. It was seen the increase in release of drug and shown more than 100% drug release in 24 hour profile. In case of tablets T7, containing drug. HPMCK4M & HPMCK15M (in mg) 200:10:10 the release profile was showing drug release more than 100%. In case of Tablets T8 containing drug. HPMCK15M (in mg) 200 : 23. The release profile was showing drug release with in 24 hours. With very slower release than all formulations containing % drug release 99.56. Results of stability studies of batch T-8 indicates that it was stable at 40°C/75% + 5% relative humidity as there was no significant difference was observed for dissolution and average drug content data after two months.

Keywords*:* Formulation Development, Evaluation, Sustained Release, Oxaprozin.

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INTRODUCTION

Retention of drug delivery systems in the stomach prolongs overall gastrointestinal transit time improving oral bioavailability of the drugs that are having site specific absorption from the stomach or upper part of the small intestine. Therefore different approaches have been proposed to retain the dosage form in the stomach including bio adhesive systems, swelling, and expanding systems and delayed gastric emptying devices to achieve gastric residence time for sustained drug release [1]. The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve promptly and then maintain the desired drug concentration [2].

This deliberate control of drug release is achieved in sustained release dosage form as it prolongs the therapeutic effect by continuously releasing medication over an extended time after administration of a single dose [3].

The most employed method to modulate the sustained drug release is to include it in a matrix system. Because of their flexibility, hydrophilic polymer matrix systems are widely used in oral controlled drug delivery to obtain a desirable drug release profile, cost-effectiveness, and broad regulatory acceptance [4]. Matrix systems are also favored because of their simplicity, patient compliance than traditional drug delivery (TDS), which have many drawbacks like repeated administration and fluctuation in blood concentration level. In this type of drug delivery system, the drug is homogeneously dispersed throughout the matrix of crosslink of linear polymer chain [5]. It is assumed that from this type of drug delivery system, drug molecule come out from matrix by dissolution and then diffusion through the polymer structure [6]. As the drug is released, the distance for diffusion becomes greater and solid particles began to deplete. Most of the highly water-soluble drugs, if not formulated properly, may readily release the drug at a faster rate, and are likely to produce toxic concentration [6]. Hydrophilic polymers have become product of choice as an important ingredient for formulating sustained release formulations of highly water soluble drugs [7]. As the dissolution medium or biological fluid penetrates the dosage form, the polymer swells and drug molecules begin to move out of the system by diffusion at a rate determined by the nature and composition of the polymer as well as formulation technology [8].

Sustained release matrix tablets prepared by wet granulation technique using microcrystalline ethyl cellulose polymer and Bees wax showed good sustaining drug release concluding that sustained release tablet could be successfully combined with accurate control and prolongation of the drug release patterns [9, 10].

In pharmaceutical practice several approaches exist for administration of drugs to the patient. If the drug is given in conventional dosage form it has to be administered several time to produce desired therapeutic effect. Because of this frequent dosing fluctuation in plasma drug level occur. The pronounced fluctuation resulting from the conventional drug administration are likely to yield period of therapeutic effects, when the concentration falls below the minimum therapeutic level. Drug concentration can be controlled within the narrow therapeutic range by the use of sustained release systems, which will minimize the severity of side effects *Oxaprozin* is an Non Steroidal Anti Inflammatory Drug , with half life of 4–4.3 hours and requires Single daily doses to maintain adequate plasma concentrations. So it is selected to prepare a sustained release tablets. The objective of this present study to develop a competitive sustained release tablets Oxaprozin which release the drug in a sustained manner over a period of 24 hours, by using different polymers and study on there effect on release pattern.

PREFORMULATION STUDY

Preformulation stability studies are usually the first quantitativeassessment of chemical stability of a drug as well as stability in presence of other excipients. The primary objectives of this investigation are identification of stable storage conditions for drug in the solid state and identification of compatible excipients for a formulation as seen in Table 1 and Table 2.

Identification of Drug

The Identification of Drug was done by FT-IR Spectroscopy.

Method

Triturate 1–2 mg of the substance to be examined with 300–400 mg, unless otherwise specified, of finely powdered and dried potassium bromide or potassium chloride. These quantities are usually sufficient to give a disc of 10–15 mm diameter and a spectrum of suitable intensity. Infrared spectrophotometers are used for recording spectra in the region of 4000 650.

