FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLET OF KETOROLAC TROMETHAMINE

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ABSTRACT

The main objective of the present research work was to establish the mouth dissolving tablet of Ketorolac Tromethamine for the management of moderate to severe pain that may get caused after Dental Procedures. The drug excipient compatibility was evaluated by Fourier transform .Infrared Spectroscopy (FTIR). It confirmed that there is no interaction between the drug and excipients used. The MDT were prepared using Direct Compression Method by using various natural and synthetic superdisintegrant such as Crosspovidone, Crosscarmellose, Modified Agar and Banana Powder. The formulation batches of mouth dissolving tablet of Ketorolac Tromethamine were designed by employing different Superdisintegrants. All Superdisintegrants were used alone and in combination at various concentrations; and were taken to see the combination effect. The effectiveness of the synthetic **(Crospovidone,Croscarmellose)** and natural disintegrants **(Banana Powder, Modified Agar)** was compared and the best combination was recorded with different concentrations and their batches were formulated. The pre-compression study was performed and the results were reported. In pre-compression study the angle of repose, bulk density, tapped density, Hausner's ratio and Carr's index was calculated and results shown the good compliance as per IP standards. The tablets parameters were

evaluated by testing weight variation thickness, hardness, friability test etc. The disintegration time for MDT was found to be **45±1.26 to 79±1.41 sec**. The formulation **F10** showed the best results of the dissolution study containing combination of **Crospovidone** and **Modified Agar**. The formulation **F10** showed **98.76%** of cumulative drug release within 30min. This unique formulation of Ketorolac Tromethamine MDT demonstrated a rapid onset of action and will be useful and practical for pediatric, geriatric, and psychiatric patients as well as those who have trouble swallowing and in circumstances where water is not readily available.

KEYWORDS – Mouth Dissolving Tablet, Ketorolac Tromethamine, Crospovidone, Modified Agar, Banana PowdeR

INTRODUCTION

Currently, oral delivery is the standard of excellence in the pharmaceutical industry. It is thought to be the safest, most practical, cost-effective, and patient-compliant method of drug delivery. The MDT had its origins in tablets made to dissolve on the buccal (cheek) mucous membrane. The medicine is absorbed by the digestive system through cheek absorption for quick systemic distribution.

The original MDTs, created to help young people more comfortable ingesting vitamins, dissolved by effervescence rather than dissolution. Through improved manufacturing techniques and the addition of ingredients (such as the addition of mannitol which increases the binding and decreases dissolution time), dissolution became more effective than.[1]

Adults with moderate to severe pain are treated temporarily with Ketorolac Tromethamine. It is typically utilised before, during, or following medical operations or surgery. In order to recuperate more comfortably and resume your regular daily activities, pain must be reduced. Nonsteroidal anti-inflammatory drugs (NSAIDs) are what this medication is.

It functions by preventing your body from producing some natural inflammatory molecules. This effect helps to decrease swelling, pain, or fever. Therefore, in this study, efforts are made to increase the onset of action and to create a Mouth Dissolving Tablet of Ketorolac Tromethamine that will have a quicker action as a NSAID.[2]

Essential Requirements of MDT's

- No need of water for administration as it should disintegrate, disperse and dissolves in mouth within seconds.
- Should have a pleasant mouth feel
  a. with improved taste
  b. without any residue in the mouth after disintegration to avoid rough texture of tablet.
- Patient compliance should be one of the most valuable requirements.
- Adequate mechanical strength should be posses and durable to withstand the rigors of manufacturing and handling.
- It should have low sensitivity to environmental conditions (temp and humidity).
- It should be cost effective also an should be Adaptable and amenable to existing process and packaging machinery.[3]

Important Criteria for excipients used in formulation of MDT's

- It must be able to disintegrate quickly.
- It should not have any interaction with the drug and other ingredients or excipients such as agents used for taste masking of bitter drug.
- The concentration of the binder must be in adequate range and the binder should not affect the final integrity means disintegration and stability of the product.[5]

Challenges in Formulation of MDT's:

- Taste masking of drugs
- Quick disintegration of tablets
- Enzymatic Reaction.

MATERIAL AND METHOD

Ketorolac Tromethamine was a purchased from Yarrow chem, Mumbai. Banana Powder and Modified Agar were received as gift samples from Aster analytical, Pune, India. Crospovidone , Croscarmellose and Microcrystalline Cellulose was purchased from Solanki Distributors, Pune. All other ingredients used were of analytical grade.

