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FORMULATION AND EVALUATION OF TASTE MASKING LORNOXICAM ORAL DISINTEGRATING TABLETS

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ABSTRACT

Lornoxicam is a non-steroidal anti-inflammatory drug with analgesic properties and belongs to the class oxicams. It is extremely bitter in taste.The purpose of this research was to develop a bitter less oral disintegrating tablet of poorly soluble drug like lornoxicam. Taste masking was done by complexing with kyron T-104 in different ratios. Three super disintegrants like sodium starch glycolate, low substituted hydroxypropylcellulose and crospovidone were used. Prepared tablets were evaluated for different properties like drug content, hardness, friability, wetting time, water absorption ratio, disintegration time and *Invitro* dissolution study. The different formulations showed disintegration time between 5-35 sec. Drug releases showed between the ranges of 5-30 min. Among all the formulations, F9 showed 98.53% drug release within 30 min. Thus, F9 was considered best among the other formulations**.** The tablets showed enhanced dissolution hence better patient compliance.

KEYWORDS

Lornoxicam, kyron T-104, Super disintegrants, Oral disintegrating tablets and Disintegrating time.

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INTRODUCTION

The demand for the development of oral disintegrating tablets (ODTs) has enormously increased as it has significant impact on the patient compliance. Oral disintegrating tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people[1]. European Pharmacopoeia (5.0, 2005) adopted the term “orodispersible tablet” as a tablet to be

placed in the mouth where it disappears rapidly before swallowing, stating a maximum DT of 3 minutes as determined in a conventional disintegration test apparatus. OD Tare also known as quick dissolves, fast melts, fast dissolving, fast disintegrating, rapid dissolve or orally dissolving tablets[2].

The bitter taste of the drugs which are orally administered often contributes to patient non-compliance in taking medicines, especially for children and elderly. Unfortunately, majority of the drugs have a natural bitter taste that can create a burning feeling in the throat or in the mouth. In particular, a bitter taste can decrease the patient compliance and thus reducing an effective pharmacotherapy[3].

Lornoxicam (chlortenoxicam) is a non-steroidal anti-inflammatory drug (NSAID) of the oxicam class and is used for the treatment of pain, especially relating to the pain resulting from inflammatory diseases of the joints, osteoarthritis, surgery, sciatica and other inflammations[10]. The main objective of the present work is to formulate oral disintegrating tablets of Lornoxiam where in which its bitter taste is masked[11]. Such taste masked formulations have been found to improve the patient compliance.

Kyron T-104 is used as ion-exchange resin for taste masking of lornoxicam. It is tasteless, nontoxic, derived from crosslinked polymer of methacrylic acid[4]. It is an effective super disintegrant as well as a dissolution improver in solid dosage forms like tablets, capsules, pellets etc. kyron T-104 is available in white free flowing powder hence it is more suitable in direct compression system.

MATERIALS AND METHODS

MATERIALS

Lornoxicam, kyron T-104, sodium starch glycolate, low substituted hydroxyl propyle cellulose, crospovidone, micro crystalline cellulose, sucralose, magnesium stearate, talc were obtained as gift samples from Yarrow chemicals (Mumbai, India).sodium hydroxide, potassium dihydrogen phosphate were obtained as gift samples from S.D Manufactures Ltd.(Mumbai, India).

METHODS

Preparation of Drug -Resinate Complex

The method used for masking the taste of bitter drug lornoxicam was complexation with ion exchange resin such as kyron T-104as for the following procedure

Step-1: Drug and resin were accurately weighed in required ratio.

Step-2: Then slurry of resin was made in sufficient quantity of demineralised water and stirred for half an hour at500rpm, in order to allow polymer structure to swell uniformly.

Step-3: The drug was added slowly under stirred conditions to step 2.

Step-4: The drug resin mixture was then continuously stirred for 8-10 hrs at 500-600rpm and the volume was made up to100ml.