Drug Excipient Compatibility Study

Compatibility studies were conducted to investigate and predict physicochemical interaction between drug substance and excipents and therefore to select suitability of chemically compatible excipients.

STANDARD CURVE OF OXAPROZIN

Preparation of Phosphate Buffer pH 6.8

Accurately weighed quantity of 27.218 g of potassium dihydrogen phosphate was dissolved in distilled water and diluted with distilled water upto 1000 ml. 50 ml of above solution was taken in a 200 ml of volumetric flask, 22.4 ml of 0.2 M NaOH was added to the solution and then diluted with distilled water upto volume.

Preparation of Standard Curve in 6.8 PH Buffer

100 mg equivalent weighed of Oxaprozin was dissolved in 100 ml of phosphate buffer pH 6.8. The 10 ml of above solution was further diluted upto 100 ml with phosphate buffer pH 6.8. The resulting solution was serially diluted with phosphate buffer pH 6.8. to get drug concentration 5,10,15,20,25 µg/ml. The absorbance of the solutions was measured against phosphate buffer pH 6.8 as a blank at 274.0 nm using double beam UV visible spectrophotometer. The plot of absorbance v/s concentration (µg/ml) was plotted, and data was subjected to obtain linear regression analysis as seen in Table 3.

Observation

The standard calibration curve of drug in phosphate buffer pH 6.8 depicted as Figure. The data of absorbance was shown in Table The datahad correlation coefficient of 0.9992.

Table 1. Formulation of batch T-1 to T-5.

Formulation Ingredients	**Trial Batches**				
	ASR-01	***ASR-02***	***ASR-03***	***ASR-04***	***ASR-05***
Oxaprozin	200	200	200	200	200
MCC	67	63	62	74	72
PVP K 30	10	9	10	8	10
I.P. A	Q. S	Q. S	Q. S	Q. S	Q. S
HPMC K4M	-	20	15	10	10
HPMC K 15	15	10	15	10	-
ACRYPOL934 P	10	-	-	-	10
MAGSTEARATE	5	5	5	5	5
AEROSIL	3	3	3	3	3

Table 2. Formulation of batch T-6 to T-10.

Formulation Ingredients	**Trial Batches**				
	ASR-06	***ASR-07***	***Final***	***ASR-09***	***ASR-10***
Oxaprozin	200	200	200	200	200
MCC	71	67	49	53	42
PVP K – 30	11	10	10	10	10
I.P. A	Q. S	Q. S	Q. S	Q. S	Q. S
HPMC K4M	-	10	-	20	25
HPMC K 15	5	10	23	-	-
ACRYPOL934 P	15	5	20	19	25
MAGSTEARATE	5	5	5	5	5
AEROSIL	3	3	3	3	3
Total Weight	310 mg	310 mg	310 mg	310 mg	310 mg

Table 3. Physical parameters of tables of each batch.

B.No	Weigh Variation (mg)		Thickness (mm)		Hardness (kg/cm^2)	Friability (%)		Drug Content (%)
T1	310	1.97	4.66	0.2	6	0.62	0.03	101.65
T2	310	1.68	4.63	0.0	4	0.62	0.02	98.22
T3	310	3.05	4.37	0.3	4	0.42	0.05	103.99
T4	310	3.01	4.72	0.2	5	0.49	0.04	100.83
T5	310	1.84	4.69	0.3	6	0.65	0.03	96.98
T6	310	2.36	4.66	0.2	6	0.59	0.04	96.89
T7	310	3.14	4.60	0.3	4	0.67	0.02	96.42
T8	310	2.15	4.66	0.2	4	0.53	0.03	99.25
T9	310	3.14	4.60	0.3	6	0.65	0.03	99.73
T10	310	1.87	4.69	0.2	4	0.45	0.02	100.75

Table 4. Dissolution profile of batch No. T-1 to T-10 and marketed sample in 6.8 pH phosphate buffer.