Preparation of calibration curve of Ketorolac Tromethamine in phosphate buffer solution pH 6.8

In a 100 ml volumetric flask with phosphate buffer solution at pH 6.8, 10 mg of Ketorolac Tromethamine that had been precisely weighed was added to create the stock solution. The volume was then increased to 100 ml by obtaining a 100 g/ml solution using a phosphate buffer solution with a pH of 6.8. A range of concentrations of 10–50 ug/ml were produced by diluting various aliquots from the stock solution in series of 1, 2, 3, and 4 and 5 ml in a 10 ml volumetric flask with phosphate buffer solution pH 6.8. A UV spectrometer was used to test the solutions' absorbance at 322 nm. The absorbance vs. concentration calibration curve was plotted, and the slope, intercept, and coefficient of correlation values were computed.[2]

DRUG – EXCIPIENT COMPATIBILITY STUDY

Fourier Transform Infrared Spectroscopy (FTIR)

FT-IR spectrum of Ketorolac Tromethamine was obtained on an FTIR spectrophotometer (FTIR 8400S, Shimadzu) using the KBr powder press technique to check its purity. Using dried potassium bromide, the baseline correction was carried out. With a resolution of cm-1 over the range 4000-400 cm-1, the instrument was operated in dry air purge. The scans were examined

for principal drug peak existence. The reported IR spectrum's primary peaks and the detected peaks were compared.[3,4]

PRE-COMPRESSION EVALUATION OF POWDER BLEND OF MOUTH DISSOLVING TABLET OF KETOROLAC TROMETHAMINE

Angle of repose

Powder mixtures that had been precisely weighed were put in a funnel. The funnel's height was adjusted such that the tip of the funnel barely (2 cm) touched the top of the pile of powder mixes. On the surface of the funnel, the powder mixtures were permitted to freely flow through. The powder cone's diameter was measured, and the following formula was used to determine the angle of repose. **$\theta = \tan^{-1}(h/r)$**

whereas, θ = angle of repose, h = height of pile, r = average radius of the powder cone.

Bulk density

It was carried out by pouring powder blend in 100 ml graduated cylinder. The sample occupied volume has been recorded. Bulk density was calculated by following formula.

Bulk density (g/ml) = Weight of the powder / Volume of the powder

Tapped density

It was carried out by pouring powder blend in 100ml graduated cylinder. The cylinder was tapped mechanically by Tap density apparatus until a constant volume was obtained. Volume occupied by the sample after tapping were recorded and tapped density was calculated by using following formula:

Tapped density (g/ml) = Weight of the powder / Tapped volume of the powder

Hausner's ratio

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula;

Hausner′s ratio = Tapped density / Bulk density

Compressibility Index

It was one of the simple techniques to determine flow property of powder. In which the bulk density and tapped density was compared and % Compressibility index was calculated from following formula.[5]

Carrs index = Tapped density −Bulk density / Tapped density × 100

MANUFACTURING OF MOUTH DISSOLVING TABLET OF KETOROLAC TROMETHAMINE BY DIRECT COMPRESSION METHOD.

All materials, with the exception of Talc and Magnesium Stearate, were accurately weighed according to the recipe and combined for 15 minutes in a mortar and pestle to ensure homogeneity. The prepared powder mixture was run through sieve #60. After 10 minutes of additional mixing, Talc and Magnesium Stearate that had passed through Sieve No. 30 were added. A 200 mg homogeneously mixed powder blend that was accurately weighed was manually fed into a 16 station tablet compression machine, where it was compressed using flat faced. Total 11 Formulation Batches were prepared.

Table 1: Formulation of Mouth Dissolving Tablet of Ketorolac Tromethamine

Ingredients	Formulation										
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
Ketorolac Tromethamine	10	10	10	10	10	10	10	10	10	10	10
Croscarmellose Sodium	5	10	-	-	-	-	-	-	-	-	-
Crosspovidone	-	-	5	10	-	-	-	-	5	7	3

Banana Powder	-	-	-	-	5	10	-	-	-	-	-
Modified Agar Powder	-	-	-	-	-	-	5	10	5	3	7
Mannitol	20	20	20	20	20	20	20	20	20	20	20
Microcrystalline cellulose	161	156	161	156	161	156	161	156	156	156	156
Magnesium Stearate	2	2	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2	2	2
Total	200	200	200	200	200	200	200	200	200	200	200

POST-COMPRESSION EVALUATION OF MOUTH DISSOLVING TABLET OF KETOROLAC TROMETHAMINE

Thickness

Vernier callipers were used to measure the thickness of 10 tablets, which were then converted to millimetres (mm).

Hardness: Hardness indicates the ability of a tablet to with stand mechanical shocks while handling. The hardness of the tablets was determined using Digital hardness tester. It is expressed in Kg/cm^2.Digital hardness tester was used to measure hardness of the tablet. In which the tablet was placed in the tester and pressure needed to break the tablet was measured.

