Section A-Research paper

ISSN 2063-5346

"Comparative Evaluation of Basil Seeds powder as superdisintegrant with other disintegrant for formulation of Ketorolac Tromethamine Tablet."

Rahul Jadhav[1], Dr.Prof. Sonia Singh[2], Pallavi R. Kaple[3], Vibhavari M.Chatur[3], Kirti Sahu[3], Harshada Gaikwad[3]

Corresponding author- Mr. Rahul Rajendra Jadhav

Email- rahuljadhavrajveer@gmail.com

[1,]Student of MPharm ,Pharmaceutics Department, Alard College of Pharmacy, SPPU, Pune

[2]Dr. Sonia Singh,Principal& Professor of Pharmaceutics Department,Alard College of Pharmacy, SPPU, Pune

[3]AssistantProfessor, Pharmaceutics Department, Alard College of Pharmacy, SPPU, Pune

ABSTRACT:

The purpose of this research was to develop fast disintegrating tablets of Ketorolac Tromethamine containing natural super disintegrant from *Ocimum basilicum seed.* The mucilage was extracted from seeds of *Ocimum basilicum* and used to develop the fast disintegrating tablet of Ketorolac Tromethamine. The disintegration property of mucilage powder in FDTs was compared with widely used superdisintegrants like Sodium StarchGlycolate (SSG), and Crosspovidone .The prepared FDTs were evaluated for uniformity of weight, hardness, thickness, friability,anddisintegration time, *In-vitro* dissolution. From the study, it was concluded that Ketorolac Tromethamine tablet containing *Ocimum basilicum* seed mucilage powder shows disintegration time 18 sec which was less than SSG and Ac-Di-Sol.

Keywords: Ketorolac Tromethamine, *Ocimum basilicum* Seed Mucilage Powder, FDT, Natural Super disintegrant

INTRODUCTION:

Fast disintegrating tablets (FDTs) are oral drug delivery systems resulting in quick disintegration of the administered medicine into solution or suspension when in contact with the saliva. FDTs are commonly known as fast melt, orally disintegrating tablets, fast dissolving tablets, mouth dissolving tablets, quick disintegrating tablet, rapid melt, melt in mouth, quick-dissolving and porous tablet. These formulations have advantages of both solid and liquid dosage systems i.e., they are convenient as solid dosage and easy to swallow as a liquid formulation. The fast-disintegrating drug delivery system provides convenient means of administering tablets especially to paediatrics, geriatrics and patients having difficulty in

ISSN 2063-5346

swallowing conventional dosage form, thus improving compliance to dosage regime. FDTs are also useful when rapid disintegration and absorption of drug is needed thereby producing rapid onset of action.[1,2]Fast disintegration is usually achieved using super disintegrants. They have greater disintegrating efficiency than conventional disintegrants and are effective at low concentrations. Examples of superdisintegrant include Crosspovidone, Sodium Starch Glycolate.[2]

The natural super disintegrants involve various natural substances like gums, mucilage, and other substances of natural origin which are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. Some natural substances like gum karaya, modified starch and agar have been used in the formulation of FDT's. Mucilage of natural origin is preferred over semi- synthetic and synthetic substances because they are comparatively cheaper, abundantly available, non- irritating and nontoxic in nature. Some natural polymer provides the fast disintegration as synthetic super disintegrants. Recently some gums and mucilage have been investigated to improve the disintegration processes. [6]

Ocimum basilicum seed mucilage powder can be used as natural super disintegrant. Ispaghula husk contains the certain amount of dried seeds of the plant which is known as*Ocimum basilicum* .the plant holds mucilage in the epidermis of the seeds. The mucilage of*Ocimum basilicum* has different features like binding, disintegrating and sustaining properties.disintegrating activity *Ocimum basilicum* mucilage provides fast disintegration of tablets. This study aimed to formulate fast disintegrating tablets of Ketorolac Tromethamine using *Ocimum basilicum* mucilage powder as a natural super disintegrant .[6,7]

Ketorolac Tromethamine is a commonly prescribed non-steroidal anti-inflammatory drug (NSAID) that is used as an analgesic, antipyretic and anti-inflammatory drug, and in treating various acute, chronic pain and inflammatory conditions. It is known to dissolve and get absorbed faster than the sodium salt and is thus, recommended in treatment that needs quick onset of action mainly for its analgesic properties. To achieve a fast onset of action, fast disintegrating tablets of Diclofenac can be designed and formulated for quick absorption in the gastrointestinal tract.

