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FORMULATION AND EVALUATION OF LORNOXICAM ORODISPERSIBLE TABLETS USING NATURAL SUPERDISINTEGRANTS

SENTHIL SELVI, BHAMA S, RAMYA R.R*, CHANDRASEKHAR Y, PERUMAL P
Dept. of Pharmaceutics, J.K.K. Nattraraja College of Pharmacy,
Komarapalayam – 638 183, Namakkal (D.T.) Tamil Nadu, India
***Author for correspondence:** Mobile No: +91 9715573518, Email Id: ramyarraami@gmail.com

ABSTRACT

Oral drug delivery is the most preferred route of drug administration. The Oro dispersible tablets are the newly introduced Oral Drug Delivery systems. There are several methods for their manufacture. Direct compression methodusing superdisintegrants is one among them. The natural superdisintegrants can be used instead of synthetic superdisintegrants as they showed equal disintegrating property as that of synthetic agents, Ispagol's mucilage, powder and husk powder etc are used for the preparation of Lornoxicam oro dispersible tablets. The study mainly focused for the use of natural superdisintegrants for manufacturing Lornoxicam Oro dispersible tablets.

1.INTRODUCTION

Oral tablets are the most widely used dosage form because of its advantage in terms of self administration, compactness, low cost and ease in manufacturing. The major demerits of conventional tablets include poor patient compliance, low bioavailability and delayed on set of action. Because of these problems scientists developed innovative drug delivery systems known as 'Oro dispersible tablets'. United States Food and Drug Administration (FDA) defined Oro dispersible tables as "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly within a matter of seconds when placed upon the tongue". The characteristic advantages of Oro dispersible tablets include administration without water, rapid on set of action and increased bioavailability.

Usually superdisintegrants are added to these drug formulations to facilitate the break up or disintegration of tablet contents into smaller particles. Many synthetic agents like Sodium Starch Glycolate, Micro Crystalline Cellulose (MCC), Crospovidone, Croscarmellose sodium have been used in the formulations of Oro dispersible tablets. Similarly, various natural super disintegrants like agar, gum karaya etc., have been used in the formulation of Oro dispersible tablets. Natural agents are preferred to semi-synthetic and synthetic super disintegrants as they are non toxic, non-irritating, abundantly available and cheaper. Ispagol (seed of Plantago Ovata) used in pharmaceutical industry, food preparation, ayurvedic medicine, unani remedies. It have various pharmaceutical formulation characteristics like binding and disintegrating properties. Ispagol mucilage, powder and husk powder were used as super disintegrants to develop Oro dispersible tables of Lornoxicam. And these were compared with that of formulated with widely used Synthetic Super disintegrants like Cros povidone, Sodium Starch Glycolate and Calcium Carboxy Methyl Cellulose.

Lornoxicam,(3E)-6-Chloro-3-[hydroxyl(pyridine-2-ylamino)Ethylene]-2-methyl-2,3-dihydro-4-H thieno [2,3e][1,2] thiazin-4-one 1.1. Dioxide) is a non-steroidal anti-inflammatory drug (NSAID) of Oxicam class. It has been indicated for various acute painful indications and proved as effective as other NSAIDS. Lornoxicam is poorly soluble in water. The solubility can be enhanced by complexation with β-Cyclodextrin.

2.MATERIALS AND METHODS

Lornoxicam, Sodium starch glycolate, sodium stearyl fumerate, Talc, Aspartame, Aerosil, Orange flavor were obtained from Bangalore Antibiotics and Biologicals (Salem, Tamilnadu). Calcium Carboxy Methyl Cellulose, Mannitol, Microcrystalline Cellulose and Crospovidone were obtained from SD Fine Chem Limited, Mumbai. Ispagol was collected from Gujarath International, Gujarath.