Weight Variation

Twenty t ablets are ingested and their individual and collective weights are calculated on an electronic weighing scale in accordance with the I.P. protocol for uniformity of weight. One tablet's average weight was determined using the entire weight.

The weight variation test would provide a reliable way to assess the uniformity of the medication content.

Friability

Friability is the measure of tablet strength. It was carried out by using Roch friability apparatus, in which the accurately weighed 20 tablets was allowed to rolling and free fall at 25 rpm, after 100 revolutions weight of tablet was again measured and % friability was calculated by following formula

$$\% \text{ Friability} = W(int) - W(final) / W(int) \times 100$$

Where,

Wint = Initial weight of the tablets

Wfinal =Final weight of the tablets

Disintegration Time

Disintegration times for sublingual tablets were determined using USP tablet disintegration apparatus with saline phosphate buffer of pH 6.8 as medium. Maintained the medium temp at 37± 2° C. The time in minute taken for complete disintegration of the tablets with no palatable mass remaining in the apparatus was measured.

Wetting Time

In that the tissue paper has been folded twice and placed in Petri dish above that tablet is placed and 6 ml water was added. The time required to get the tablet completely wet was measured.

Water Absorption Ratio

In this method, A piece of tissue paper folded twice was placed in a small Petri dish containing 6ml of water. A tablet was put on the tissue paper and allowed to completely wet. The wetted tablet was then weighed. Water absorption ratio was determined using following equation.

$$\text{Water absorption ratio} = Wa - Wb \backslash Wb \times 100$$

Where,

Wa – weight of tablet after absorption; Wb – weight of tablet before absorption.

Drug Content

This method is performed as per Indian Pharmacopoeia. Two tablets were crushed and added to 30 ml of 0.1M NaOH in 100 ml volumetric flask sonicated to disintegrate, then diluted by acetonitrile and then this solution was filtered and diluted the filterate with a mixture of seven volumes acetonitrile and three volumes of 0.1M NaOH. Absorbance was measured by UV spectroscopy at 322nm

In-vitro Dissolution Study

The in-vitro drug release study of formulated sublingual tablets F1-F11 was carried out using USP dissolution apparatus type II (Electro Lab Dissolution Tester USP II) at 50 rpm. A temperature of 37±0.5 ^{0}C was maintained throughout the study. The dissolution test was carried out using 900ml of saline phosphate pH 6.8. A sample (5 ml) of the aliquot was withdrawn from the dissolution apparatus at 5, 10, 15, 20, 25and 30min. The samples were replaced with fresh dissolution. The samples were filtered through Whattman filter paper and analyzed using UV-visible spectrophotometer (UV-1800, Shimadzu, Japan) at 284nm and the percentage drug release was calculated.[6,7,8,9]

STABLITY STUDY

The formulation F10 was selected for stability studies on the basis of their high cumulative % drug release and also results of in vitro disintegration time studied. The stability studies were carried out at 40˚C±2˚C/75˚C±5% relative humidity for the selected formulation up to two months. For every 1-month time interval the tablets were analyzed for drug hardness, disintegration time, content uniformity, % drug release up to three months.[10]

RESULTS AND DISCUSSIONS

Scanning of Ketorolac Tromethamine:

In UV spectroscopy study, the maximum wavelength (λmax) of Ketorolac Tromethamine in water was found to be 322nm. The reported λmax value of Ketorolac Tromethamine in water was also 322nm respectively, so the values similar with the reported values indicate that the given sample of Ketorolac Tromethamine was in pure form.