MATERIALS:

Ketorolac Tromethamine (Research lab fine chem ,Mumbai), Crosspovidone (Analab fine chemicals ,Mumbai), Mannitol (Analab fine chemicals ,Mumbai), Sodium Starch Glycolate (Hilab chemicals) ,SSG(research lab fine chem ,Mumbai), Micro crystaline cellulose (Analab fine chemicals, Mumbai) Magnesium Stearate(AG traders, Pune), MCC (Analab fine chemicals, Mumbai), *Ocimum basilicum* seed was purchased at a local market in pune and processed into powder in the laboratory.

METHODS: Preparation of *Ocimum basilicum* Mucilage Powder

Seeds of *Ocimum basilicum* were used for isolation of mucilage .they were soaked in distilled water for 24 h and then boiled for 30 min for complete release of mucilage into water. the material was filtered by squeezing in a muslin cloth to remove marc, then equal volume of acetone was added to filtrate to precipitate the mucilage. The mucilage was

ISSN 2063-5346

separated and dried in oven at a temperature less than 60℃, powdered (60 mesh) and stored in desiccator.[2]

Evaluation of Ketorolac Tromethamine[3,4,5]

Determination of ⋋max for Ketorolac Tromethamine:

Ketorolac Tromethamine Pure drug 100 mg was transferred into 100 ml of Phosphate buffer pH 6.8 in a volumetric flask to prepare Standard stock solution. From this Std stock solution 10ml was diluted to 100 ml with Phosphate buffer 6.8 solution and scanned for Ketorolac Tromethamine drug over range of 200-400 wavelength. The ⋋max 323 nm was determined from this scan.

Standard calibration curve of Ketorolac Tromethamine in buffer pH 6.8

Accurately weighed 100 mg of Ketorolac Tromethamine was added to 100 ml volumetric flask, volume made up to 100 ml with Phosphate buffer pH 6.8 as stock solution. From this Std stock solution working solutions of 5,10,15,20,25,30 ppm were prepared separately. Absorbance was measured for each solution at ⋋max 323 nm using UV spectrophotometer. Calibration curve was plotted for absorbance vs. Concentration to confirm linearity.

Formulation of Fast Disintegrating Tablet: Direct Compression method- FDT of Ketorolac Tromethaminewere formulated by using direct compression method. The composition of tablet are given in table 1 below.All the ingredient except Magnesium Stearate as shown in table were pass through mesh 60 and mixed thoroughly. The above blend was lubricated with Magnesium Stearate and the powder blend was compressed into tablets on a 12 station rotary tablet punching machine using 8 mm flat round bevelled edged punch.[8, 9]

Table 1 :Formulation of Fast disintegrating tablet of Ketorolac Tromethamine.

Sr. no.	Ingredient mg/tablet	F1	F2	F3	F4	F5	F6
1	Ketorolac Tromethamine	25	25	25	25	25	25
2	Sodium Starch Glycolate	20.5	37.5	—	—	—	—
3	Crosspovidone	—	—	20.5	37.5	—	—
4	*Ocimum basilicum* powder	—	—	—	—	20.5	37.5
5	Mannitol	172	155	172	155	172	155

ISSN 2063-5346

8	Micro-Crystalline Cellulose	20	20	20	20	20	20
9	Magnesium Sterate	2.5	2.5	2.5	2.5	2.5	2.5
10	Talc	10	10	10	10	10	10
11	Total weight	250	250	250	250	250	250

Pre-CompressionEvaluation Parameter Prior to compression, the powder blends should be evaluated for their Bulk and Tapped density and CompressibilityIndex and Hausner'sRatio calculated.[10,11]The Angle of Repose was also determined.

