Research Article

Formulation, Development and Evaluation of Fast dissolving Tablet of Meclofenamate Sodium by using Natural Superdisintegrant (Banana Powder)

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ABSTRACT

The demands for fast dissolving tablets have received ever increasing day by day during the last decade. In the present projected study, the effect of natural Super disintegrants was compared with synthetic Super disintegrants and conventional Super disintegrants in the of fast dissolving tablet formulation of Meclofenamate Sodium. Meclofenamate sodium NSAID is used for the treatment of mild to moderate pain in various conditions like (e.g., dental pain, osteoarthritis) and to decrease pain and blood loss during menstrual periods. It is also used for other treatments like reducing pain, swelling, and joint stiffness caused with rheumatoid arthritis. In the present work 9 formulations of FDT (Fast dissolving tablet) of Meclofenamate Sodium were prepared by using Super disintegrants was evaluated and compiles with the official parameters and specifications. Various formulations were prepared using four different super disintegrants namely natural super disintegrant Banana Powder, sodium starch glycolate, crosscarmelose sodium with three concentrations (2%, 4%, 6%) by direct compression method. The blend was evaluated for pre-compression parameters like Angle of repose, bulk density, tapped density, and then tablet evaluated with various post-compression parameters like thickness, drug content, hardness, weight variation, wetting time, friability, disintegration time, dissolution time, drug release study. Formulation F2 showed the lowest disintegration time and in-vitro dissolution studies recorded that formulation F2 showed 98.55% drug release at the end of 3 minutes. The best formulations among these were also found to be stable and optimized formulations were subjected to the stability studies as per ICH guideline.

Keywords: Fast dissolving tablet, Natural Super disintegrants, menstrual periods, Meclofenamate Sodium, sodium starch glycolate, Banana powder, direct compression, dissolution time.

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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 these conventional tablets is difficulties 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 contact saline without requirement of additional water. The advantage of FDT (Fast dissolving tablet) is onset of action, higher patient acceptance, and increased bioavailability.[3-4]

Meclofenamate Sodium is the sodium salt form of potent NSAID Meclofenamate sodium, an anthranilic acid and non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory, antipyretic and analgesic actions. Meclofenamate sodium acts inhibiting the activity of the enzymes cyclo-oxygenase I and II, which decreased the formation of precursors of prostaglandins and thromboxanes. Meclofenamate sodium is also used for the treatment of primary dysmenorrheal (painful menstrual periods) and for the treatment of idiopathic heavy menstrual blood loss.

It undergoes rapid first-pass metabolism in the liver (approximately 95% of a dose). This leads to lower bioavailability of Meclofenamate Sodium. Such drugs shows first-pass metabolism effect, so the drug is selected for fast dissolving tablet.[5-10]

MATERIALS AND METHOD

Material

Meclofenamate Sodium was received as gift sample by Pro Lab Marketing Pvt. Ltd., Delhi, Magnesium stearate used were procured from Reckon animal health care, Jaipur ,Banana powder was gifted by Ayursatva, Madhya-Pradesh, Asparteme used was procured from Sweetener India, Delhi, and other reagents and chemicals used were of analytical grade.

Method

Fast dissolving tablet of Meclofenamate Sodium 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 every formulation (Table No. 1). The powdered drug, Mannitol and Lactose were mixed uniformly with continuous trituration using mortar and pestle. Then weighed quantity of super disintegrates and aspartame taken for each formulation and properly 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**)**. A Batch of 50 tablets of each formulation was prepared for all the designed tablet formulations. 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.[11-12]

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 of the 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.[13]

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

$\tan \theta = h/r$

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

Where θ = Angle of repose, r = Radius of the cone, h = height of the cone

Bulk Density

Density defined as weight per unit volume. Bulk density can be 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 any powder primarily depends on its various parameters such 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 was the ratio index of 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 tapped volume was noted. 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 by percentage and is given by:

$I = Dt - Db/Dt \times 100$

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]

Evaluation of Tablet

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

Weight Variation

Twenty tablets of Meclofenamate Sodium formulation were selected randomly from each of the formulation and weighted individually using Citizen Digital Balance for their weight data. The average weight of the tablets calculated was found in standard range.[21]

Hardness

Hardness of the Meclofenamate Sodium 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]

Friability

The friability of the Meclofenamate Sodium tablet, a sample of twenty tablets was measured using USP type Roche fraibilator. The tablets reweighed and percentage weight-loss was calculated, was found in standard range.[24]

% 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 of every batch was placed on the paper and time for complete wetting of the tablet was measured in seconds. Three random 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.[25-27]

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 then the average wetting time was noted.[28-29]

Disintegration Study

Disintegration time study was carried out by selecting 6 tablets of Meclofenamate Sodium and performed disintegration test using 900 ml distilled water at temperature ($37^0C±2^0C$)[30]

Dissolution Study

The In-vitro for the dissolution study was carried out in the USP (United states pharmacopeia) dissolution test apparatus type 2 known as Paddle dissolution apparatus, used phosphate buffer as dissolution medium as 900 ml containing PH 6.8 was taken in vessel and the temperature maintained at $37±0.5^0C$ as per standard guidelines. The speed of the dissolution apparatus 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 formulation was performed in replicates of three .[31-32]