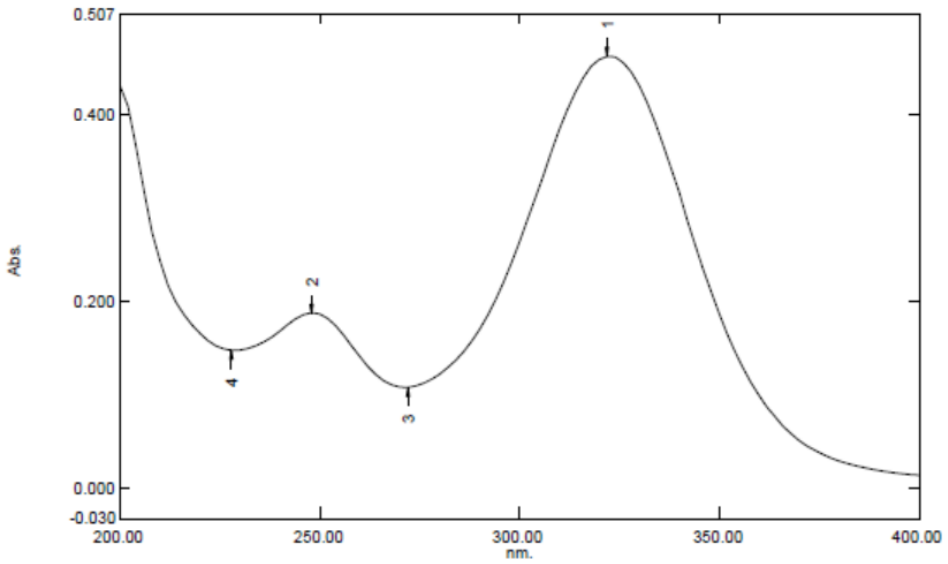


Figure 1: UV spectra of Ketorolac Tromethamine in water at 322nm

Calibration Curve of Ketorolac Tromethamine in Phosphate Buffer 6.8

The UV spectroscopy method was selected as an analytical tool for Ketorolac Tromethamine to calculate the data and percent (%) release data of prepared formulation. Calibration curve of Ketorolac Tromethamine in phosphate buffer pH 6.8 was developed at 322nm and it showed good linearity and absorbance with R^2 value 0.988, which reveals that, the drug Ketorolac Tromethamine obeys the Beers lamberts law.

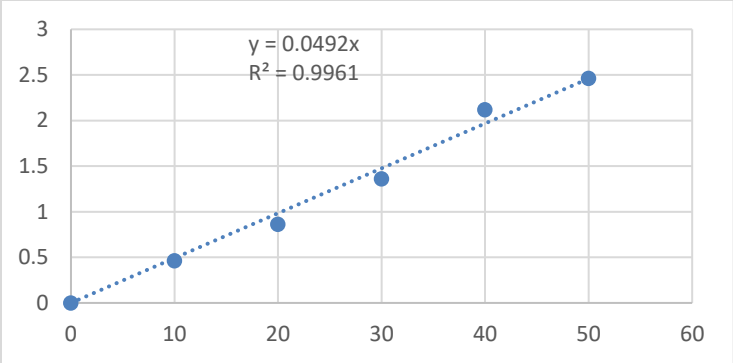
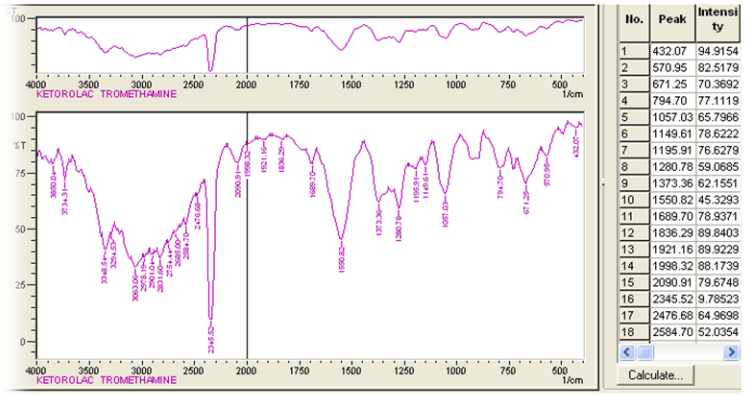