Bulk density and Tapped density : An accurately weighed amount of powder should be introduced in 100 ml measuring cylinder. Note the initial volume as Bulk Volume, then the cylinder should be tapped 100 times on a plane hard surface and tapped volume of material should be recorded. Bulk density (BD) and TappedDensity (TD) should be calculated using following formula:

BD = Mass/BulkVolume ……(1)

TD = Mass/TappedVolume. ……(2)

Hausner Ratio: Hausner's ratio is an index of ease of powder flow. It is calculated by the ratio of Tapped density andBulk density as given in formula :

HI = Tapped Density / Bulk density ……(3)

Angle of repose : It is determined by the funnel method. The blend was poured through a funnel, that can be raised vertically to a maximum cone height (h). The radius of the heap (r) was measured. The Angle of Repose is calculated by following formula(12)

TanØ= h / r ……. (4)

Carr's index (Compressibility) : The difference between tapped and bulk density divided by the tapped density was calculated and ratio expressed as a percentage. The equation is as given below:

CI = (TD- BD)/ TD ……..(5)

Post- Compression Evaluation Parameters :

General Appearance and OrganolepticProperties: Itinvoles measurement of tablet size,shape,colour,surfacetexture.volunteers opinion for bitterness were recorded.[13,14]

ISSN 2063-5346

Weight variation test : Individually weigh 20 tablets, which are selected at random and calculate the average weight. Then calculate differnce of individual weigh from average weight.

Tablet hardness: Monsanto hardness tester can be used to determine the force required to break the tablet.

Tablet Friability : Weigh twenty tablets and subject them to abrasion by employing a Roche friability Apparatus at 25 rpm for 4 min. Weigh the tablets and compare with their initial weights to obtain percentage friability.

Thickness: The thickness in millimetres (mm) should be measured individually by Verniercalliper.

Disintegration time : For this test, six tablets are used in water at 37^0 C using a tablet disintegration tester. The time required for disintegrating all tablets and passing completely through the sieve is recorded.

***In vitro* dissolution study :**The release rate of drug from FDTs is determined using USP dissolution testing apparatus 2 (paddle method). The dissolution test is performed using 900 ml of Phosphate buffer 6.8 at 37±0.5 ^{0} C at 100 rpm.upto30 min by withdrawing 5ml sample every 5 min intervals and replacing with Phosphate buffer.

Drug Content : Accurately weighed 10 tablets are powdered and quantity equivalent to 25 mg of Ketorolac Tromethamineweighed and transferred into 100 ml volumetric flask. Initially 5 ml Ethanol was added and shaken for 10 min, then volume made up with Phosphate buffer pH 6.8. This solution filtered.diluted suitably and evaluatedspectro-photometrically at 276 nm.

Drug excipient compatibility study by FTIR : Compatibilty of drug with excipient was confirmed by carrying out IR studies,using FTIR spectrophotometer. The pure drug along with excipient were subjected to IR studies.IR of pure drug and IR of FDT were carried out by PotassiumBromide pellet was employed.

RESULT AND DISCUSSION :

Determination of ⅄max for Ketorolac Tromethamine :

