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DESIGN AND FORMULATION OF FAST DISSOLVING TABLET OF LORNOXICAMUSING BANANA POWDER AS NATURAL SUPERDISINTEGRANT BY DIRECT COMPRESSION METHOD.

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ABSTRACT

The demands for fast dissolving tablets have received ever increasing day by day during the last 15 years. In the present designed study, the effect of Natural superdisintegrant was compared with synthetic super disintegrants and conventional super disintegrants in the of fast dissolving tablet formulation of Lornoxicam. Lornoxicamis a potent NSAID of oxicam class with analgesic anti-inflammatory and antipyretic properties with management of pain, inflammatory disease of joints, osteoarthritis, surgery sciatica and other inflammations. In the present work 9 formulations of FDT (Fast dissolving tablet) of Lornoxicam were prepared by using isolated Raw Banana powder was evaluated and compiles with the official parameters and standard specifications. Various formulations were prepared using four different superdisintegrants namely- Banana, sodium starch glycolate, cross carmelose sodium with three concentrations (2%, 4%, 6%) by direct compression method. The blend was evaluated for various pre-compression parameters like Angle of repose, tapped density, and then tablet evaluated post-compression parameters like thickness, drug content, hardness, weight variation, wetting time,friability, disintegration time, dissolution time, drug release study. Formulation 5 showed the lowest disintegration time and in-vitro dissolution study data recorded that formulation 5 showed 99.25% drug release at the end of 3 minutes. The best formulations

were also found to be standard and optimized formulations were subjected to the stability studies as per ICH guideline.

KEYWORDS: Fast dissolving tablet, NSAID, Lornoxicam, Banana powder, sodium starch glycolate, direct compression, dissolution time.

INTRODUCTION

The tablet is most widely used dosage for because of its convenience in term of self-administration, compactness, accurate dosage and ease in manufacturing. Over this one drawback of conventional tablet is difficulty in swallowing by pediatric and geriatric patients.[1-2]

To beat these issues the scientists have developed novel drug delivery system that known as fast dissolving tablet. The fast dissolving tablets that dissolving in few seconds in the mouth when they come with the contact of saline without requirement of additional water. The advantage of FDTs (Fast dissolving tablets) is onset of action, higher patient acceptance, and increased bioavailability.[3-4]

Lornoxicam is a non-steroidal anti-inflammatory drug of the oxicam class with analgesic, anti-inflammatory and antipyretic properties. It is available in oral and parenteral formulations. Lornoxicam differs from other oxicam compounds in its potent inhibition of prostaglandin biosynthesis, a property that particularly explains the pronounced efficacy of the drug. Lornoxicam is used for the treatment of various types of pain, especially resulting from inflammatory diseases of the joints, osteoarthritis, surgery, sciatica, and other inflammations.

IUPAC name: (3E)-6-chloro-3-[hydroxy(pyridin-2- ylamino)methylene]-2-methyl-2,3-dihydro-4Hthieno[2,3-e][1,2]thiazin-4-one 1,1-dioxide
Molecular formula: C13H10ClN3O4S2
Molecular mass: 371.8192 g/mol
Drug Bank accession number: DB06725
CAS number: 70374-39-9
Half life: 3-4 hrs
Therapeutic category: Non steroidal anti inflammatory drug (NSAID)
Route: Oral, Parenteral

Solubility: Poorly soluble in water, Soluble in 0.1N NaOH solution.

Mechanism of action

Lornoxicam's anti-inflammatory and analgesic activity is related to its inhibitory action on prostaglandin and thromboxane synthesis through the inhibition of both COX-1 and COX-2. This leads to the reduction of inflammation, pain, fever, and swelling, which are mediated by prostaglandins. However, the exact mechanism of lornoxicam, like that of the other Non steroidal anti-inflammatory drugs (NSAIDs), has not been fully determined.

Bioavailability of Lornoxicam is about 40% to 60% and its half-life is 3-4 hrs. The drug is distributed throughout the body and 30% of drug binds to plasma proteins. It undergoes rapid first-pass metabolism in the liver (approximately 95% of a dose). This leads to lower bioavailability of Lornoxicam. In order to overcome such extensive first-pass metabolismeffect, so the drug is selected for fast dissolving tablet. 5-10.