Preparation of Lornoxicam Oro dispersible Tablets: Orodispersible tablets of Lornoxicam were prepared by direct compression method. The Lornoxicam β-Cyclodextrin complexes were prepared in 1:2 ratio. All ingredients were passed through sieve (#80) to ensure better mixing. Micro Crystalline Cellulose was used as directly compressible vehicle. Mannitol included because of its sweet taste. It will help to mask the bitter taste of drug. Sodium Stearyl fumerate was used as lubricant. Talc was used as glidant. Orange flavor was used as flavoring agent. Aerosil was used to enhance the compressibility.

Preparation of Lornoxicam, β-Cyclodextrin complex: Preparation of Lornoxicam β-Cyclodextrin Complexes (1:2 ratio) was prepared by kneading method. Both Lornoxicam and β-Cyclodextrin were weighed separately. The pre weighed quantity of Cyclodextrin dissolved in minimum quantity of water. It is triturated in glass mortar using pestle.

To this the weighed quantity of Lornoxicam added little by little until uniform slurry obtained. Kneading method also known as slurry complexation. The prepared slurry dried in hot air oven at 60^0C.

Preparation of Ispagol mucilage, powder and husk powder: Ispagol seed and husk were washed and dried well. After drying it powdered and grinded using automatic grinder. Grinding done is several time until these pass through #80. After grinding these were stored in desiccator until use.

Preparation of Ispagol mucilage: Ispagol were soaked in distilled water for 2 days. Then it boiled for few minutes. Then the mucilage was completely released into the water. The material collected was squeezed through muslin cloth. The mucilage squeezed out and the marc separated. Then the mucilage(filtrate) treated with equal volume of Acetone to precipitate . The separated mucilage was dried in oven t a temperature less than 60^0C. After proper drying it powdered and pass through sieve no.#80 and stored in desiccator until use.

Preformulation study of natural superdisintegrants: The prepared natural superdisintegrants were evaluated for their flow property (Angle of Repose) and swelling property (Swelling index). The swelling index is the volume in milliliters that is occupied by 1g of drug. This is one of the identification test for Ispagol (specified in Pharmacopoeia).

Angle of Repose was found out using funnel method. The preweighed quantity of Ispagol Mucilage, powder and husk powder were used for study.

Evaluation of Powder blend: The parameters like Bulk density, tapped density, compressibility index(%), Hausner's ratio and Angle of repose were found out.

Preparation of Lornoxicam Oro dispersible Tablets: For the preparation of Lornoxicam Orodispersible tablets direct compression method by adding superdisintegrants were used. Both synthetic and Natural superdisintegrants were included in the formula. Superdisintegrants were used in two different concentrations like 4.5% and 6%. The formula shown in Table No.3. All ingredients separately passed through sieve no.#80 and mixed to get the uniform mixture. Then compressed using a single-punch tableting machine (Cadmach Machinery Co. Pvt. Ltd., India).

Evaluation of Oro dispersible Tablets: Quality Control tests for Orodispersible tables of all formulations were performed and the average values were calculated. The following tests were performed.

Weight variation: The weight variation was determined by weighing 20 tablets individually, the average weight and percent variation of tablet was calculated.

Thickness: The thicknesses of tablets were measured using Vernier calipers. The values were expressed in mm.

Hardness: Hardness was determined using Monsanto hardness tester. The average values were determined.

Friability: The friability of the tablets were determined using Roche friabilator. The preweighed 20 tablets were placed in a friability tester, which was rotated for 4 minutes at 25rpm. After dusting, the total remaining mass of tablets was recorded and percent friability was calculated.

Friability, $F = 100 \times \frac{W_0 - W_f}{W_0}$

Where, W_0 = initial wt. of tablets, W_f = final wt of tablets

Disintegration time: The test was performed using Disintegration apparatus with water which was heated to 25^0C. A tablet was added to each of 6 tubes of apparatus and the time in seconds for complete disintegration of the tablets were found out. The test performed three times and average values were found out.