Table 1: Formulation of fast dissolving tablet of Meclofenamate Sodium

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Meclofenamate	100	100	100	100	100	100	100	100	100
Banana Powder	3	6	9	-	-	-	-	-	-
Sodium Starch Glycolate	-	-	-	3	6	9	-	-	-
Cross carmellose Sodium	-	-	-	-	-	-	3	6	9
Aspartame	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Flavour	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium Stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Mannitol	20	17	14	20	17	14	20	17	14
Lactose	21	21	21	21	21	21	21	21	21
TOTAL	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**

RESULT AND DISCUSSION

Table 2: Pre-compression parameters of Meclofenamate Sodium FDTs

Parameters / Formulation	Bulk Density (mg/ml)	Tapped Density (mg/ml)	Hausners Ratio	Compressibility Index (%)	Angle of Repose
F_1	0.500± 0.011	0.576±0.011	1.103±0.051	13.19± 0.15	24.77± 1.38
F_2	0.471± 0.022	0.538±0.019	1.177±0.090	12.00± 0.03	23.96± 1.35
F_3	0.517± 0.019	0.576±0.014	1.121±0.019	12.66± 0.18	23.19± 1.40
F_4	0.391 ± 0.09	0. 455± 0.02	1.151 ± 0.02	13.11± 0.60	31.14 ± 1.20
F_5	0.365 ± 0.15	0.421± 0.03	1.162 ± 0.04	15.22± 0.75	30.08 ± 1.55
F_6	0.410 ± 0.02	0.481± 0.02	1.171 ± 0.01	14.12± 1.23	35.12 ± 1.42
F_7	0.521± 0.16	0.621± 0.11	1.161± 0.07	15.01± 0.22	30.20± 0.16
F_8	0.582± 0.04	0.482± 0.14	1.141±1.00	16.19± 0.56	28.28± 0.23
F_9	0.495± 0.10	0.572± 0.19	1.103±1.11	17.27± 1.58	29.31± 1.15

Table 3: Post-Compression parameters of Meclofenamate Sodium FDTs:

Parameters Formulation	Diameter (mm)	Thickness (mm)	Weight (mg)	Hardness (Kg/cm²)	Friability (%)	Disintegration Time (Sec)	Swelling Time (Sec)
F_1	4	3	145.05±0.55	3.15±0.15	0.60±0.84	44±1.44	15±1
F_2	4	3	147.57±0.78	3.09±0.01	0.62±0.25	39±1.14	14±2
F_3	4	3	146.01±0.11	3.24±0.09	0.59±0.17	45±1.46	16±1
F_4	4	3	138.02±0.25	3.18±0.12	0.61±0.16	48±1.25	21±1
F_5	4	3	140.01±0.11	3.28±0.01	0.60±0.12	40±1.52	22±2
F_6	4	3	142.05±0.15	3.22±0.10	0.62±0.32	46±1.36	18±2
F_7	4	3	141.01±0.15	3.32±0.05	0.65±0.13	41±1.01	19±2
F_8	4	3	143.50±0.04	3.50±0.09	0.62±0.23	42±1.59	22±2
F_9	4	3	142.02±0.22	3.41±0.18	0.68±0.19	43±1.58	17±1

