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FORMULATION AND EVALUATION OF FAST DISSOLVING TABLETS OF LORNOXICAM

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ABSTRACT

Mouth dissolving tablets are also known as fast disintegrating, fast dissolving, fast melt, quick melt tablets. Lornoxicam is an NSAID with 100% bioavailability having a bitter taste. So by formulating it as an ODT the absorption and the bioavailability of the drug will fasten and hence the action of the drug will be faster .The mode of action of Lornoxicam is mainly by inhibition of prostaglandin synthesis (inhibition of cyclooxygeanase enzyme). So the purpose of the present work is to formulate a taste masked mouth dissolving tablet of Lornoxicam. Taste masking was done by using Eudragit (EPO 100) in different ratios. Three superdisintegrants were used namely sodium starch glycolate, crospovidone, crosscarmellose sodium. The tablets were evaluated for various parameters like hardness, friability, drug content, disintegration and in vivo dissolution. Among all the formulations F5 showed 98% drug release with in 15 min. So it was considered as best formulation.

Keywords: Lornoxicam, Eudragit EPO 100, Super disintegrants, Mouth dissolving tablets.

INTRODUCTION

Oral drug delivery has been known for decades as the most widely used route of administration among all the routes that have been used for the systemic delivery of drugs via various pharmaceutical products of different dosage forms. The reason for that the oral route achieved such popularity mainly be due to its ease of administration as well as the traditional belief that by oral administration the drug is well absorbed as the food stuffs ingested daily. In fact, the development of pharmaceutical products for oral delivery, irrespective of physical form involves varying extents of optimization of dosage form within the inherent constraints of GIT physiology. For the successful development of a dosage form for an oral drug delivery system consists of a basic understanding of the following aspects:

i. Physicochemical, pharmacokinetic and pharmacodynamic characteristics of the drug,
ii. The anatomic and physiologic characteristics of the GIT, and
iii. Physicochemical characteristics and the drug delivery mode of the dosage form to be designed[1].

Oral route of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules. Apart from that drinking water plays an important role in the swallowing of oral dosage forms[2].

The orally disintegrating tablets are also called as oral dispersible tablets, quick disintegrating tablets, fast disintegrating tablets, porous tablets, rapimelts,mouth disintegrating tablets. However of all the above terms, United States Pharmacopoeia (USP) approved these dosage forms as ODTs. Recently, European Pharmacopoeia has used the term "oral dispersible tablet" for tablets that disperse readily and within three minutes before swallowing. United States Food and Drug Administration (FDA)

defined ODT as "A solid dosage form containing medicinal substances or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue". The disintegration time for ODTs generally ranges from several seconds to about a minute[5].

MATERIALS AND METHODS

Chemicals: Lornoxicam was obtained as a gift sample from Ranbaxy Pvt Ltd,Gurgoan; Mannitol,Qualigen fine chemicals ,Bombay .India;Magnesium stearate , Oxford laboratory,Mumbai,India ;Na2HPO4,KH2PO4, FINAR reagents,Ahemadabad,India;Sodium saccharine , Jhonson and george chemicas co , Mumbai, India;Aerosil,Yarrow chem. Products,Mumbai,India;SSG,CCS , CP,L-HPC A to Z chemicals,chennai,India.

Compatability studies:The compatability of Lornoxicam with different excipients was tested using FTIR Spectrophotometer.

Preparation of Taste masked granules using Eudragit EPO: Lornoxicam taste was masked by the following procedure: The taste masking agent (i.e) Eudragit EPO was maintained at about 50-55^{0}c for 3 minutes. When the taste masking agent started melting the drug was added and mixed. The drug: taste masking agent ratio was maintained at 1:2.

PEPERATION OF MOUTH DISSOLVING TABLETS BY DIRECT COMPRESSION

Method: Oral dispersible tablets are prepared by direct compression. The various disintegrants like crospovidone, croscarmellose and sodium starch glycolate were used. Required quantity of each ingredient is taken for each specified formulation and all ingredients were mixed. Aerosil and magnesium stearate were then passed through mesh no.60 mixed and blended with initial mixture. The resulting mixture is compressed into tablet using 16 station rotary press.

POST FORMULATION STUDIES

Weight variation: 20 tablets were selected randomly from the lot and weighted individually to check for weight variation. The weight variation test was performed and the weights of the tablets were between 99 to 101 mg, As the weight of the tablet is 100mg, The weight variation limit is ± 7.5%.

Hardness, Friability (F) and Thicknes: Hardness or tablet crushing strength is the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester and the friability was tested using a Roche friabilator. The thickness of the tablets was measured using a Vernier callipers.