ISSN 2063-5346

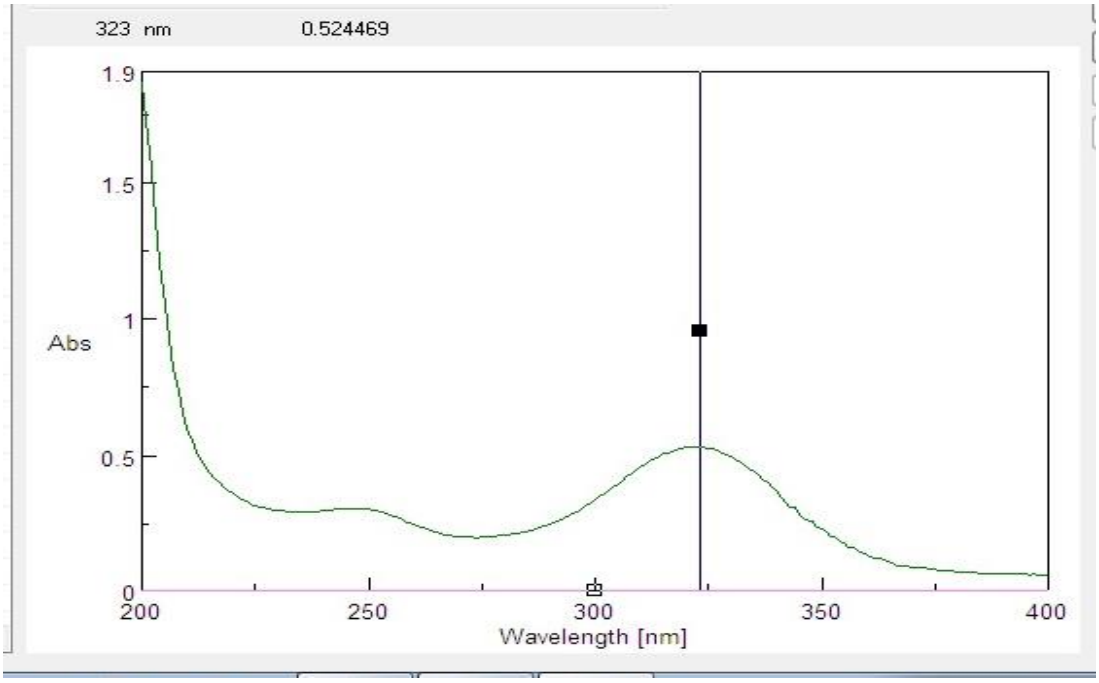

Fig. 1: **Determination of ⅄max of Ketorolac Tromethamine** at 276nm

Calibration Curve of Ketorolac Tromethamine :

The calibration curve of Ketorolac Tromethamine in Phosphate buffer pH 6.8 , its dilutions used for absorbance are given in table 2.

Table 2: Calibration curve of Ketorolac Tromethamine

Sr No	Conc.(µg/ml)	Absorbance
1	5	0.132
2	10	0.342
3	15	0.462
4	20	0.582
5	25	0.712

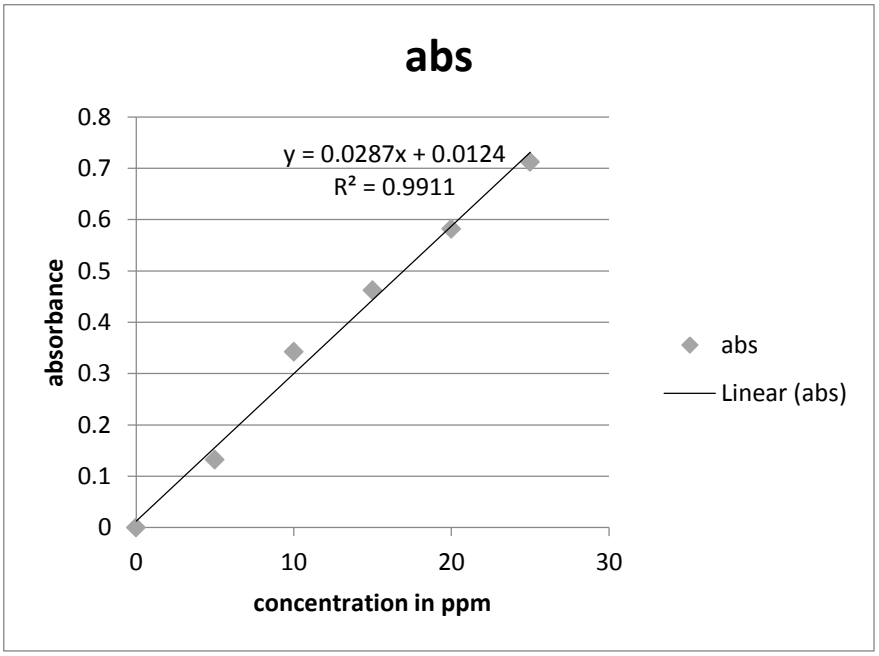

Fig. 2 Calibration curve: Ketorolac Tromethamine in PBS 6.8

ISSN 2063-5346

Pre- Compression Parameters : The values of all pre-compression parameters are given in Table 3.