Drug content: Twenty tablets were weighed and powdered. An amount of powder equivalent to 20mg of Lornoxicam was dissolved in 0.1 N Hydrochloric acid, filtered, diluted the sample suitably and analyzed for drug content at 378 nm using UV-Visible Spectrophotometer.

Wetting time: A piece of tissue paper(12cm x 10.75cm) folded twice was placed in Petri dish(internal diameter =9cm) containing 9ml of water. A tablet was placed on the tissue paper and the time for complete wetting of tablet was measured in seconds. The test performed thrice and average value was determined.

In vitro dissolution study: Dissolution study was carried out using a digital tablet dissolution apparatus in 900ml of 0.1 N Hydrochloric acid as dissolution media kept at 37 ± 0.5^0C. The test carried out for 30 minutes. The aliquots of sample were withdrawn at 0,5,10,15,20,25 and 30 minutes filtered suitably diluted and analyzed at 378nm using UV-Visible Spectrophotometer. The data thus obtained were fitted to various kinetic models.

Water absorption ratio (R): The weight of the tablets prior to placement in the Petri dish containing water was noted. The weight of tablets after placing the water also noted. The water absorption ratio, R was then determined according to the following equation.

Water absorption ratio, $R = 100 \times \frac{(W_a - W_b)}{W_b}$

Where, Wb = weight of tablets before water absorption, Wa = weight of water after absorption

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3.RESULTS AND DISCUSSION

Superdisintegrants generally use either for developing orodispersible tablets or for improving dissolution of active pharmaceutical ingredients from the solid dosage form. In this work superdisintegrants were used in two different concentrations like 4.5% and 6.5 %. Drug compatibility study carried out by FTIR Spectrophotometer (Fig no.1) The results showed that drug and excipient were compatible. Natural superdisintegrants were evaluated by their swelling property and flow property (Table no.1). Swelling index value is highest for Ispagol mucilage and lowest for Ispagol husk powder. All of these agents showed excellent flow properties. The powder blend was evaluated by determining bulk density, tapped density, compressibility index, Hausner's Ratio and Angle of Repose (Table no.2). All values come within specified limits and showed that it is suitable for direct compression (Table no.3). The evaluation tests like weight variation, hardness, friability, drug content, thickness, disintegration time, wetting time, water absorption ratio (Table no.4) and In Vitro drug release studies were carried out (Table no.5). The lowest disintegration time and high drug release was shown by F2 formulation and selected as optimized formulation. The stability studies of optimized formulation was carried out. It complies with stability conditions.

CONCLUSION

In the present work , both natural and synthetic superdisintegrants were used for the formulation of Orodispersible tablets. The evaluation studies showed that natural and synthetic super disintegrants were differed in their ability to disintegrate the Lornoxicam Orodispersible tablets when used in different concentrations. Hence such difference can potentially affect the drug dissolution rate. The Orodispersible tablets developed in this study will hopefully contribute to improve the drug administration to the patients with difficult to access water (travelers and mentally ill) and also suffering swallowing problems. These tablets much useful for treating acute pain conditions.