B.No	Time in Hours (cumulative % drug release)						
	6.8 PH buffer						
	0	*2*	*4*	*8*	*12*	*16*	*24*
T1	0	25.65	50.48	79.25	91.25	99.52	102.
T2	0	22.68	40.17	72.58	89.24	97.77	100.
T3	0	18.85	39.45	65.95	90.58	99.01	100.
T4	0	20.65	40.25	72.56	92.68	99.67	102.
T5	0	26.98	49.65	75.82	95.62	101.24	101.
T6	0	24.98	42.78	70.98	85.24	92.57	101.
T7	0	25.64	45.65	75.58	90.14	99.65	102.

Manufacturing procedure of sustained release tablet of Oxaprozin Wet Granulation Method

Weight accurately Drug + HPMC K15M + PVP K-30 and Microcrystaline cellulose pass through 40 no sieves and mix properly for 3–5 minutes in a steel tub.

Prepare binder solution by dispersing PVP K30 in isopropyl alcohol as seen in Table 4.

Granulation of above mixture is done by prepared binder solution by kneading up to granulation end point is obtained (Dough mass). Pass the dough mass through 12 mess and keep it in a tray dryer for drying and finaly keep the loss on drying (LOD) up to 2–3%. Remove the driedgranules from oven and pass through 20 mess sieve to get optimum size granules. Lubrication is done by using Mg.stearate and passed through 60 mesh of the granules for 3 to 4 min. in a steel tub and then in polybag.

Compression is done by using 16 stations single rotary CADMA CH machine by using 9.6 mm round, biconcave, both side plane punch as seen in Table 5.

DESIGN AND DEVELOPMENT OF OXAPROZIN SRMATRIX TABLETS

Determination of Similarity & Disimilarity Factor.

STABILITY STUDY OF TABLETS OF BATCH T8.

The batch T8 was selected as an optimum batch and the stability study was carried out at accelerated condition. of 40 C/75% RH condition for a period of two months.

Table 5. Disimilarity factor.

Time (hours)	R	T	R-T	SQR	MOD (sqrt)	Cumulative OD	Cumulative R	F1
0	0	0	0	0	0	0	0	0
2	11.41	15.56	-4.15	17.22	4.15	4.15	11.41	36.37
4	21.63	25.63	-4	16	4	8.15	33.04	24.66
8	71.64	69.85	1.79	3.20	1.79	9.94	104.68	9.49
12	78.46	82.46	-4	16	4	13.94	183.14	7.61
16	89.27	92.02	-2.75	7.56	2.75	16.69	272.41	6.12
24	100.35	99.56	0.79	0.62	0.79	17.48	372.76	4.68

Table 6. Similarity factor.

Time in (hours)	R	T	R-T	(R-T)2	Cumulative (R-T)2	Cum (RT)2*1/N	Cum (RT)2*1/N+1	SQRT	1/SQRT	100*1/SQR
0	0	0	0	0	0	0	1	1	1	100
2	11.41	15.56	-4.15	17.22	17.22	2.87	3.87	1.96	0.50	50.83
4	21.63	25.63	-4	16	33.22	5.53	6.53	2.55	0.39	39.11
8	71.64	69.85	1.79	3.20	36.43	6.07	7.07	2.65	0.37	37.60
12	78.46	82.46	-4	16	52.42	8.73	9.73	3.12	0.32	32.04
16	89.27	92.02	-2.75	7.56	59.98	9.99	10.99	3.31	0.30	30.15

Table 7. Drug content of batch T 8 kept for stability.

Time	Drug Content (%)
Zero Month	99.25

Table 8. Dissolution profile of batch T-8 kept for stability.

Dissolution Medium	Time (hrs)	Cumulative % Release	
		Initial	*Two months*
	0	*0*	*0*
	2	15.56	14.12
	4	25.63	23.69
6.8 PH Buffer	8	69.85	69.12
	12	82.46	81.78
	16	92.02	91.23
	24	99.56	99.31

Method.

Ten tablets were individually wrapped using aluminum foil and packed in ambered color screw cap bottle and put at above specified condition in incubator for 2 months. After two-month tablets were evaluated for content uniformity and in-vitro drug release.

Observation.

E results of stability study after two months are given in Tables 6 & 7. The plot of cumulative % drug release v/s Time (hr) depicted in graph.

Drug Content

Comparative content uniformity of the Tablet after two-month stability.

RESULTS AND DISCUSSION.

The procured sample of Oxaprozin was tested for its identification. The manufacturer also confirmed the quality and purity of sample.