Table 3 : Pre Compression Parameter

Formulation	Bulk Density (g/ml)	Tapped Density (g/ ml)	Angle of repose (^{o})	Hausners ratio	Carr's Index %
F1	0.66±0.01	0.53±0.01	27.70^0 ±0.01	1.24±0.02	19.69 ±0.02
F 2	0.64±0.01	0.53±0.01	26.74±0.01	1.20±0.01	18.18±0.02
F 3	0.67±0.01	0.54±0.01	27.21±0.01	1.24±0.01	19.40±0.03
F 4	0.67±0.01	0.55±0.01	26.93±0.02	1.21±0.02	17.91±0.01
F 5	0.69±0.01	0.56±0.01	27.35±0.01	1.23 ±0.02	18.84±0.02
F6	0.69±0.01	0.53±0.01	27.72±0.01	1.24 ±0.02	19.69±0.02

Post Compression Parameters : The values of compression parameters are shown in table 4 below.

Table 4: Compression parameters of trial batches.

Trial no .	Wt mg	Hardness kg	Thickness mm	Friability (%)	D.T (sec)	Drug Content
F 1	248.3	3.38±0.1	4.09±0.15	0.62	1min 7	95.23
F 2	248.2	3.4 ±0.2	3.89± 0.01	0.66	39 s	96.30

ISSN 2063-5346

F 3	249.2	3.5 ±0.1	3.70 ± 0.1	0.66	49se	95.28
F 4	247.8	3.5 ±0.3	3.40± 0.05	0.64	1min 38 sec	94.65
F 5	249.5	3.3 ±0.2	4.53± 0.01	0.64	43 sec	92.08
F 6	249.7	3.3±0.2	3.85±0.15	0.66	18 sec	97.76

Comparative study of all batches i.e F1 to F6 shown in below pie chart with respect to disintegration time. From pie chart, it can be seen that batch F6 shows minimum disintegration time i.e .18 sec compare to others (with *Ocimum basilicum* seed mucilage powder natural superdisintegrant)

Dissolution Study:

The % dissolution release data shows that F2 contain(37.5 mgCrosspovidone) 91.44%DR,F2 contain (37.5 mg SSG)93.06%DR,F6 contain (37.5 mg *Ocimum basilicum* seed mucilage powder) 98.22%DR,To compare %DR graph plotted as time/%DR for batches F3,F5,and F6.

Comparative %DR of F4 (Crosspovidone),F2(SSG),F6(*Ocimum basilicum* seed mucilage powder)

Disintegration time of batch F4 (contain Crosspovidone)-39 sec F2(contain SSG)-49 sec,F6(*Ocimum basilicum*seed mucilage powder)-18 sec. batch F6 shows lowest D.T compared to F2 and F4.

Drug content (%) of batch F1,F2,F3,F4,F5,F6 were determined. which is obtained as (F1-95.23),(F2-96.30),(F3-95.28),(F4-94.65)),(F5-92.08),(F6-97.76)..compared to others batch F2,F6,F3 and batch F6 shows maximum % drug content.% Dissolution release of batch F2-93.06%,F4-91.44%, and F6-98.22 %,here F6 shows maximum % drug release compared to F2 and F4.All pre-compression and post compression parameters of F6 was also in limits. Batch F6 with (*Ocimum basilicum* seed mucilage powder) as a natural superdisintegrant shows optimum result compared to F2 and F4 with (SSG) and (Crosspovidone).

CONCLUSION : In the Present work FDT of Ketorolac Tromethamine by using *Ocimum basilicum* seed mucilage powder were prepared by direct compression method.use

ISSN 2063-5346

of other superdisintegrant like SSG, Crosspovidone to compare with natural superdisintegrant. F4 contain (Crosspovidone),F2 contain(SSG),and F6 contain (*Ocimum basilicum* seed mucilage powder as a natural superdisintegrant) compared D.T obtained F4-39 sec,F2-49sec,F6-18sec.Batch F6 found to be more optimum compared with F2 and F4,comparative %DR vs time graph also indicates F6 shows 98.22% drug release. Hencewe can say natural superdisintegrant shows more efficiency than commercial disintegrants.i.e (Crosspovidone),(SSG).The FTIR spectra study shows that no interaction between drug and excipient,drug is compatible with all excipient used in optimized formulation. Hence it is concluded that the Ketorolac Tromethamine FDT using *Ocimum basilicum* seed mucilage powder as a natural superdisintegrant can be successfully prepared by direct compression method.