Fig 1: FTIR Spectrum of Lornoxicam

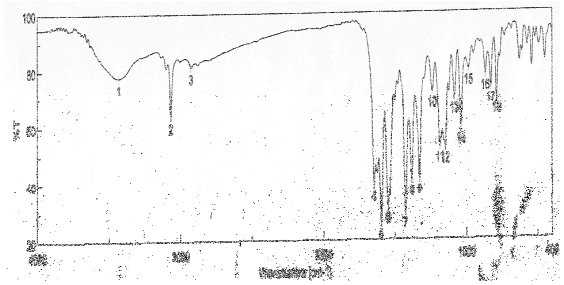

Fig 2:Characterization of Lornoxicam Betacyclodextrin complex

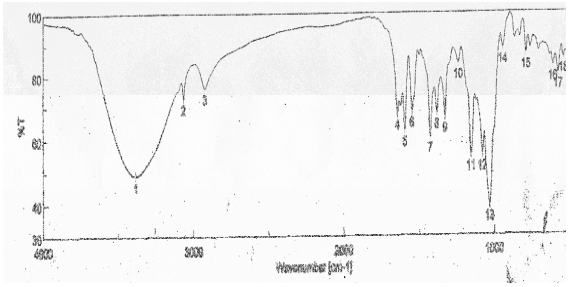

Fig 3: Drug complex with physical mixture

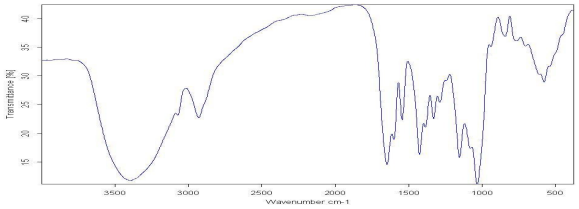

Table No.1: Evaluation of natural superdisintegrant

Parameters	Ispagol mucilage	Ispagol powder	Ispagol powder
Swelling index(%)	21.80	18.30	13.30
Angle of repose (o)	19.20 ± 0.32	20.13 ± 0.23	22.06 ± 0.32

Table No.2: Evaluation of powder blend

Formulation code	Bulk density (gm/ml)	Tapped density(gm/ml)	Hausners Ratio	Carr'index(%)	Angle of repose
F1	0.293	0.331	1.13	11.48	19.35 ±0.23
F2	0.289	0.321	1.11	9.96	19.01 ±0.11
F3	0.287	0.322	1.12	10.86	23.35 ±0.31
F4	0.289	0.321	1.11	9.96	23.12 ±0.13
F5	0.285	0.324	1.14	12.03	20.21 ±0.15
F6	0.276	0.312	1.13	11.53	20.05 ±1.3
F7	0.280	0.317	1.012	11.67	19.32 ±0.17
F8	0.288	0.322	1.12	10.56	19.11 ±0.23
F9	0.284	0.326	1.15	12.88	21.19 ±0.21
F10	0.285	0.324	1.14	12.03	21.01 ±0.26
F11	0.283	0.325	1.15	12.92	23.32 ±0.23
F12	0.285	0.323	1.13	11.76	23.06 ±0.20

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Table No.3: Formulation of Oro dispersible Tablets

Code	Wt.variation n=3±SD	Thickness in mm n=3±SD	Hardness (Kg/cm^2) n=3±SD	Friability (%)	Drug content(%) n=3±SD	Disintegration time (sec) n=3±SD	Wetting time(sec) n=3±SD	Water absorption ratio
F1	198.63 ±0.26	2.97 ±0.021	3.54 ±0.12	0.36	99.63 ±0.26	22.33 ±2.10	50.66 ±1.9	65.41
F2	199.63 ±0.21	2.99 ±0.012	3.58 ±0.13	0.30	99.88 ±0.24	21.00 ±1.52	47.66 ±1.5	65.31
F3	197.63 ±0.36	2.96 ±0.023	3.98 ±0.21	0.31	100 ±0.41	31.33 ±2.30	63.00 ±2.3	73.81
F4	200.63 ±0.46	2.97 ±0.022	3.46 ±0.17	0.40	98.60 ±0.53	30.62 ±2.00	66.33 ±2.2	74.01
F5	198.63 ±0.26	3.01 ±0.02	3.18 ±0.15	0.38	100.03 ±0.65	26.66 ±2.50	63.33 ±2.2	66.62
F6	196.63 ±0.45	2.98 ±0.022	3.06 ±0.17	0.30	98.85 ±0.41	25.66 ±3.00	57.67 ±2.1	67.17
F7	198.73 ±0.36	2.97 ±0.018	3.24 ±0.20	0.33	99.54 ±0.43	26 ±2.50	54.33 ±1.9	65.31
F8	197.63 ±0.31	2.98 ±0.021	3.26 ±0.23	0.31	99.78 ±0.38	24.66 ±2.10	52.66 ±2.3	65.17
F9	199.63 ±0.26	2.96 ±0.023	3.03 ±0.19	0.34	99.61 ±0.56	28.00 ±2.20	52.00 ±2.2	66.17
F10	198.63 ±0.26	2.93 ±0.014	3.38 ±0.17	0.42	99.43 ±0.41	26.66 ±3.10	53.33 ±2.7	66.98
F11	199.63 ±0.26	2.94 ±0.016	3.14 ±0.21	0.35	99.21 ±0.60	33.66 ±2.10	65.33 ±2.6	74.12
F12	199.63 ±0.26	2.96 ±0.021	3.08 ±0.19	0.33	99.56 ±0.51	32.23 ±2.20	63.00 ±2.3	73.65