The drug–excipients compatibility was done at accelerated temperature 40ºC/75% ± 5% and 30ºC/65% ± 5% relative humidity. Opened and closed vial methods were used. The result doesn't show any physical change to the mixture after 30 days. This fact concluded that the drug and Excipient are compatible with each other as seen in Table 8.

The sustained release tablets of Oxaprozin were prepared by wet granulation method, They were evaluated for weight variation, drug content, friability, hardness, and thickness for all batches (T-1 T10).

No significant difference was observed in the weight of individual tablets from the average weight. Tablet weights of all batches were found within recommended pharmacopoeia limits. The data of uniformity of content indicated that tablets of all batches had drug content within pharmacopoeia limits. The hardness of tablets of all batches are in acceptable limits, as shows in the literature. All the formulation showed % friability less then 1% that indicates ability of tablets to withstands shocks, which may encounter. No significant difference was observed in the thickness of individual Tablet from the average weight.

Standard calibration curve of Oxaprozin was prepared in phosphate buffer medium 6.8 pH. Correlation coefficient values indicate the linear correlation between concentration and absorbance and following lamberts beers law.

The release of Oxaprozin from sustained release tablet of various formulations varied according to the ratio and degree of the polymer. In case of tablet of T1containing drug & HPMCK15M (quantity in mg). 200:15 the release profile, was showing the release 102.69%. In case of tablets of T2 containing drug and HPMC K15M & HPMC K4M (in mg). 200:10:20 it was showing 100.25% release in 24 hours. In case of tablets of T3 containing drug polymer's (HPMCK15M, HPMCK4M in mg) 200 15 15 prepare to be seen in the effect of combination of polymers in release of drug but it was showing same release given 100.25% upto 24 hour. In case of tablets T4 containing drug and HPMC K15M & HPMCK 4M (in mg) 200: 10: 10 the release profile was showing drug release more than 100%. In case of tablets of T5 containing drug and HPMC K 4M & HPMC K15M PVP K30 (in mg) 200: 10: 10:10. Prepared the tablets. But it cannot maintain the release with in 100%. In case of tablets of T6 containing drug and HPMC K 15M (in Mg) 200 5 It was seen the increase in release of drug and shown more than 100% drug release in 24 hour profile. In case of tablets T7, containing drug. HPMCK4M & HPMCK15m (in mg) 200 10:10 the release profile was showing drug release more than 100%. In case of Tablets T8 containing drug.

HPMCK15M (in mg) 200 23. The release profile was showing drug release with in 24 hours. With very slower release than all formulations containing % drug release 99.56.

In case of tablets T9, containing drug. HPMCK4M (in mg) 200:20 the release profile was showing drug release more than 100%. In case of tablets T10, containing drug.

HPMCK4M (in mg) 200:25 the release profile was showing drug release less than 100%.

For similarity, F2 calculation was done in 6.8 pH phosphate buffer showing the value of similarity factor (F2) i.e., 73.9

Results of stability studies of batch T-8 indicate that it was stable at 40ºC/75% + 5% relative humidity as there was no significant difference was observed for dissolution and average drug content data after two months.

CONCLUSION

The study was undertaken with an aim to formulate Develop and evaluation of Oxaprozin sustained release tablets using different polymers as release retarding agent. Preformulation study of Oxaprozin was done initially and results directed for the further course of formulation. Based on preformulation studies different batches were prepared using selected excipeints. Granules were evaluated for tests LOD, Bulk density, tapped density, compressibility index, Hausner ratio before being punched as tablets. Tablets were tested for weight variation, thickness, hardness and friability as per official procedure. Dissolution of batch T-8 was carried out in 6.8 pH media and compared with marketed preparation. Based on dissolution tests and F-2 values in pH 6.8 phosphate buffer as release medium, it was concluded that T-8 satisfactory performs in the same manneras that of marketed formulation. F-2 (similarity factor) value of T-6 was found to be 73.90.

From the above results and discussion, it is concluded that formulation of sustained release tablet of Oxaprozin containing HPMC K 15M & 200 :23 (in mg) T8 can be taken as an ideal or optimized formulation of sustained release tablets for 24-hour release as it fulfills all the requirements for sustained release Tablet and our study encourages for the further clinical trials on this formulation.

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