REFERENCES :

1. Femi Joseph,K. Premaletha, Natural Superdisintegrants for the Formulation of Orally Disintegrating Tablets,International Journal of Research and Review,vol-8,2021,Pg,No.126.

2. OgochukwuAugustinaMeko,Formulation& Evaluation of Fast disintegrating tablet of Ketorolac Tromethamine using Pleurotus tuber-regiumpowder,International Journal of Pharmacy & Pharmaceutical Research,vol-1 2020,Pg.No.218,231.

3. The united states pharmacopeia,the national formulary,by authority of the united states pharmacopial convention prepared by the council of experts and its expert committees,vol-2,2014,pg no-2592-2593.

4. Sonia Singh, Rahul Bomma,Nalanda Rangari,Sonal Bore, Ganesh Dubale Formulation and evaluation of ofloxacin alginate microspheres for lung infection in the form of dry powder inhaler, International Journal of Food and Nutritional Sciences 2022 11(1), 1373-1393

5. Indian pharmacopia,goverment of india ministry of health and family welfare,published by the indianpharmacopia commission ghaziabad,vol-1,2014,pg no-757.

6. British Pharmacopoeia, the department of health,social services and public safety,published by medicines and healthcare product regulatory agency,vol-1,2013,pg no-701.

7. S.M.Shahidulla,MohibKhan.Formulation& Evaluation of Fast disintegrating tablet of Domperidone by using *Ocimum basilicum* mucilage, Dr.Samuel George Institue of Pharmaceutical sciences,2012,Pg.No.1527.

8. TadiousChimombe,SubhankarMukhopadhyay,Orally Disintegrating Tablets: Formulation, Preparation, Evaluation And Recent Advances: A Review,Dr.Samuel George Institue Of Pharmaceutical Sciences,2012,Pg.No.1527.

9. BhiseSucheta D, JarandeKiran,Isolation and Evaluation of Natural Superdisintegrant from *Ocimum basilicum* in MDTs of Telmisartan,IJPI's Journal of Pharmaceutics and Cosmetology,2012,Pg.No.11,15.

10. TanselComoglu,AysegulDogan,Formulation& Evaluation of Fast disintegrating tablet of Diclofenac Potassium and their clinical application in migraine patients,Drug Development and Industrial Pharmacy,2011,Pg.No.261,262.

11. EragaSO,AkpanFE.Evaluation of fast disintegrating tablet of paracetamol prepared from cross carmellose and pleurotus tuber regium powder. Pakistan journal of pharmaceutical science.2018,2503-2508.

12. Sonia Singh, Shubhangi Parbhane, Nalanda Rangari, Dnyaneshwar Lingse, Rosalin Alexander, Vishal More Formulation and evaluation of oral soluble film of Dapagliflozin using permeation enhancer International Journal of Health Sciences 2022 11(1), 1394-1407

13. Hartsell T, Long D and Kirsh JR. The efficacy of postoperative ondansetron (Zofran) orally disintegrating tablets for preventing nausea and vomiting after acoustic neuroma surgery. Anaesthesia and Analgesia. 2005;105(5): 1492-1496.

14. Iwuagwu MA and Onkeyweli AO. Preliminary investigation into the use of pleurotustubberregium. Mushworld publication 2004; 1: 29-37.

15. Markl D and Zeitler JA. A review of disintegration mechanism and measurements techniques. Pharmaceutical research. 2017; 34(5): 890-917.

16. Reddy LH, Ghosh B and Rajneesh. Fast dissolving drug delivery system: A review of literature. Indian Journal of pharmaceutical Sciences. 2002; 64(4): 331-336.