Figure.2 : Calibration curve of Ketorolac Tromethamine in Phosphate Buffer 6.8

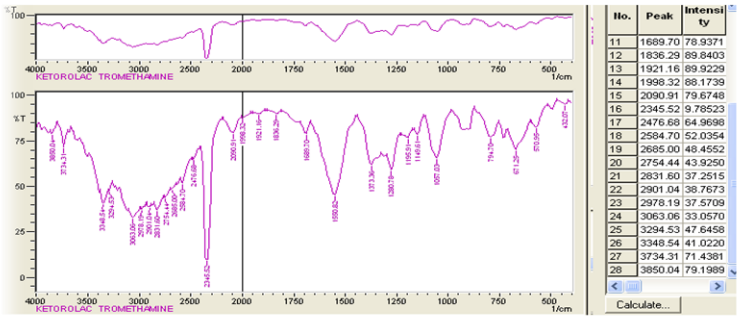
DRUG – EXCIPIENT COMPATIBILITY STUDY

(FTIR) Interpretation of Ketorolac Tromethamine



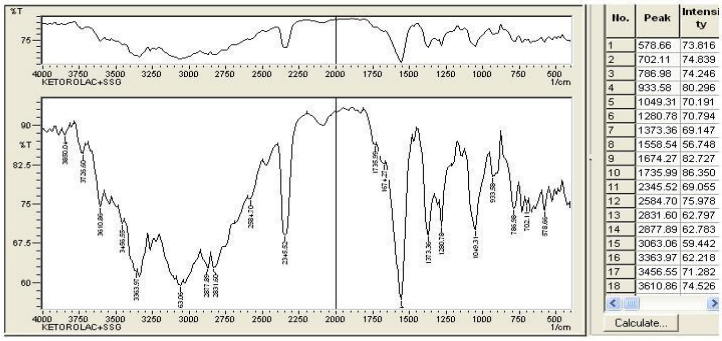
No.	Peak	Intensity
1	432.07	94.9154
2	570.95	82.5179
3	671.25	70.3692
4	794.70	77.1119
5	1057.03	65.7966
6	1149.61	78.6222
7	1195.91	76.6279
8	1280.78	59.0685
9	1373.36	62.1551
10	1550.82	45.3293
11	1689.70	78.9371
12	1836.29	89.8403
13	1921.16	89.9229
14	1998.32	88.1739
15	2090.91	79.6748
16	2345.52	9.78523
17	2476.68	64.9698
18	2584.70	52.0354

Calculate...



No.	Peak	Intensity
11	1689.70	78.9371
12	1836.29	89.8403
13	1921.16	89.9229
14	1998.32	88.1739
15	2090.91	79.6748
16	2345.52	9.78523
17	2476.68	64.9698
18	2584.70	52.0354
19	2685.00	48.4552
20	2754.44	43.9250
21	2831.60	37.2515
22	2901.04	38.7673
23	2978.19	37.5709
24	3063.06	33.0570
25	3294.53	47.6458
26	3348.54	41.0220
27	3734.31	71.4381
28	3850.04	79.1989

Figure 3: FTIR Studies of Ketorolac Tromethamine



No.	Peak	Intensity
1	578.66	73.816
2	702.11	74.839
3	786.98	74.246
4	933.58	80.296
5	1049.31	70.191
6	1260.78	70.794
7	1373.36	69.147
8	1558.54	56.748
9	1674.27	82.727
10	1735.99	86.350
11	2345.52	69.055
12	2584.70	75.978
13	2831.60	62.797
14	2877.89	62.783
15	3063.06	59.442
16	3363.97	62.218
17	3456.55	71.282
18	3610.86	74.526

Fig 4: FTIR Studies of Ketorolac Tromethamine + Crospovidone.