Characterization of complex for drug content

Drug resinate complex equivalent to 8 mg of drug was stirred by using magnetic stirrer with 100ml of 6.8 phosphate buffer for 60 mins, till the entire drug leached out from complex, then the solution was filtered through the whatmann's filter paper. Further, the solution was diluted with p^H 6.8 phosphate buffer and the drug content was determined spectrophotometrically at 376nm (Table No.1).

On the basis of these observations Drug and kyronT-104 complex ratio 1:3 was finalized for further study.

Preparation of drug resinate granules and lubrication

After drug-resin mixtures were stirred for required time, the drug-resinates were thoroughly washed with demineralized water for several times then filtered by using whatmann's filter paper and dried. The powderd drug-resinate particles are wetted made into damp mass, then passed through sieve no.60 and dried at 60^0C for 30minutes and these granules were taken in a poly bag along with other excipients and mix for 15minutes. And then finally add talc and blend for 5mins. Then it is subjected to pre-compression parameters followed by direct

compression using 9mm concave punches (Table No.2).

EVALUATION PARAMETERS OF LORNOXICAM ORAL DISINTIGRATING TABLETS

Weight variation test[5]

Weighed 20 tablets selected at random and calculated the average weight. Then percentage deviation from the average was calculated.

Thickness[5]

The thickness of five tablets for all batches was measured using verniercaliper. The diameter was also determined by using verniercaliper.

Hardness and Friability[6]

Hardness is the tensile strength of tablets expressed in Kg/cm^2, which is determined using Monsanto hardness tester. Preweighed sample of tablets were placed in the friabilator (Roche friabilator), and operated for 100 revolutions. Tablets were dedusted and reweighed. The test complies if tablets not lose more than 1% of their weight.

Water absorption ratio[7]

Small piece of tissue paper folded twice was placed on a small Petridish containing 6ml of water. A tablet was put on the paper and the time required for complete wetting was measured. The wetted tablet was then reweighed.

$$\text{Water absorption ratio} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

Wetting time[8]

5 circular tissue papers of 10cm diameter were placed in a petridish containing water soluble dye methylene blue (w/v) solution 6ml. a tablet was carefully placed on surface. The time required for developing the colour on the upper surface of the tablet is noted as "wetting time".

***In vitro* disintegration test**[9]

This test is performed to ensure disintegration of tablets in 6.8 Phosphate Buffer. Disintegration test is performed by using disintegration apparatus IP and the disintegration time is noted accordingly.

Drug content uniformity test

5 tablets of each formulation were weighed and powdered. The quantity of powder equivalent to 100mg of drug was transferred to 100ml volumetric flask. Small quantity of pH-6.8 phosphate buffer is taken and sonicated for 30min. After sonication filter it and volume is adjusted with pH-6.8 phosphate buffer to 100ml. Suitable concentration was diluted and absorbance was observed at 376nm.

***Invitro* drug release**

Invitro dissolution study was performed in 900ml PH 6.8 Phosphate buffer using USP type-II (paddle) apparatus at 50 rpm for 30 mins (37 ± 0.5^0C). Aliquots of the dissolution medium (5ml) were withdrawn at specific time intervals (0, 5, 10, 15, 20, 25,30mins respectively) and replaced immediately with equal volume of fresh buffer. The samples were filtered and analysed for drug content by measuring the absorbance at 376 nm.The drug concentration was calculated in order to get %cumulative drug released.

RESULTS AND DISCUSSION

Fourier transform infra-red spectroscopy (FTIR)

The interaction study between the drug and kyron T- 104 in the ratio of 1:3 and crospovidone performed using FTIR spectrophotometer. The pellets were prepared on KBr press. The spectra were recorded over the wave number range of 3500 to 1000 cm^{-1}. The FTIR spectrum of lornoxicam showed a characteristic peak at 3,289.79 cm^{-1} corresponding to -NH stretching vibration. Other peaks were observed at 1,521.86 cm^{-1} and were assigned to bending vibrations of the N–H group in the secondary amide. The stretching vibrations of the O=S=O group appeared at 1,185 $cm^{-1}$and 746.74 cm^{-1} due to the C–Cl bending vibration, which indicates groups is match with structure of drug and confirm the purity of the drug. FTIR-spectra of drug and kyron T-104 complex and also in combination with crospovidone are exactly same, and there is no shift of peaks or disappearance of principle peaks or modification of the principle peaks indicating that there is no interaction between the drug and excipients. FT-IR spectrum of pure drug is represented in Figure No.1 and 2.