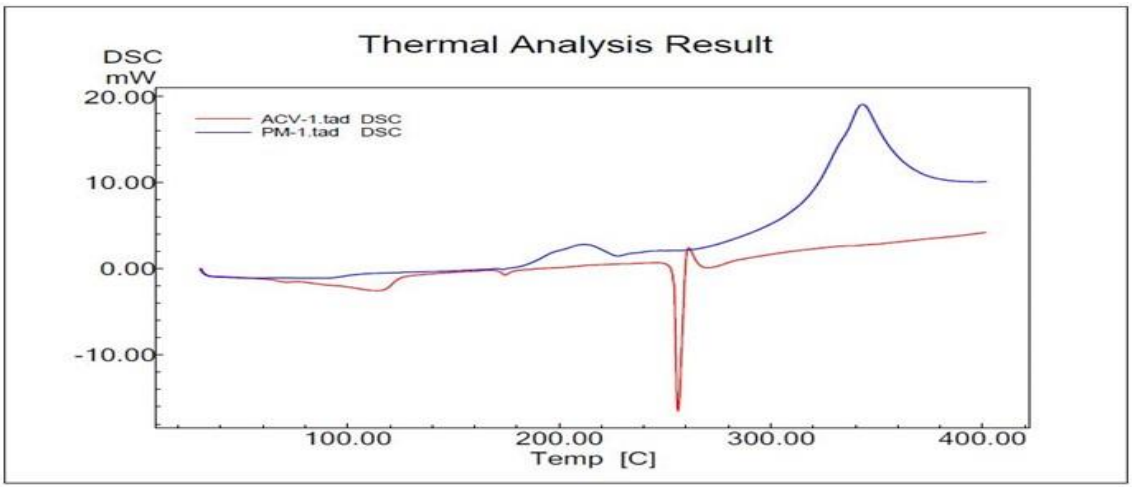

Figure 2: DSC Thermogram of Meclofenamate Sodium

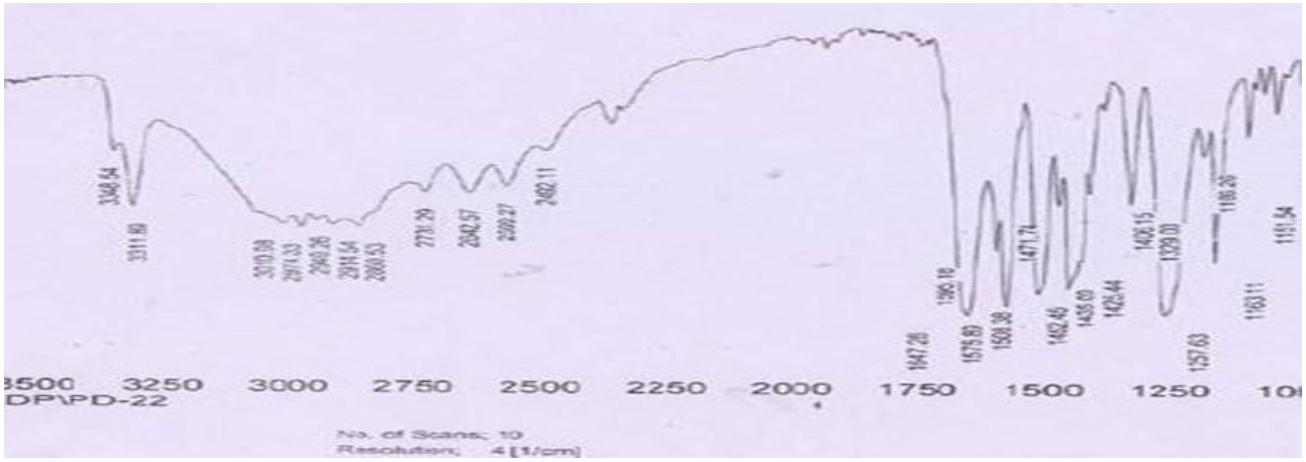

Figure 3: IR spectra of Meclofenamate Sodium

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 23.19 to 35.12°. Formulations with Natural Super disintegrants (Banana Powder) (F1-F3) as a disintegrate showed angle of repose values ≤ 24.77°. Other the formulation Sodium Starch Glycolate containing (F4-F6) was showed angle of repose values <35.12° and last Cross carmelose sodium (F7-F9) was showed angle of repose values ≤30.20° indicating only fair flow property of the powder blend. Compressibility index was found to be in the range 12.00 % to 17.27 %. All formulations showed good flow properties. Hausner's ratio was found to be in the range 1.103 to 1.177 and that indicated that all formulation has good flow properties. The batches showed low hardness 3.09 and higher 3.50. F9 shows Higher friability and F3 show low friability (0.59%).

Table 4: Drug Content in the Fast-Dissolving Tablet of Meclofenamate Sodium

Parameters / Formulation	Drug Content (mg per Tablet)	% Drug Content
F_1	145.66±0.015	97.10
F_2	147.83±0.031	98.55
F_3	145.32±0.115	96.88
F_4	144.33±0.010	96.22
F_5	142.20±0.085	94.80
F_6	143.37±0.151	95.58
F_7	145.33±0.158	96.88
F_8	146.96±0.085	97.97
F_9	145.25±0.150	96.83

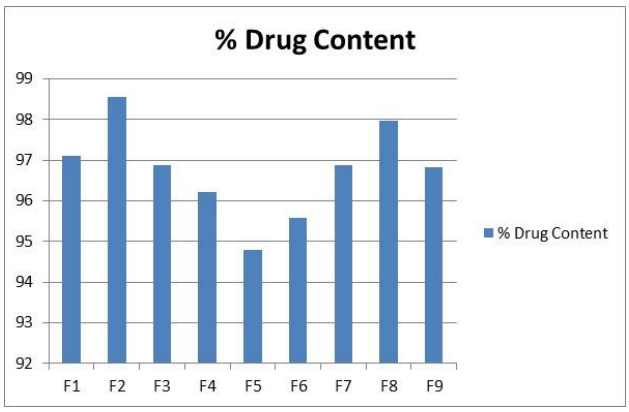

Figure 1: Drug Content in the Fast-Dissolving Tablet of Meclofenamate Sodium

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 F3contain Banana powder 4% found to be better formulation in terms of rapid dissolution and but maximum percentage drug release was found 98.55% of formulation F3, with Banana Powder (4%).

CONCLUSION

It can be concluded from the whole study that fast dissolving tablets of Meclofenamate Sodium drug. Natural Super disintegrants can be used as pharmaceutical excipients for oral drug delivery. So Natural Super disintegrants like Banana Powder 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 F3 maximum percentage drug release was found 98.55%, with Banana Powder.

From the study, it was concluded that Natural Super disintegrants like Banana Powder showed better disintegrating property over the synthetic super disintegrate like, SSG (Sodium starch glycolate) and CCS (Cross Carmellose 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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