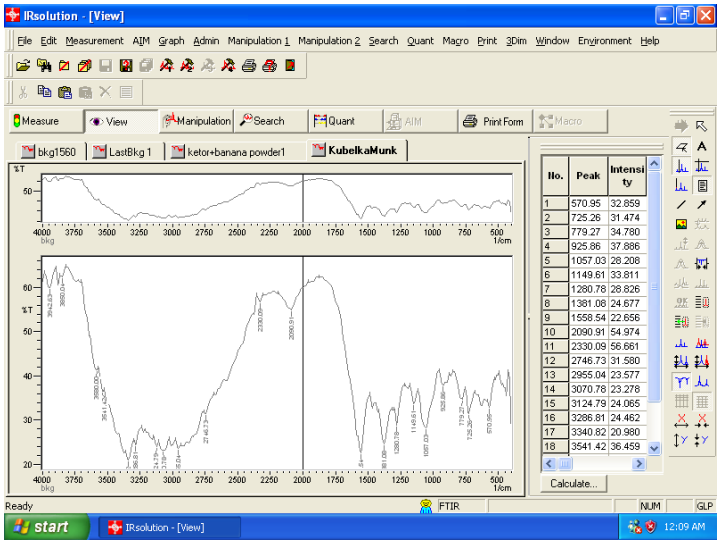


Fig 5: FTIR Studies of Ketorolac Tromethamine +Banana Powder

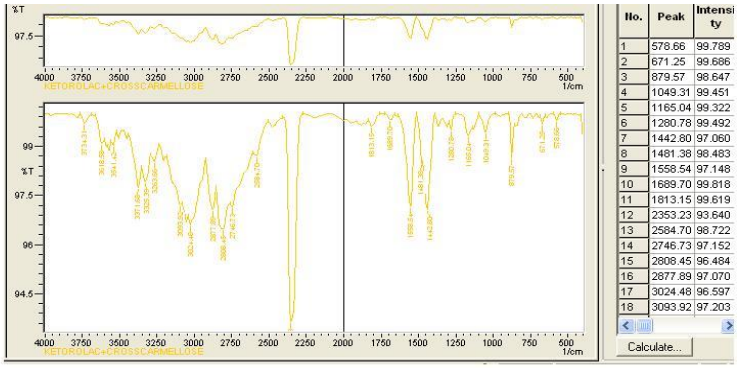


Fig 6: FTIR Studies of Ketorolac Tromethamine +Croscarmellose

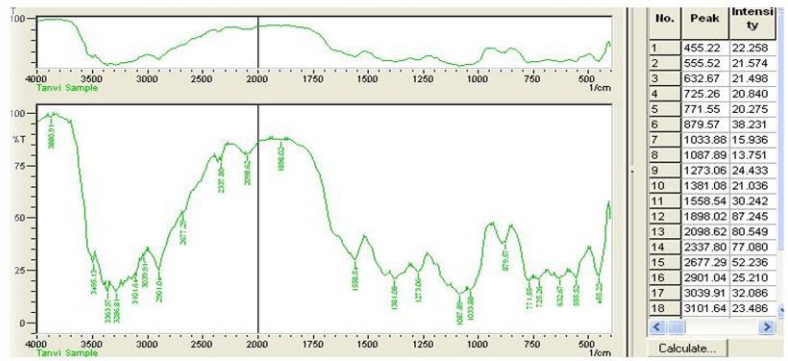


Fig 7 : FTIR Studies of Ketorolac Tromethamine and Excipients.

EVALUATION OF POWDER BLEND OF MOUTH DISSOLVING TABLET OF KETOROLAC TROMETHAMINE.

The characterization of mixed blend was done for determination of mass-volume relationship parameter. The evaluated parameter angle of repose, bulk density, tapped density, hausner's ratio and compressibility index was reported in table below.

Table 2: Evaluation of tablet blend for Mouth Dissolving Tablets

For mulations	**Angle of repose (Ɵ)**	**Bulk Density (gm/cm^3)**	**Tapped Density (gm/cm^3)**	**Hausner's Ratio (H_R)**	**Carr's Compressibility index (%)**
F1	20.58±1.50	0.35±0.01	0.41±0.01	1.17±0.10	14.63±0.12
F2	21.82±1.22	0.35±0.01	0.39±0.02	1.11±0.21	10.25±0.24
F3	24.76±1.94	0.38±0.01	0.40±0.01	1.05±0.20	5.00±0.36

F4	26.15±1.28	0.36±0.02	0.41±0.01	1.13±0.32	12.19±0.39
F5	27.63±1.15	0.33±0.02	0.39±0.01	1.18±0.28	15.38±0.32
F6	24.34±1.08	0.33±0.01	0.40±0.01	1.21±0.18	17.5±0.20
F7	26.45±0.97	0.39±0.01	0.46±0.02	1.17±0.16	15.21±0.18
F8	24.36±1.26	0.34±0.02	0.42±0.01	1.23±0.13	19.04±0.16
F9	23.59±1.10	0.36±0.01	0.41±0.01	1.13±0.10	12.19±18
F10	28.60±1.00	0.40±0.01	0.45±0.02	1.12±0.15	11.11±20
F11	27.37±0.09	0.38±0.02	0.41±0.01	1.07±0.19	7.31±26

Results are mean of three determinations.

10.4.1 Angle of Repose

Angle of repose of various powder mixed blends (F1-F11), prepared with different Superdisintegrants (synthetic and natural), and was measured by funnel method. Angle of repose was found in the range 20.58±1.50- 28.60±1.00. The good flow ability of powder blend was also evidence with angle of repose.

10.4.2 Bulk density

The bulk density of various powder mixed blends (F1-F11) prepared with different Superdisintegrants was measured by graduated cylinder. The bulk density was found in the range 0.31±0.01- 0.39±0.01 g/ml.

10.4.3 Tapped Density

The Tapped density of various powder mixed blends (F1-F11) prepared with different Superdisintegrants was measured by using measuring cylinder. The tapped density was found in the range 0.38±0.02 - 0.46±0.02 g/ml. These values indicate good packing characteristics and the powder was not bulky.

10.4.4 Hausner's ratio

The Hausner's ratio of various powder mixed blends (F1-F11), prepared with different Superdisintegrants, it is calculated by using bulk density and tapped density data. It was found in the range of 1.07±0.19 – 1.23±0.13, reveals good flow properties (<1.25)

10.4.5 Compressibility Index

The Compressibility index of various powder mixed blends (F1-F11), prepared with different Superdisintegrants, using bulk density and tapped density data, compressibility index was calculated. It was found in the range 5.00±0.36- 19.04±0.16. This indicates good flow properties.

EVALUATION OF MOUTH DISSOLVING TABLETS OF KETOROLAC TROMETHAMINE TABLETS

Table 3: Evaluation of Mouth Dissolving Tablets.