Determination of λ_{max}

The UV absorption spectrum shows peak at 376 nm .The same was selected as λ_{max} for Lornoxicam, for obtaining calibration curve (Figure No.3).

Micromeritic properties

The values for Angle of repose were from20.10 to23.17.All the formulations shown angle of repose below 30^o. It indicated that all the formulations are having good flow properties. The bulk and tapped density values used for the calculation of Compressibility Index and Hausner's ratio. The Hausner's ratio values were observed below 1.18. The compressibility index were observed below 11 -15, which indicates that all the formulation were having good compressibility (Table No.3).

Kinetic study

To know drug release kinetic of the optimized formulation the dissolution data were subjected to different kinetic models such as zero order, first order, Higuchi, Korsmeyerpeppas, Hixoncrowel etc.

From the above observations the tablets showed the Hixoncrowel model (R^2=0.992) indicates that the drug release by diffusion (Table No.6).

SUMMARY AND CONCLUSION

In the present research investigation work under taken, an attempt was made to explore the use of ion exchange resins as taste masking agents and Superdisintegrants in the formulation of orally disintegrating tablets of Lornoxicam. The purpose was to enhance patient compliance and provide rapid onset of action.

Kyron T-104 (polacrillic acid) was used as ion exchange resin for taste masking of the bitter drugs. The polymer was mixed with the drug in differentiation's i.e., drug: resin form 1:1, 1:2, 1:3.These drug-resinate mixtures were then converted into granules. These granules were lubricated and used for compression as required. Results showed that the bitterness was masked with 1:3 ratio and the percentage drug content for 1:3 ratio was found to be 95.11. The trail number F9 has high % cumulative drug release. FTIR studies showed that all the functional groups present in 1:3 ratio of drug-resin complex and that of final formula containing crospovidone along with drug-resin complex are same with that of the individual structures. Hence, they are compatible with each other.

Trail No.: F9 is taken for the selection of the suitable super Disintegrant. Trails ware taken with different disintegrating agents to get less disintegration time as it is one of the essential parameter for the orally disintegrating tablets. From trail No. F1 to F9, trails were taken with different disintegrating agents and the disintegration time was observed in the order of Sodium Starch Glycolate, Low substituted hydroxypropyl cellulose, Crospovidone. So the disintegration time of tablets containing Crospovidone was less as compared to the tablets containing Sodium Starch Glycolate or Low substituted hydroxypropyl cellulose.

Trail No. F9 showed pleasant mouth feeling without any bitterness thus fulfilled the requirements of orally disintegrating tablets. So trail no. F9 is finalized as final composition which is having all the desirable properties for the orally disintegrating tablets.

The lubricated blends were characterized for Angle of repose, Bulk density, tapped density, Compressibility index and Hausner's ratio. All the formulations were shown good flow properties and good compressibility.

The compressed tablets were subjected to evaluation studies for the parameters like general appearance, thickness, diameter, and hardness, weight variation, wetting time, water absorption ratio, friability, *invitro* disintegration and dissolution tests respectively(Table No.4 and 5).

Drug Content uniformity studies were conducted for all the formulations and found satisfactory. For all the formulations the content uniformity was within 85% to 115 % limit only. *Invitro* dissolution studies showed a drug release up to 98.53% in 30 minutes, whichwas found to be better than a commercial product (85.83%) (Figure No.5-8).

