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Formulation and Development of Oral Fast Dissolving Tablet of Etoricoxib

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ABSTRACT

In this investigation, development of oral fast dissolving tablet of Etoricoxib was developed to overcome solubility problem of Etoricoxib. Dissolution of Etorioxib enhanced by solid dispersion technique in which Etoricoxib-carrier Urea solid dispersion were prepared by physical mixture (PM), kneading (KN) and by fusion method (FM) techniques, in three molar rations (1:1, 1:2 and 1:3). In formulation Mannitol used to maintain rapid disintegration and Urea added which acts as hydrophilic carrier and superdisitigrant. Preparation of tablet by direct compression and evaluation were done. From dissolution study results, method of solid dispersion technique and drug- carrier ratio was optimized. Taste masking of bitter Etoricoxib was done by using Aspartame, In vitro and In vivo taste evaluation was done. Compatibility between drug and excipient examine by FTIR study.

Key words- Solid dispersion technique, super disintigrant, taste masking, Urea, Aspartame.

INTRODUCTION

The tablet is the most widely used dosage form because of its convenience in terms of self-administration, compactness, and ease in manufacturing. However, geriatric and pediatric patients experience difficulty in swallowing conventional tablets, which leads to poor patient compliance. To overcome this weakness, scientists have developed innovative drug delivery systems known as fast dissolving tablets. Their characteristic advantages such as administration without water, anywhere, anytime lead to their suitability to geriatric and pediatric patients. They are also suitable for the mentally ill, the bedridden and patients who do not have easy access to water. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability, and good stability make these tablets popular as a dosage form of choice in the current market [1, 2] .

The Oral fast dissolving tablet prepared by many techniques, direct compression is one of main method to prepare oral fast dissolving tablet. Direct compression represents the simplest and most cost effective tablet manufacturing technique. This technique can now be applied to preparation of Orodispersible tablet because of the availability of improved excipients especially superdisintegrants and sugar based excipients [3].

Clinically, nonsteroidal anti-inflammatory drugs (NSAIDs) are the most frequently prescribed by physicians for inflammatory disorders. NSAIDs exert their effect through inhibition of cyclooxygenase-II, the main form of isozyme associated with inflammation. But the simultaneous inhibition of cyclooxygenase-I and the resulting gastric and renal dysfunction limit their frequent use [4]. Etoricoxib is a cyclooxyginase-II (COX-II) selective NSAID used in the treatment of rheumatoid arthritis, osteoarthritis, postoperative dental pain, chronic low back pain, acute gout and primary dismenorrhoea [5]. The COX-I to COX-II selectivity ratio is higher than other COX-II inhibitors such as Rofecoxib, Valdecoxib and Celecoxib [6] . Etoricoxib is practically insoluble in water and peak blood level

reaches after 1 h of oral administration [7, 8]. The rate and extent of dissolution of the drug from any solid dosage form determines rate and extent of absorption of the drug. In the case of poorly water-soluble drugs, dissolution is the rate-limiting step in the process of drug absorption that in turns dependent on disintegration. The dissolution rate and bioavailability of poorly soluble drug from solid dosage form depend much on formulation additives and formulation characteristics.

In this investigation, development of oral fast dissolving tablet of Etoricoxib was developed to overcome solubility problem of Etoricoxib. Dissolution of Etorioxib enhanced by solid dispersion technique in which Etoricoxib-carrier Urea solid dispersion were prepared by physical mixture (PM), kneading (KN) and by fusion method (FM) techniques, in three molar rations (1:1, 1:2 and 1:3). In formulation Mannitol used to maintain rapid disintegration and Urea added which acts as hydrophilic carrier and superdisitigrant [9]. Preparation of tablet by direct compression and evaluation were done. From dissolution study results, method of solid dispersion technique and drug- carrier ratio was optimized. Taste masking of bitter Etoricoxib was done by using Aspartame, In vitro and In vivo taste evaluation was done. Compatibility between drug and excipient examine by FTIR study.

MATERIALS AND METHODS

MATERIALS

Etoricoxib obtained as free gift sample from Cadila Pharma, Ahmadabad, India. Urea obtained from Loba. Cheme. Pvt. Ltd, Mumbai, India. Cross Carmellose Sodium obtained as free gift sample from Leben Laboratories Pvt. Ltd, Akola, India. Avicel PH 102 purchase from Nicholas Piramal Health care Pvt. Ltd. Ahmadabad, India. Mannitol, aspartame, aerosil, magnesium Stearate and talc were obtained from Samar chemicals, Nagpur, India.

METHOD

Preparation of standard curve in 0.1 N HCl [89]

100 mg Etoricoxib was dissolved in 100ml of water. 10ml of the resulting solution was further diluted up to 100ml with 0.1 N HCL to make a stock solution of concentration 100µg/ml. Further serial dilutions were carried out with 0.1 N HCL to get drug concentration between 1 to 12µg/ml. The absorbances of the dilutions were measured against water as a blank at 234nm using Shimadzu double beam UV visible spectrophotometer. The plot of absorbance vs. concentration was plotted and was found to obey Beers Lambert's law in the range of 0 to 100 µg/ml. Data in this range was subjected to linear regression analysis. The plot for standard calibration curve of drug in 0.1N HCL.