Content uniformity: Ten tablets were randomly selected and tested for their drug content. Each tablet was powdered and dose of the drug equivalent was taken and to it 10 ml of 6.8 pH phosphate buffer was added and the resulting solution was diluted appropriately and measured for its absorbance at 375nm using a UV-Visible spectrophotometer.

Disintegration time: Tablet was placed in the disintegrating apparatus or a disintegrator having pH 6.8 phosphate buffer solutions at 37 ± 0.5^o C. Time required for complete dispersion of a tablet was measured.

Wetting time or water absorption Ratio: The water uptake characteristic of the loose disintegrant powder allows and evaluation of both the intrinsic swelling and the wettability of the super disintegrants .Water uptake were performed at room temperature. Water absorption ratio R was determined by using the following formula.
Water absorption = [Wa-Wb / Wb] *100

In-vitro Release studies: The invitro drug release studies were carried out in an USP Type II (Paddle) dissolution apparatus to suite the physiological conditions of the GIT. The medium used for dissolution is Phosphate buffer with a pH of 6.8.The volume of the medium in the dissolution apparatus was maintained at 900ml.The stirring rate was 50 rpm and the temperature was maintained at 37± 0.5^{0}C.Aliquots of dissolution medium were withdrawn at predetermined time intervals and the same volume of medium was replaced to maintain the constant volume.

RESULTS AND DISCUSSIONS

Compatability study: From the FT-IR study the drug was found to be compatible with all the excipients.

Micromeritic properties: Lornoxicam powder blends were free flowing as indicated by the values of bulk density(0.39 to 0.55 gm/cc),Tapped density(0.49 to 0.64 gm/cc), Hausner's ratio(1.12 to 1.25), Compressibility index (11.36 to 21.39 %) and the Angle of repose ranged from 24.02 ^{0} to 28.61$^{0.}$ The values are given in **table 2.**

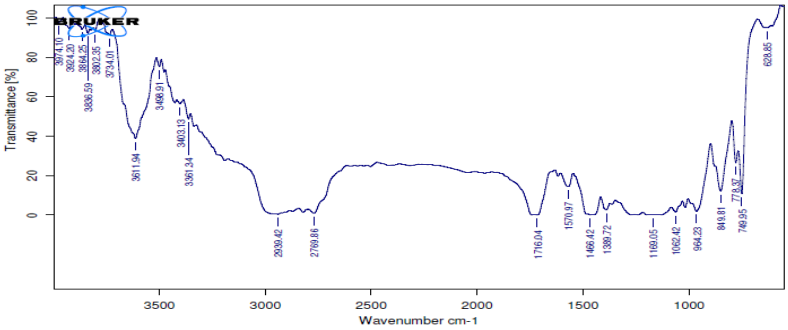
Post Compression Evaluation parameters of formulated ODT's: Lornoxicam tablets were uniform in weight (99.9 to 100.2 mg), the thickness (0.210 to 0.213 mm) of all tablets were uniform. The hardness of all the tablets was found to be between 3.00 to 3.03kg/cm^2 ,While the friability of the ODT'S ranged from 0 .10 to 0.26%.The content uniformity of all the formulations were ranged from 98.28% to 100.02% w/w .The disintegration time of all the formulations ranged from 30 to 10 seconds, the modified disintegration test values ranged from 33 to 13 seconds and the wetting time values ranged from 35 to 16 seconds .Fifteen formulations were tried by taking different superdisintegrants with different ratios. The post compressional parameters are presented in the table 3.

InVitro release study of the tablets: Invitro dissolution study of formulations using Eudragit EPO as taste masking agent: F1 to F15 formulations were prepared using Eudragit EPO as taste masking agent. F1 to F5 formulations were prepared using crospovidone as the superdisintegrant at a concentration of 2,3,4, 5 and 7.5% .F6 to F10 formulations were prepared using cross carmellose sodium as the superdisintegrant at a concentration of 2,3,4, 5 and 7.5% .F11to F15 formulations were prepared using croscarmellose sodium as the superdisintegrant at a concentration of 2,3,4,5, and 7.5%.It was observed that all the formulations showed a gradient and proportional increase in the drug release.The results were tabulated in Table 4 .

CONCLUSION

F1 to F5 batches were formulated using crospovidone as superdisintegrant at different concentrations of 2,3,4,5%,5% and 7.5% respectively. F5 batch with 7.5% crospovidone showed better results. Though the results indicate that crosspovidone showed concentration dependent disintegration and dissolution in which higher concentration of crosspovidone is responsible for faster water uptake, It facilitates wicking action and brings about faster disintegration and dissolution when compared to other superdisintegrants like used crosscarmellose sodium and sodium starch glycolate.