Table No.1: Characterization of complex for drug content

S.No	Drug and kyron t-104 ratio	% drug content in complex
1	1:1	87.94
2	1:2	90.80
3	1:3	95.11

Table No.2: Composition of Lornoxicam Oral Disintegrating Tablets Formulations and their excipients (mg)

S.No	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	DRC(1:3)equivalent to 8 mg of drug	32	32	32	32	32	32	32	32	32
2	SSG	6	8	10	-	-	-	-	-	-
3	L-HPC	-	-	-	6	8	10	-	-	-
4	Crospovidone	-	-	-	-	-	-	6	8	10
5	MCC	106	104	102	106	104	102	106	104	102
6	Sucralose	2	2	2	2	2	2	2	2	2
7	Mg.Sterate	2	2	2	2	2	2	2	2	2
8	Talc	2	2	2	2	2	2	2	2	2
9	Total weight	150	150	150	150	150	150	150	150	150

Table No.3: Pre-compression parameters

S.No	Formulation code	Angle of repose (Ɵ)	Bulk density	Tapped density	Carr's index (%)	Hausner's ratio
1	F1	20.10	0.312	0.347	10.08	1.11
2	F2	25.81	0.316	0.337	6.23	1.06
3	F3	24.22	0.308	0.347	11.23	1.12
4	F4	20.47	0.312	0.342	8.77	1.09
5	F5	22.58	0.308	0.333	7.50	1.08
6	F6	24.08	0.316	0.347	8.93	1.09
7	F7	21.80	0.320	0.342	9.09	1.06
8	F8	20.98	0.312	0.337	7.41	1.08
9	F9	23.17	0.308	0.328	6.09	1.06

Table No.4: Post compression parameters

S.No	Formulation Code	Thickness (mm)	Hardness (kg/cm^2)	Weight variation (mg)	Friability	Water absorption ratio	Wetting time (sec)	Disintegration time (sec)	Drug content uniformity
1	F1	3.01	3.52	148	0.67	86.66	40	35	98.61
2	F2	2.99	3.45	146	0.33	88.00	46	30	98.02
3	F3	2.98	3.33	147	0.40	90	52	28	99.05
4	F4	3.01	3.23	148	0.60	85.33	57	23	99.05
5	F5	2.98	3.44	149	0.66	91.33	54	20	98.41
6	F6	2.97	3.49	147	0.53	93.33	52	18	99.11
7	F7	2.99	3.55	147	0.46	83.33	58	12	99.38
8	F8	2.98	3.27	150	0.40	90.66	56	10	99.27
9	F9	2.96	3.35	149	0.47	96.66	48	5	99.64

Table No.5: Dissolution profile of prepared formulations

S.No	Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9	Marketed preparation
1	0	0	0	0	0	0	0	0	0	0	0
2	5	38.73	50.47	51.52	50.34	53.47	69.65	71.86	73.82	73.95	50.21
3	10	42.34	54.41	54.02	56.62	57.29	78.38	77.49	78.26	81.93	63.53
4	15	44.27	61.1	63.45	63.33	63.61	85.73	82.22	82.48	90.34	68.84
5	20	47.38	64.06	70.18	68.11	70.71	88.94	83.72	84.37	94.22	76.92
6	25	48.16	66.1	74.87	72.87	75.92	90.6	85.87	87.96	96.31	83.86
7	30	51.82	71.29	77.88	77.51	78.16	92.01	90.25	91.83	98.53	85.88

Table No.6: Different Dissolution kinetic parameters of optimized formulation F9

S.No	Formulation code	Zero order R^2	First order R^2	Higuchi model R^2	Korsmeyer peppas R^2	Hixoncrowel R^2
1	F9	0.610	0.984	0.863	0.790	0.992