MATERIAL AND METHOD

MATERIAL

Lornoxicam was received as gift sample by Ultra drugs, Solan, Banana powder, Magnesium stearate used were procured from Rescue Laboratories, Jaipur, Lactose used was procured from RDPL, Jaipur, Asparteme used was procured from Sweetener India, Delhi, and other reagents and chemicals used were of analytical grade.

METHOD

Fast dissolving tablet of Lornoxicam were prepared by direct compression method. Pure drug and excipients were passed through # 60 No. mesh, Required amount of drug and excipients were taken for each formulation (Table No. 1).

The powdered drug, Mannitol and Lactose were mixed uniformly with continuous trituration using mortar and pestle. Then required quantity of super disintegrates and aspartame taken for each formulation and mixed, finally magnesium stearate and talc powder were added and mixed well.

The mixed blend of drug and excipients were compressed using 10 station tablet punching machine. (Shakti pharmaceuticals**)** 4Mm punch. A Batch of 25 tablets of each formulation was prepared for all the required formulation. Before the tablet preparation /punch the mixture blend of all designed formulations were subjected to compatibility studies (IR) and

pre-compression parameters like-Angle of repose, Bulk density, Tapped density, compressibility index, Hauser's ratio.

Pre-formulation studies

Angle of Repose (θ)

Angle of repose is defined as, the maximum possible angle between the surface of the pile of the powder and the horizontal plane of the powder. When more quantity powder is added to the pile, it slides down, until the mutual friction of the particles producing a surface angle θ, is equilibrium with the gravitational force.

The angle of repose is determined by the funnel method suggested by the scientist Newman. Angle of repose is determined by the following formula;

$\text{Tan } \theta = h/r$

$\theta = \text{Tan}^{-1}\ h/r$

Where,

θ = Angle of repose

r = Radius of the cone

h = height of the cone

Bulk Density

Density defined by the value weight per unit volume. Bulk density is defined as the mass of the powder is divided by the bulk volume of powder and is expressed as gm/ cm^3.The bulk density of a powder primarily depends on its, particle shape, particle size, distribution and the tendency of particles to adhere together. There are two types of bulk density.[14]

Low bulk density

The particles are pack in such a way so as to leave large gaps between their surfaces resulting up in light powder of low bulk density.

High bulk density

Here the smaller particles shift between the large particles resulting in heavy powder of high bulk density.

Tapped Density (Dt)

It is expressed as the ratio indexof total mass of the powder to tapped volume of the powder. Volume was reported by tapping the powder for 500 times and the tapped volume was

recorded, if the difference between these two volumes was less than 2%. If it more than 2%, then tapping was continued for 750 times and more 1000 times and tapped volume was recorded. Tapping was continued until the difference between volumes was less than 2% in bulk density apparatus. It was expressed in g/ml and was given as following;

Dt= M/Vt

Where, M is the mass of powder

Vt is the tapped volume of the powder.[15-17]

Carr's index (or) % compressibility

Carr's index indicates powder flow properties. It is expressed bypercentage and is given by:

$I=Dt-Db/Dt\times100$

Where, Dt denotes the tapped density of the powder

And Db is the bulk density of the powder.[18-19]

Hausner ratio

Hausner ratio is an indirect index of ease of powder flow properties. It is calculated by the following formula:

Hausner ratio=Dt/Db

Where, Dt show the tapped density.

Db is the bulk density.

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).[20]

EVALUATATION OF TABLET

All the prepared tablets of Lornoxicamwere evaluated for the following parameters as per IP guideline; all the calculations are represented in the table No. 3.