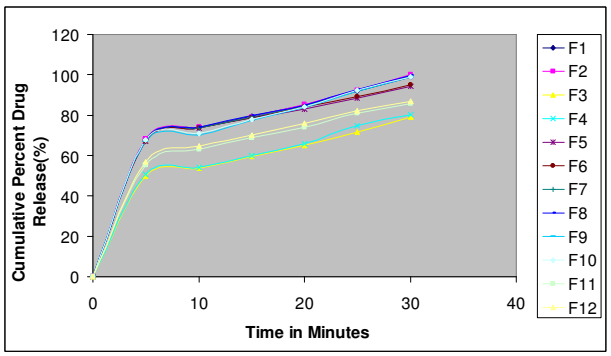
Table No.4: Evaluation tests for ODTS

Ingredients	Quantity in mg/tablet											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Complex eq.to 4mg drug	11.23	11.23	11.23	11.23	11.23	11.23	11.23	11.23	11.23	11.23	11.23	11.23
M.C.C.	92.0	92.0	92.0	92.0	92.0	92.0	92.0	92.0	92.0	92.0	92.0	92.0
Mannitol	79.0	76.0	79.0	76.0	79.0	76.0	79.0	76.0	79.0	76.0	79.0	76.0
Isp.mucilage	9.0	12.0	-	-	-	-	-	-	-	-	-	-
Isp.husk powder	-	-	9.0	12.0	-	-	-	-	-	-	-	-
Isp.powder	-	-	-	-	9.0	12.0	-	-	-	-	-	-
Cross povidone	-	-	-	-	-	-	9.0	12.0	-	-	-	-
S.S.G.	-	-	-	-	-	-	-	-	9.0	12.0	-	-
Ca. C.M.C.	-	-	-	-	-	-	-	-	-	-	9.0	12.0
S S F	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Talc	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Aspartame	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Aerosil	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
Orange flavor	0.27	0.27	0.27	0.27	0.27	0.27	0.27	0.27	0.27	0.27	0.27	0.27
Total weight	200	200	200	200	200	200	200	200	200	200	200	200

Table No.5: Dissolution profile of formulations

Code	Time						
	0	5	10	15	20	25	30
F1	0	67.83	73.88	79.50	84.91	91.82	99.03
F2	0	68.33	74.06	79.06	85.18	92.16	99.98
F3	0	49.83	53.88	59.50	64.91	71.82	79.03
F4	0	50.70	54.28	60.08	65.89	74.98	80.28
F5	0	67.13	73.48	78.88	83.17	88.41	94.31
F6	0	67.15	73.51	78.88	84.17	89.31	94.91
F7	0	67.63	73.75	79.13	84.37	92.01	99.51
F8	0	67.80	74.05	79.76	84.98	92.82	99.88
F9	0	67.01	70.23	77.45	83.76	91.78	98.88
F10	0	67.75	70.91	77.93	84.01	92.15	99.08
F11	0	55.14	63.20	68.78	74.08	81.23	85.53
F12	0	56.75	64.77	70.15	75.85	82.18	86.86

Fig 4: Comparitive dissolution studt



REFERENCES

Birader S S, Bhagavathi S T, Kuppasad I.J, Fast Dissolving Drug Delivery Systems Abrief overview, International Journal of Pharmacology, 2006, 516-519.