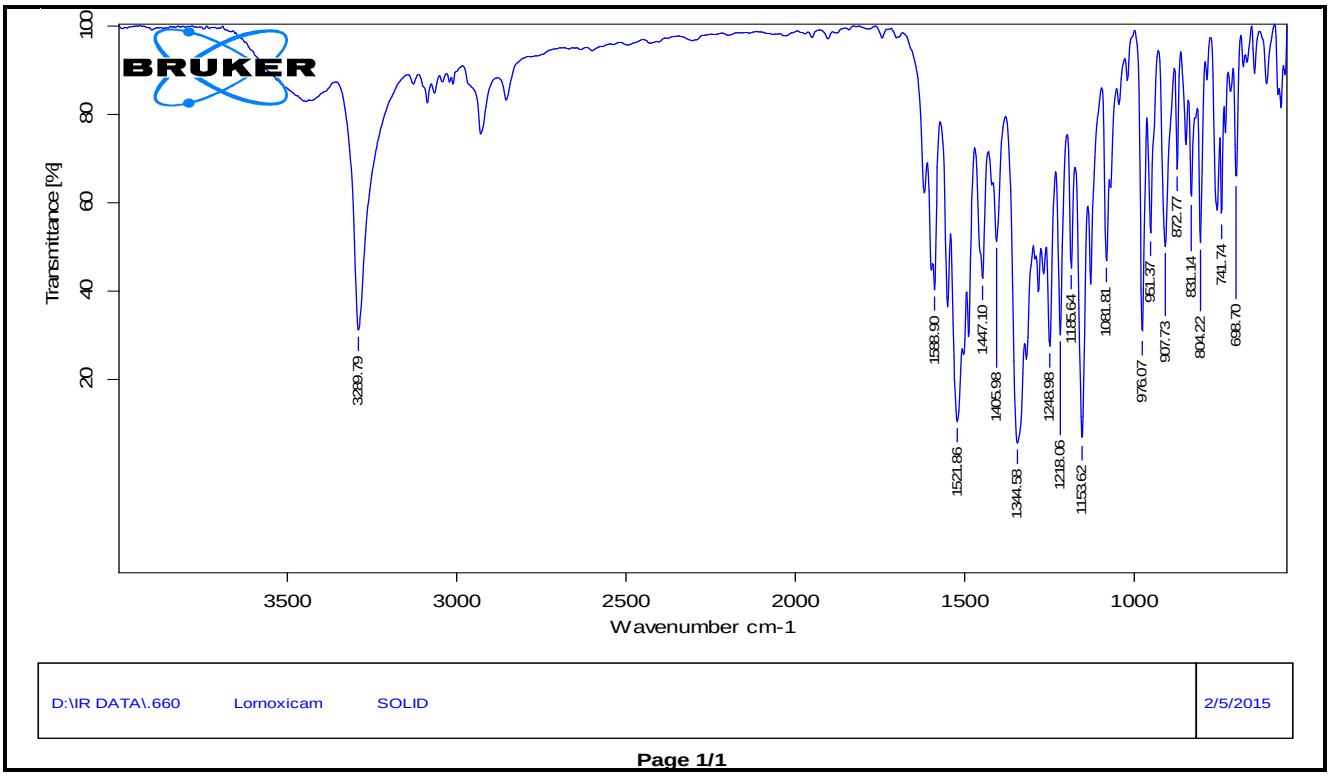

Figure No.1: Pure Drug (Lornoxicam)