FTIR STUDIES FOR DRUG AND EXCIPIENTS



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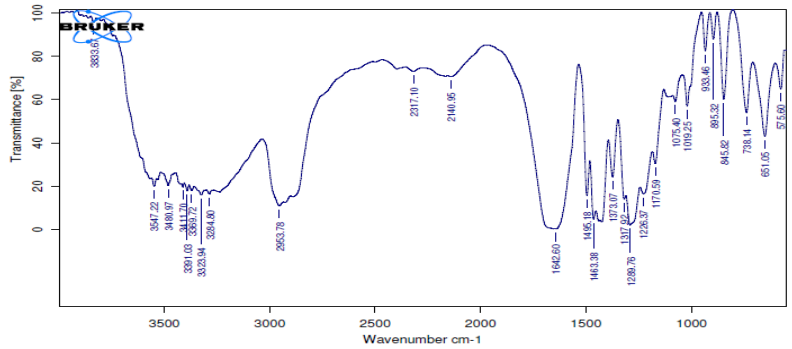

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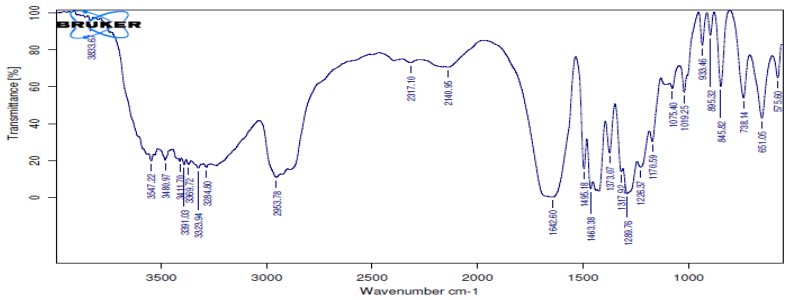
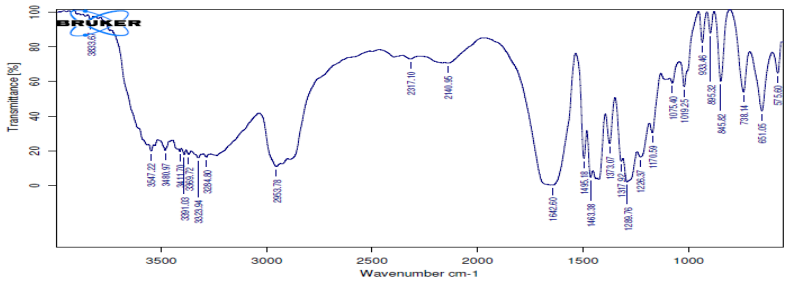
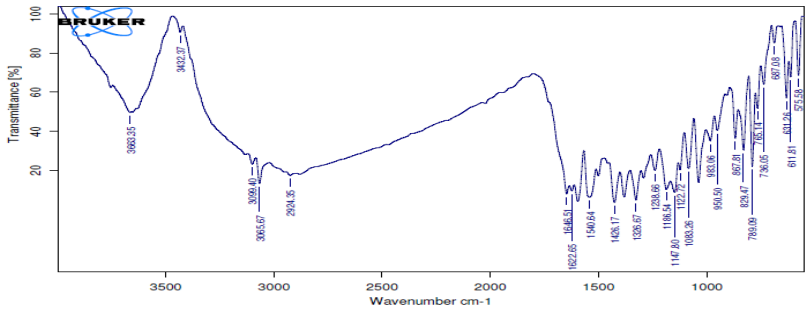


LORNOXICAM



LORNOXICAM + EPO



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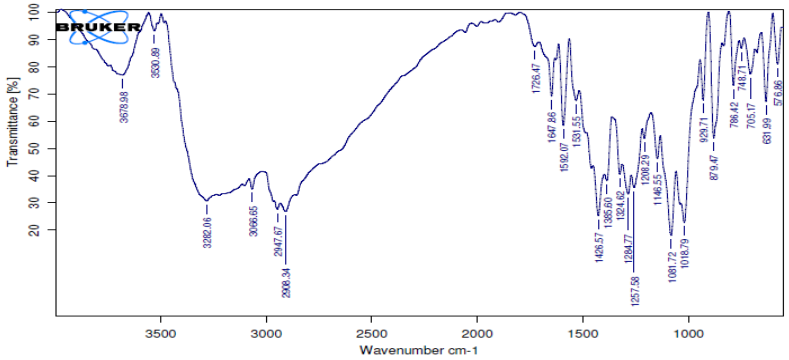