Brahmakar D.M and Sunil B.Jaiswal, Biopharmaceutics and pharmacokinetics, A Treatise, Edition1, Vallabh Prakashan, Delhi , 1, 19-20,150-177.

Charles R Craig and Robert E Stitz , Modern Pharmacology with clinical application, Edition 6, Bettyson, 316.

Crollman, Pharmacology and Therapeutics, Edition 11, 313-330.

Desai S.A, Kharede S.V, Petkar K.C and Kuchekar B.S, Orodispersible tablets of Promethazine Hydrochloride, Indian Journal of Pharmaceutical Education and Research, 4(3), 2006, 172-174.

Desari and Gandhi, Desari and Gandhi's Elements of Pharmacology, Edition 9, 1, 340-345.

Devi V.K, Asha A.N, Pai R.S and Reddy, Orodispersible Fluconazole tablets-Preparation and evaluation, Indian Drugs, 43(7), 2006, 548-552.

Dr. Gaud R.S, Yadav A.V, Dr.Yeole P.G, Gokhale S.B, Text Book Of Pharmaceutics, Edition 10, Nirali Prakasan, 51-55.

Iman saad Ahmed, Mona Hassan Aboul Einien, InVitro and InVivo evaluation of Fast Disintegrating lyophilized dry emulsion tablets containing Griseofulvin, European Journal of Pharmaceutical Sciences, 32, 2007, 58-68.

Ishiwa T, Mukai B, Sriraishi S and Fuji M, Preparation of Rapidly Disintegrating Tablets containing new types of Microcrystalline Cellulose and low substituted HydroxyPropyl Cellulose or spherical sugar granules by direct compression method, Chemical and Pharmaceutical Bulletin, 44(11), 1996, 213-236.

Jeevanadham S, Dachinamurthy D and Chandrasekhar K.B, Formulation and evaluation of Naproxen Sodium Orodispersible tablets-A sublimation technique, Asian Jornal of Pharmaceutics, 2010, 48-51.

Jinichi Fukami, Yasuo Yoshihashi and Etsuo Yonemmoochi, Evaluation of Rapidly Disintegrating tablets containing Glycine and Carboxy Methyl Cellulose, Science direct International Journal of Pharmaceutics, 310, 2006, 101-110.

Mahajan H.S, Badhan A.C, Kuchekar B.S, Mouth Dissolving Tablets of Sumatriptan Succinate, International Journal of Pharmaceutical science, 66(2), 2004, 238-240.

Nangude T.D, Saifee Maria, Bhaise K.S, Formulation and evaluation of Fast Disintegrating Tablets of Diphen hydramine Tannate, Asian Journal of Pharmaceutics, 1, 2006, 41-45.

Sameer H.Ladake, Formulation development and evaluation of Mouth Dissolving Tablets of Odancetron Hydrochlodide, Asian Jouranal Of Pharmaceutics, 1, 2007, 150-157.

Shailesh Sharma, Sudhir Bharatwaraj and G D Gupta, Fast dissolving Tablets of Promethazine Theoclate by using natural super disintegrants, Research journal of Pharmaceutical Technology, 1 (3), 2008, 218-220.

Venkatalakmi R ,Sasikala C and Swathi R, Formulation and evaluation of Granisetron Hydrochloride mouth dissolving tablets, International Journal of Pharmaceutical Sciences, 1, 2009, 336-341.

Yadav A.V, Shete A.S and Dhabke A.P, Formulation and evaluation of Orodispersible liqusolid compacts of Aceclofenac, Indian Journal of Pharmacuetical Educational Research, 44(3), 2010, 237-235.