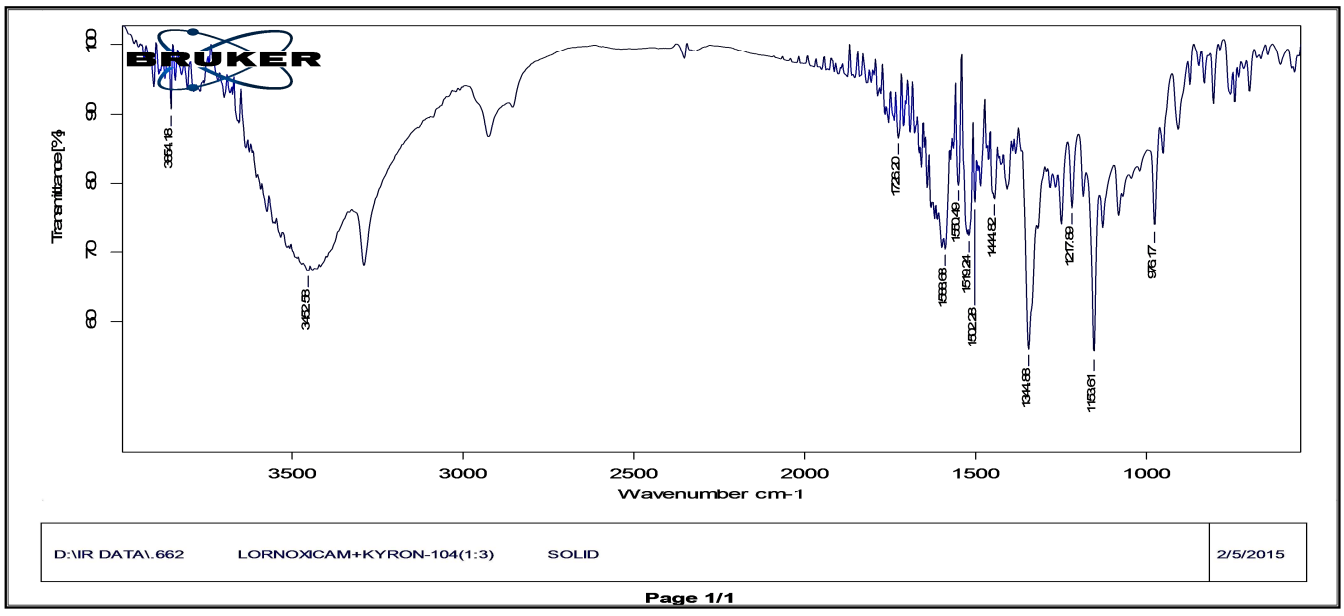

Figure No.2: Pure Drug (Lornoxicam) and KYRON-104(1:3)