WEIGHT VARIATION

Twenty tablets of Lornoxicamwere selected randomly from each of the formulation and weighted individually using Citizen Digital Balance for their weight data. The average weight of the tablets as well as percentage deviation was calculated.[21]

HARDNESS

Hardness of theLornoxicam tablet was measured with the tablet hardness testing apparatus known as Monsanto tablet harness tester.[22]

THICKNESS

The thickness of the tablet was measured in mm by the Vernier Calipers for all the designed formulation batches.[23-24]

FRIABILITY

The friability of the Lornoxicam tablet, a sample of twenty tablets was measured using USP type Roche Friabilator. The tablets were dusted reweighed and percentage weight-loss was calculated.[25-26]

%Friability= Initial Weight−Final Weight * 100/ Initial Weight

Water absorption ratio

A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in small Petri-plate (ID = 6.5 cm) containing 10 ml of water. A tablet was placed on the paper and time for complete wetting of the tablet was measured in seconds. Three trials for each batch were performed and the standard deviation was also determined. The wetted tablet was weighed and water absorption ratio R, was determined by following equation.

R = {(Wa – Wb) / Wa} × 100

Where, Wa and W_b were weights of the tablets after and before study.[27-29]

Wetting Time

A piece of tissue paper (12cmX10.75cm) folded twice was placed in a small Petri dish (ID = 9 cm) containing 6ml pH 6.8 phosphate buffer, A tablet was placed on the paper and the time taken for complete wetting was noted. Three tablets from each formulation were randomly selected and the average wetting time was noted.[30-31]

DISINTEGRATION STUDY

Disintegration time study was carried out by selecting6 tablets of Lornoxicamand performed disintegration test (Lab India) using 900ml distilled water at temperature ($37^0C \pm 2^0C$).[32-33]

DISSOLUTION STUDY

The In-vitro for the dissolution study was carried out in the USP (United state pharmacopeia) dissolution test apparatus type 2 known as Paddle dissolution apparatus, used phosphate buffer as dissolution medium as 900ml containing PH 6.8 was taken in vessel and the temperature maintained at 37 ± 0.5^0C. The speed of the paddle was set at RPM 50, then 5 ml dissolution medium was withdrawn and the same amount (5ml) of fresh medium was

replenished to the dissolution medium. The calculations of the Concentration were calculated by absorbance base. The release of the drug was performed in replicates of three.[34-36]

Table No. 1: Formulation of fast dissolving tablet of Lornoxicam.

Ingredients(mg)	FL1	FL2	FL3	FL4	FL5	FL6	FL7	FL8	FL9
Lornoxicam	8	8	8	8	8	8	8	8	8
Cross carmellose Sodium	2	4	6	-	-	-	-	-	-
Banana powder	-	-	-	2	4	6	-	-	-
Sodiumstarc glycolate	-	-	-	-	-	-	2	4	6
Aspartame	2	2	2	2	2	2	2	2	2
Flavour	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2	2	2	2	2
Mannitol	30	30	30	30	30	30	30	30	30
Lactose	25	25	25	25	25	25	25	25	25
MCC	27	25	23	27	25	23	27	25	23
TOTAL	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

RESULT AND DISCUSSION

Table No. 2: Pre-compression parameters of Lornoxicam FDTs.

Parameters / Formulation	Bulk Density (mg/ml)	Tapped Density (mg/ml)	Hausners Ratio	Compressibilty Index (%)	Angle of Repose 0
FL_1	0.472±0.012	0.521±0.011	1.103±0.051	09.40±0.15	24.19±1.38
FL_2	0.461±0.021	0.543±0.019	1.177±0.090	15.10±0.03	25.32±1.35
FL_3	0.451±0.018	0.506±0.014	1.121±0.019	10.86±0.18	24.45±1.40
FL_4	0.481±0.017	0.529±0.012	1.099±0.015	09.07±0.05	24.52±0.55
FL_5	0.492±0.015	0565.±0.019	1.148±0.021	12.92±0.03	28.11±1.25
FL_6	0.466±0.011	0.541±0.017	1.160±0.025	13.86±0.19	24.19±1.89
FL_7	0.458±0.15	0.535±0.010	1.168±0.019	11.21±0.15	25.29±0.15
FL_8	0.475±0.012	0.525±0.019	1.105±0.0.29	09.52±0.05	26.20±0.29
FL_9	0.495±0.017	0.584±0.011	1.179±0.025	15.23±0.16	24.32±1.11

Table No. 3: Post-Compression parameters of Lornoxicam FDTs.