LORNOXICAM FORMULATION

Table:1 Formulation design of an oral disintegrating tablet

Ingredients/Formulation(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15
Lornoxicum	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Eudragit EPO	16	16	16	16	16	16	16	16	16	16	16	16	16	16	16
Mannitol	65.8	64.8	63.8	62.8	60.3	65.8	64.8	63.8	62.8	60.3	65.8	64.8	63.8	62.8	60.3
L – HPC	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Crospovidone	2	3	4	5	7.5	-	-	-	-	-	-	-	-	-	-
Crosscarmellose sodium	-	-	-	-	-	2	3	4	5	7.5	-	-	-	-	-
Sodium starch glycolate	-	-	-	-	-	-	-	-	-	-	2	3	4	5	7.5
Aerosil	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Aspartame	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Magnesium stearate	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Peppermint Flavour	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Total Wt in mg	100	1000	100	100	100	100	100	100	100	100	100	100	100	100	100

Table 2 :Micromeritic properties of the powder blend: (Pre formulation studies)

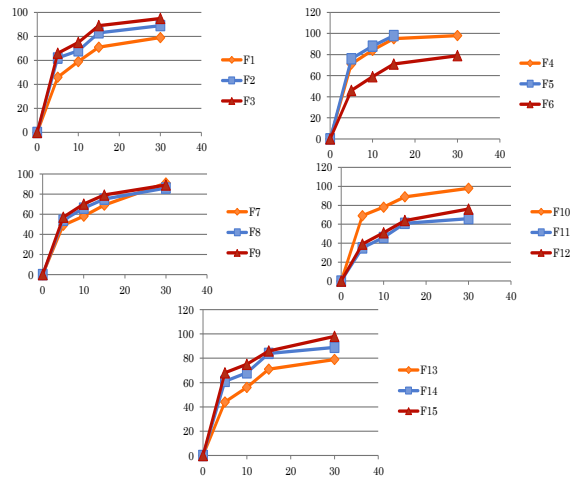
Formulation code	Bulk Density(g/cc)	Tapped density (g/cc)	Angle of repose (degrees)	Carr's index(%)	Hausner's ratio
F1	0.49	0.57	27.40	14.04	1.16
F2	0.48	0.55	26.06	12.72	1.14
F3	0.46	0.53	24.38	13.20	1.15
F4	0.43	0.49	25.72	12.24	1.14
F5	0.41	0.47	26.94	12.76	1.14
F6	0.39	0.44	28.48	11.36	1.12
F7	0.55	0.64	26.21	14.06	1.16
F8	0.53	0.61	25.74	13.11	1.15
F9	0.50	0.58	24.02	13.79	1.16
F10	0.49	0.56	23.51	12.50	1.14
F11	0.47	0.54	25.68	12.96	1.15
F12	0.475	0.565	26.45	16.03	1.19
F13	0.48	0.56	28.61	14.28	1.16
F14	0.451	0.565	26.34	20.17	1.25
F15	0.469	0.561	25.42	21.39	1.19

Table3: Postcompressional charecteristics of the Formulated ODT:

Formulation code	Weight variation	Hardness (Kg/cm^2)	Thickness (mm)	Friability (%)	Content uniformity (%)	Disintegration time (Sec)	Modified disintegration time	Wetting time (sec)
F1	Passed	3.00	0.210	0.12	99.92	24	26	28
F2	Passed	3.01	0.213	0.15	98.3	20	22	24
F3	Passed	3.02	0.212	0.14	100.01	16	18	20
F4	Passed	3.01	0.212	0.21	99.24	12	15	17
F5	Passed	3.02	0.213	0.34	98.28	10	13	16
F6	Passed	3.00	0.212	0.19	98.52	28	31	32
F7	Passed	3.03	0.214	0.19	98.98	21	24	25
F8	Passed	3.02	0.213	0.10	100.02	18	21	22
F9	Passed	3.01	0.212	0.16	99.84	15	18	21
F10	Passed	3.0	0.212	0.22	99.65	13	16	20
F11	Passed	3.01	0.210	0.11	98.62	30	33	35
F12	Passed	3.03	0.212	0.14	100.01	25	24	30
F13	Passed	3.01	0.213	0.12	99.2	23	21	26
F14	Passed	3.01	0.210	0.26	99.54	19	22	25
F15	Passed	3.0	0.212	0.23	99.75	15	18	21

Table 4: Invitro dissolution studies of formulated ODT's

Time/ Formulation code	5 min	10 min	15 min	30 min
F1	41	54	68	72
F2	59	66	81	84
F3	62	71	86	94
F4	67	82	94	98
F5	72	86	98	-
F6	42	51	62	74
F7	46	54	66	79
F8	50	64	72	81
F9	54	67	76	86
F10	67	82	94	98
F11	32	44	59	64
F12	36	49	61	71
F13	41	54	68	76
F14	59	66	81	84
F15	66	73	86	98
F15	66	73	86	98



X-AXIS: Time (min); Y-AXIS: % Drug Release

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