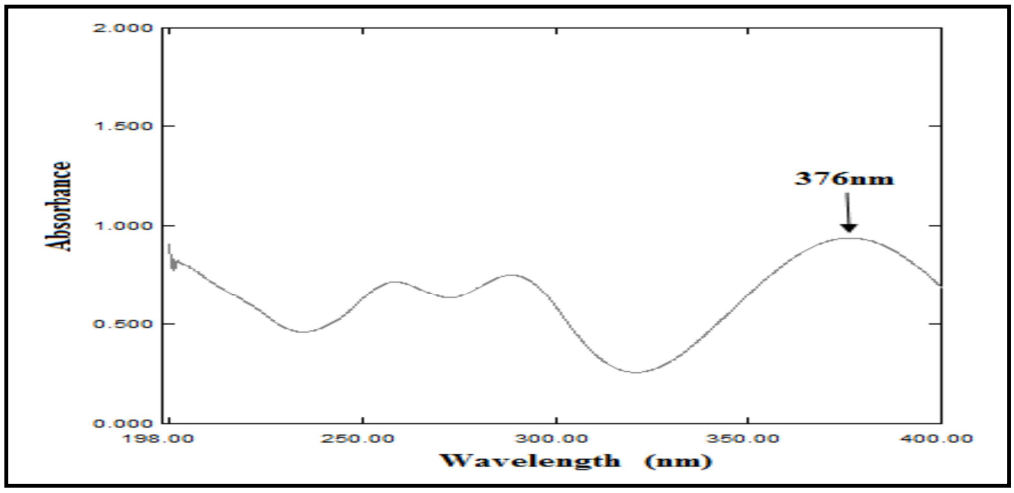

Figure No.3: Determination of λmax of Pure Lornoxicam

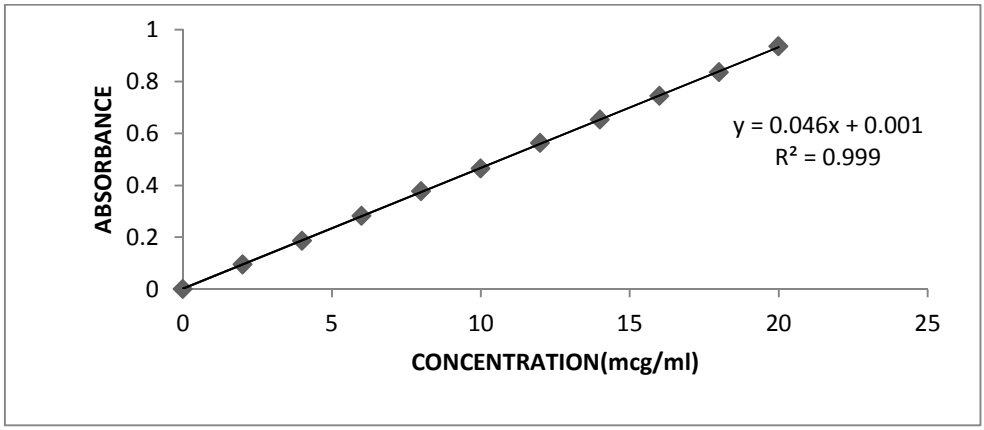

Figure No.4: Standard Calibration curve for Lornoxicam

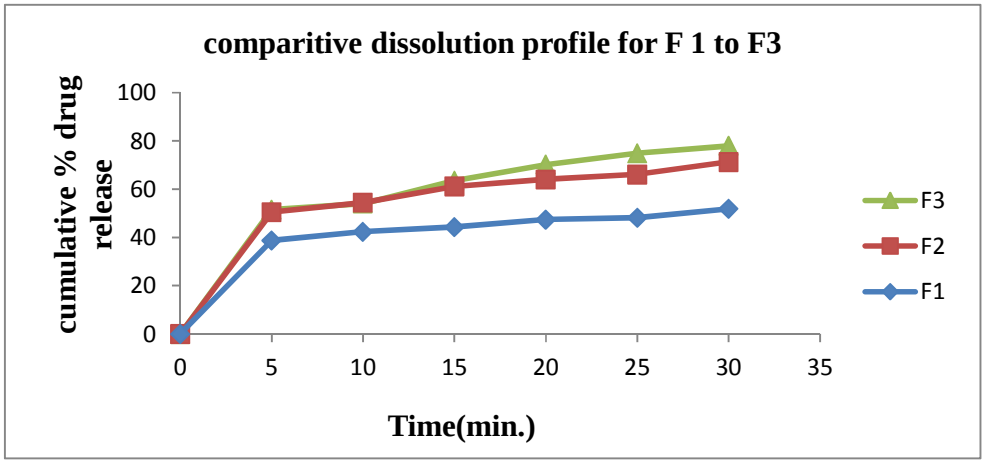

Figure No.5: Comparative *In vitro* dissolution profiles for formulation I - III

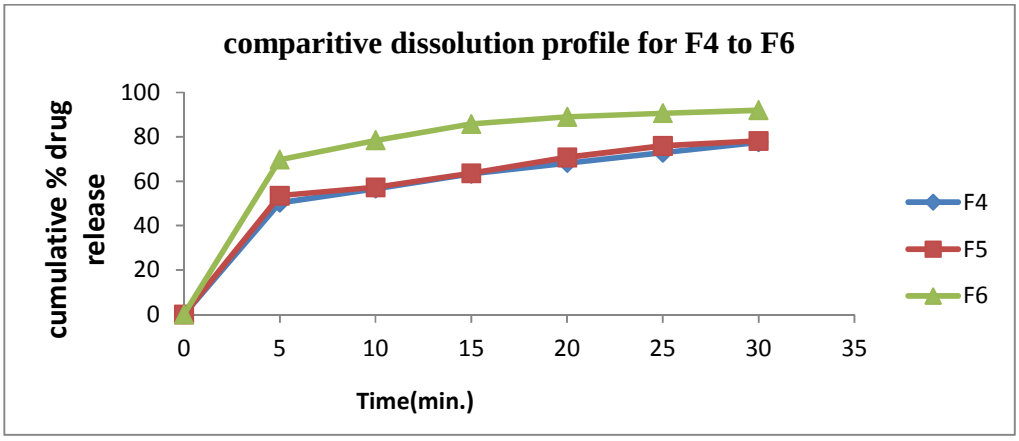

Figure No.6: Comparative *In vitro* dissolution profiles for formulation IV-VI

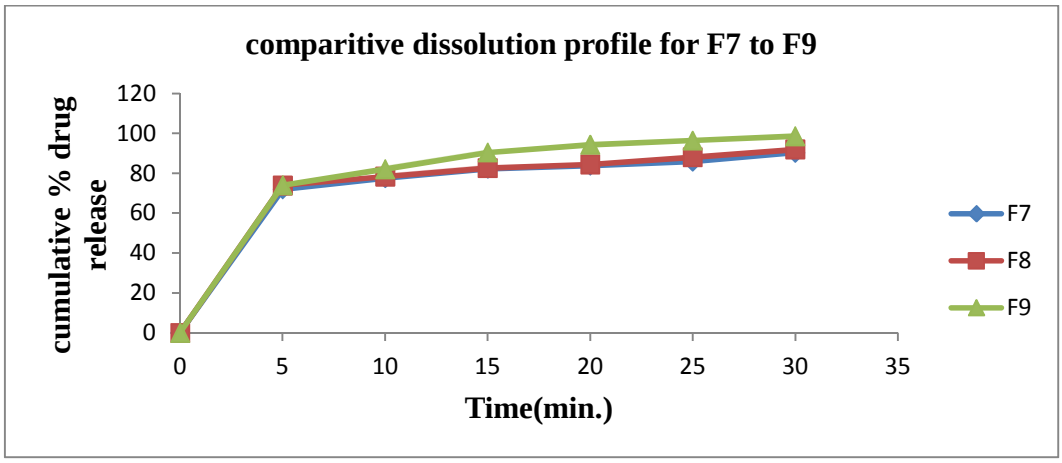

Figure No.7: Comparative *In vitro* dissolution profiles for formulation VII to IX

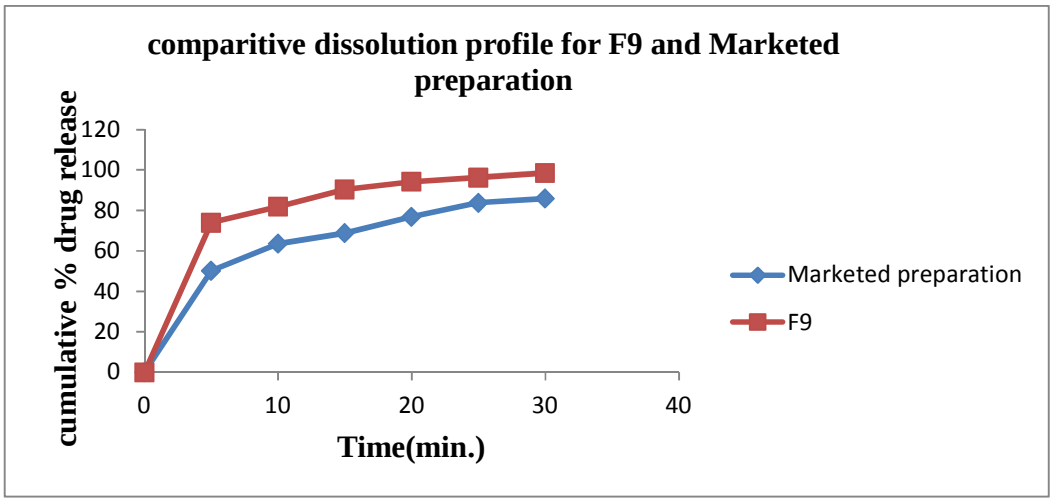

Figure No.8: Comparative *In vitro* dissolution profiles for formulation F9 and Marketed preparation

CONCLUSION

Hence, from the present research investigation it was concluded that, the taste masking polymer i.e Polacrillic acid have been proved to be useful as taste masking agent for bitter drug like Lornoxicam as well as super disintegrating agent. The superdisintegrants like Crospovidone is effectively reducing the disintegration time less than 8 seconds. Good mouth feel was achieved by using suitable sweetener. Thus, we are able to achieve our objective of preparing highly compatible orally disintegrating tablets of Lornoxicam with minimum excipients and simple method of manufacture.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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