Parameters Formulation	Weight (mg)	Hardness (Kg/cm^2)	Friability (%)	Disintegration Time (Sec)	Swelling Time (Sec)
FL_1	98.05±0.55	3.25±0.15	0.51±0.84	44±1.44	15±1
FL_2	97.57±0.78	3.19±0.01	0.59±0.25	39±1.14	14±2
FL_3	100.01±0.11	3.34±0.09	0.57±0.17	45±1.46	16±1
FL_4	102.02±0.25	3.50±0.12	0.51±0.16	63±1.25	21±1
FL_5	99.99±0.11	3.51±0.01	0.65±0.12	40±1.52	13±2
FL_6	101.05±0.15	3.29±0.10	0.73±0.32	49±1.36	17±2
FL_7	102.01±0.15	3.35±0.05	0.65±0.13	31±1.01	13±2
FL_8	102.50±0.04	3.50±0.09	0.62±0.23	30±1.59	22±2
FL_9	101.02±0.22	3.40±0.18	0.68±0.19	33±1.58	13±1

Drug Content in the Fast Dissolving Tablet of Lornoxicam.

Parameters Formulation	Drug Content (mg per Tablet)	% Drug Content
FL_1	93.51±0.02	93.51
FL_2	95.83±0.04	95.83
FL_3	93.65±0.12	93.65
FL_4	97.25±0.13	97.25
FL_5	99.25±0.15	99.25
FL_6	98.27±0.21	98.27
FL_7	95.23±0.18	95.23
FL_8	97.14±0.14	97.14
FL_9	96.85±0.20	96.85

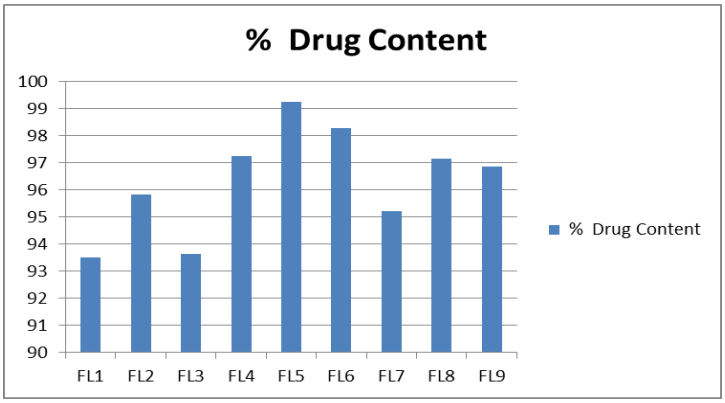


Figure: Drug Content in the Fast Dissolving Tablet of Lornoxicam.

RESULTS AND DISCUSSION

Bulk density and tapped density of powder blend has been evaluated. The angle of repose for the entire formulations blend was found to be in the range 24.19 to 28.11°. Formulations with Crosscarmelose Sodium (FL1-FL3) as a disintegrant showed angle of repose values ≤ 25.32°. Other the formulation Banana powder containing (FL4-FL6) was showed angle of repose values <28.11° and Sodium starch glycolate (FL7-FL9) was showed angle of repose values ≤26.20° indicating only fair flow property of the powder blend. Compressibility index was found to be in the range 09.40 % to 15.23 %. All formulations showed good flow properties. Hausner's ratio was found to be in the range 1.099 to 1.179 and that indicated that all formulation has good flow properties. The batches FL2, showed low hardness (3.19±0.01kg/cm^2) and FL5 higher (3.51±0.01kg/cm^2). Higher friability was of FL6 (0.73±.32) and low friability FL4 (0.51±0.16%). All parameters show weight variation, thickness, Disintegration time (sec) within standard limit. All formulation was subjected to dissolution. From all the above observations it was concluded that the formulation FL5 containg Banana powder 4% found to be better formulation in terms of rapid dissolution and

but maximum percentage drug release was found 99.25% of formulation FL5, with Banana 4%.