Formulations	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Drug Content (%)	Weight variations (mg)	Disintegration time (sec)
F1	2.04±0.10	3.26±0.05	0.8±0.05	98.50±0.11	199± 0.93	76±3.28
F2	2.08±0.17	3.36± 0.11	0.8±0.09	98.75±0.01	200±1.01	70±1.41
F3	2.08±0.25	3.26± 0.15	0.7±0.11	98.25±0.15	200±1.70	68±1.41
F4	2.11±0.10	3.36± 0.15	0.8±0.08	98.25±0.13	200± 0.93	63±1.89
F5	2.17±0.17	3.33± 0.25	0.7±0.07	98.50±0.06	200±1.17	79±1.41

F6	2.04±0.10	3.43± 0.10	0.7±0.09	98.70±0.23	198±1.51	72±1.91
F7	2.08±0.11	3.42± 0.10	0.7±0.06	98.75±0.14	199±1.67	71±0.98
F8	2.08±0.05	3.43± 0.10	0.7±0.10	98.75±0.17	200±0.90	65±1.41
F9	2.22±0.10	3.30± 0.10	0.8±0.05	98.75±0.01	199±1.70	61±1.19
F10	2.04±0.10	3.41±0.15	0.9±0.08	98.70±0.08	200±0.80	45±1.26
F11	2.12±0.11	3.36±0.20	0.7±0.10	98.65±0.01	198±1.30	70±1.26

Results are mean of three determinations.

Thickness

The thickness of the tablets was measured by using Vernier caliper by picking the tablets randomly. The values are almost uniform in all formulations. Thickness was found in the range from 2.04±0.10 mm – 2.22±0.10 mm. Uniform in the values indicates that formulations were compressed without sticking to the dies and punches.

Weight variation

Tablets were prepared using direct compression technique. Since the material was free flowing, tablets were obtained of uniform weight due to uniform die fill. Tablets were obtained in the range with acceptable weight variations as per Pharmacopoeia specifications, limit of ±5%. It was found to be from 198±1.30 to 200±1.70.

Hardness

Tablets were evaluated by using Monsanto Hardness tester. Hardness of the tablets was in the range 3.26±0.05 to 3.43± 0.10 kg/cm^2. Uniform hardness was obtained due to equal compression force. The obtained hardness range showed good mechanical strength with an ability to withstand physical and mechanical stress conditions.

Friability

Tablets were evaluated by using Roche Friabilator and friability of tablets was observed in acceptable range. 0.7±0.06 to 0.9 ± 0.08 (less than 1%) This indicated a good mechanical resistance of the prepared mouth dissolving tablets

Disintegration time

Tablets were subjected for the *in-vitro* disintegrates time in the USP Disintegration test apparatus. The *in-vitro* disintegration time for all 11 formulations varied from 45±1.26 to 79±1.41 seconds. The rapid disintegrate was seen in the formulations containing Modified Agar Powder and Crospovidone. This is due to rapid intake of the water from the medium, swelling and burst effect. Increased, the time taken for the disintegration was reduced. The formulations with highest concentration of Crospovidone and Modified Agar powder was shown significant for rapid disintegration. Disintegrate time was to be found very less for F10 formulation which contains highest concentration and efficiency of Crospovidone and Modified Agar.

Wetting time test

The values of wetting time for all formulations lie between 21±1.01- 48±1.02 and it was observed that as the concentration of disintegrant increases the time taken for wetting decreases.

Water absorption ratio

Water absorption ratio which is important criteria for understanding the capacity of disintegrants to swell in presence of little amount of water. It was found in the range of 52.64±0.22 to 70.10±0.56%. The Water absorption ratio (R) increases with the increased concentration of combination of natural and synthetic superdisintegrants.

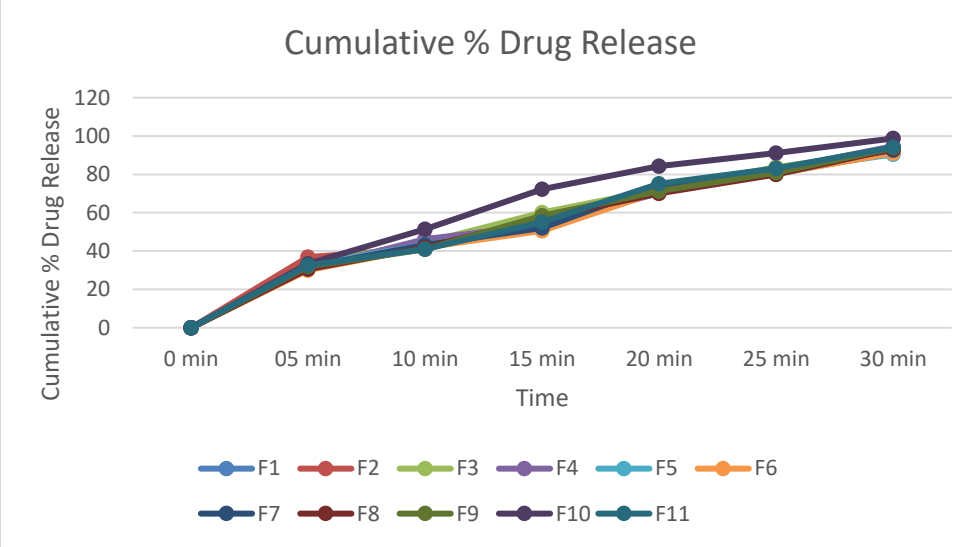
In vitro % Drug Release of Drug from Tablet