Fit of Various Kinetic Models for Fast Dissolving Tablet of Lornoxicam.

Formulation Code	Zero Order R^2	First Order R^2	Higuchi Model R^2	Korsemeyer Model R^2
FL1	0.836	0.981	0.972	0.993
FL2	0.815	0.964	0.966	0.952
FL3	0.821	0.967	0.969	0.973
FL4	0.796	S0.965	0.963	0.941
FL5	0.807	0.989	0.965	0.996
FL6	0.791	0.985	0.962	0.984
FL7	0.790	0.977	0.963	0.959
FL8	0.789	0.992	0.964	0.974
FL9	0.795	0.990	0.966	0.991

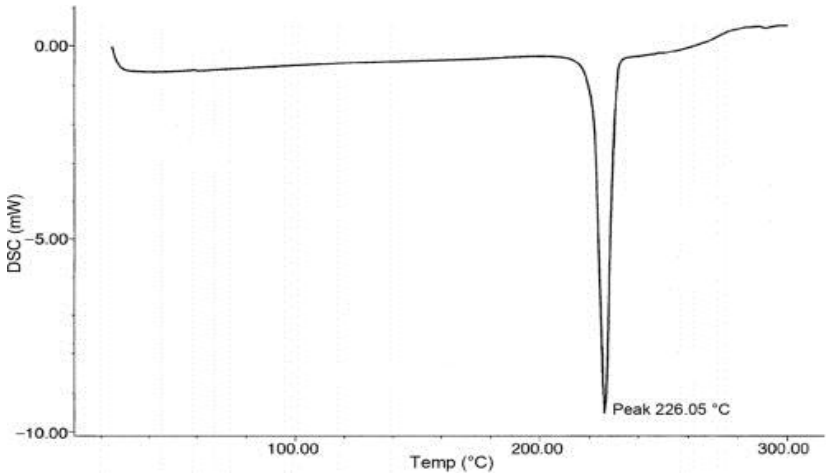
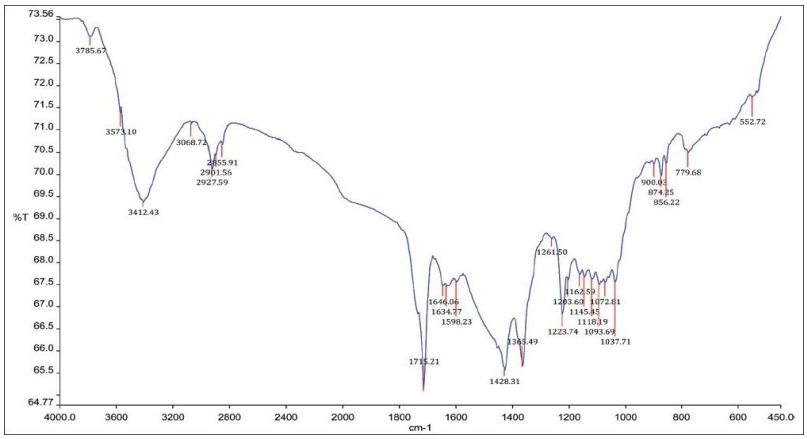


Figure: DSC Thermogram of Lornoxicam.



CONCLUSION

It can be concluded from the whole study that fast dissolving tablets of Lornoxicam drug. Natural Superdisintegrants can be used as pharmaceutical excipients for oral drug delivery. So natural superdisintegrant like Banana exhibited faster drug dissolution which leads to improve bioavailability, effective therapy (Therapeutic ratio), improve patient compliance, and satisfies all the standards as fast dissolving tablet. It was concluded formulation FL5 maximum percentage drug release was found 99.25 with Banana 4%.

From the study, it was concluded that Natural Super disintegrate like Banana powder showed better disintegrating property over the synthetic super disintegrate like, SSG(Sodium starch glycolate) CCS (Crosscarmelose Sodium).

Hence the Banana powder can be used at higher concentration at it has advantage of being non-toxic, low cost, biodegradable and biocompatible with no side effect.

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