All ten tablet batches of mouth dissolving tablet of Ketorolac Tromethamine were subjected for the in vitro dissolution studies using tablet dissolution apparatus (USP). Phosphate buffer 6.8 was used as dissolution medium.

Table 4: In vitro % Drug Release of Drug from Tablet

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
0 min	0	0	0	0	0	0	0	0	0	0	0
05 min	30.83	36.91	33.28	30.72	32.54	30.11	31.78	30.55	31.98	33.34	32.47
10 min	42.37	41.14	44.32	46.16	43.35	41.96	43.25	41.86	40.96	51.34	41.13
15 min	57.23	58.24	60.09	53.59	51.86	50.49	52.13	57.22	58.41	72.3	55.04
20 min	70.65	71.93	72.31	70.32	72.43	71.05	74.31	70.16	71.33	84.21	75.14

25 min	80.69	80.49	83.74	82.47	81.83	80.31	82.65	80.01	80.89	91.06	83.09
30 min	91.16	92.67	92.26	94.7	90.39	91.18	92.7	93.26	93.89	98.76	94.15



The rapid dissolution was observed in formulation. F10 releases 98.76 % drug at the end of 30 minutes. The remaining formulation batches released 91.16% to 98.76 % at the end of 30 min. Rapid dissolution might be due to fast breakdown of particles and rapid absorption of drugs. The drug release was completely achieved in shorter duration of time. In all the formulations the drug release within 30 minutes. High dissolution may occur due to faster breakdown.

In comparative study F10 formulation gives higher percent drug release compare to other remaining nine formulations at the end of 30 minutes and graphical representation is shown in Figure 10.9. Therefore it was concluded that the best optimized batch was found to be F10 because of lesser disintegration time and highest percentage drug release at the end of 30 min among all the formulations.

10.4. STABILITY STUDY

The formulation F11was selected for stability studies on the basis of their high cumulative % drug release and also results of in vitro disintegration time studied. The stability studies were carried out at 37˚C±2˚C/40˚C±5% relative humidity for the selected formulation up to three

months. For every 1-month time interval the tablets were analysed for drug appearance, hardness, disintegration time, content uniformity, % drug release up to three months. The results obtained in Table below;

Table 5: Stability Study for MDT of Ketorolac Tromethamine

Parameters Evaluated	**Initial**	**After 2 Month**	**After 3 Months**
Thickness	2.04±0.10	2.03±0.86	2.03±0.50
Hardness (kg/cm2)	3.41±0.15	3.29± 0.16	3.27± 0.10
Disintegration time (Sec)	45±1.26	43±1.53	45±1.19
Content Uniformity (%)	99.70±0.08	98.75±0.53	98.75±1.02
Cumulative % release	98.76	97.89	96.08

CONCLUSION

The purpose of present research work was achieved successfully as formulation of Ketorolac Tromethamine for the management of moderate to severe pain that may get caused after Dental Procedures was done. This unique formulation of Ketorolac Tromethamine MDT demonstrated a rapid onset of action and may be useful and practical for pediatric, geriatric, and psychiatric patients as well as those who have trouble swallowing and in circumstances where water is not readily available. All raw materials were subjected to pre-formulation studies such as bulk density, tapped density, Compressibility index and Hausner's ratio showed good flow properties. In FTIR spectra there is no physical interaction between drug and all excipients. From the dissolution Profile of formulation batches F1 to F11 the effect of superdisintegrant concentration

on dissolution profile of tablet can be seen clearly. As concentration of superdisintegrant increases the drug release decreases. The Batch **F10** was chosen as optimized formulation which showed satisfactory results. As high and optimum concentration of Crospovidone and Modified Agar used in the formulation **F10** showed **98.76 %** of drug release at the end of 30mins. Crospovidone and Modified Agar were found to be the best combined superdisintegrants among other used. The stability study of optimized batch **F10** was performed which showed stable formulation after three months.

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CONFLICT OF INTEREST

All authors declared no conflicts of interest.

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