Drug- carrier interaction study

Pure Drug, Pure urea and mixture of Drug+Urea were analyzed for interaction by Fourier Transform Infrared Spectroscopy (FTIR) using KBr disk method.

Manufacturing of fast dissolving tablets of Etoricoxib

A. Preparation of solid dispersion [82, 87,88]

The preparations of drug Etoricoxib-carrier Urea solid dispersion were prepared by physical mixture (PM), kneading (KN) and by fusion method (FM) techniques, in three molar rations (1;1, 1:2 and 1:3) which are described below in table no.1

Table no. 1 Ratio Etoricoxib + Urea

Name of Method	Drug : Carrier Ratio	Solid Dispersion Code
Physical Mixture	1:1	PM1
	1:2	PM2
	1:3	PM3
Kneading Method	1:1	KM1
	1:2	KM2
	1:3	KM3
Fusion Method	1:1	FM1
	1:2	FM2
	1:3	FM3

A.I. Physical Mixture

Accurately weighed quantity of carrier was placed into a mortar. Then weighed quantity of drug was introduced slowly and triturate for 30 min. The ratio of drug and carrier in the ratio of 1:1, 1:3 and 1:5 were prepared by the modified technique.

A.II. Kneading Method

Accurately weighed quantity of carrier was placed into a mortar moistened with water and kneaded to the paste consistency. Then weighed quantity of drug was introduced slowly and kneaded for 30 min. During this process appropriate quantity of water was added to maintain suitable consistency. Finally the obtained paste was dried in an oven at 40 °C until the water was removed completely and stored in desiccators over fused calcium chloride.

A.III. Fusion Method

The accurately weighed amount of carrier urea was melted in a porcelain dish at 80-85^{o}C in melted polymer .Calculated amount of Etoricoxib was added with thorough mixing for 1-2 minutes followed by quick cooling .The ratio of drug and carrier in the ratio of 1:1.,1:3 and 1:5 were prepared by the modified technique.

B. Formulation and Preparation of Tablet

Formulation of tablet represent in table no. 2. Preparation of tablet by direct compression method.

Table no. 2 Formulation table [82-85, 89, 90]

Ingredients(mg)	Formulation Code								
	PM1	PM2	PM3	KM1	KM2	KM3	FM1	FM2	FM3
Etoricoxib (equivalent to 60 mg)	120	180	240	120	180	240	120	180	240
Avicel PH 102	31	10.5	13	31	10.5	13	31	10.5	13
Mannitol	20	20	20	20	20	20	20	20	20
CCS(9%)*	18	27	31.5	18	27	31.5	18	27	31.5
Aspartame	5	5	5	5	5	5	5	5	5
Aerosil (1%)	2	2.5	3.5	2	2.5	3.5	2	2.5	3.5
Magnesium Stearate(1%)	2	2.5	3.5	2	2.5	3.5	2	2.5	3.5
Talc (1%)	2	2.5	3.5	2	2.5	3.5	2	2.5	3.5
Total Weight	**200**	**250**	**320**	**200**	**250**	**320**	**200**	**250**	**320**

Evaluation of tablets[82,89]

Rapid dissolving tablets were evaluated for following parameters.

a. Drug Content

Ten tablets were taken and triturated in a glass mortar. The powdered tablet equivalent to 60 mg of drug was dissolved in a 900ml of 0.1 N HCL and the drug content was determined spectrophotometrically at 234 nm.

b.Hardness

Tablets require a certain amount strength or hardness and resistance to friability to withstand mechanical shock of handling in manufacturing, packaging and shipping. Hardness was measured using Monsanto hardness tester.

c.Friability

Friability was evaluated as the weight loss of tablets, tumbled in a friabilator (Roche) Dolphine, Pvt. Ltd., Mumbai) for 4 min at 25 rpm. The tablets then were dedusted, and the loss in weight caused by fracture or abrasion was recorded as percentage friability. The percentage friability was measured using the formula no.1

$$\%F = \{(W - Wo)/Wo\} \times 100 \qquad (1)$$

Where, % *F* is friability in percentage, Wo is initial weight of tablet and *W* is weight of tablet after test.

d. Weight variation

For weight variation, 20 tablets were weighed individually. Average weight was calculated and individual tablet weights were compared to the average. All the tablets were found to pass the weight variation test.

e. Wetting time and Water absorption ratio

A piece of tissue paper folded twice was kept in a culture dish (i.d. 5.5 cm) containing about 6ml of purified water. A tablet having small amount of amaranth powder on the upper surface was placed on the tissue paper. Time required to develop red color on the upper surface of the tablet was recorded as a wetting time. The same procedure was repeated for determining water absorption ratio without using amaranth. The wetted tablet was then weighed and water absorption ratio, R, was determined according to following formula no. 2

$$R = \{(Wa - Wb)/Wb\} \times 100 \qquad (2)$$

Where, Wb is weight of tablet before study and Wa weight of tablet after study.

Disintegration time[90]

For rapid dissolving tablets, drug formulation was intended to disperse rapidly (less than 1 min) in oral cavity, so that dose swallows easily. Hence the assessment of the disintegration profile of rapidly disintegrating tablet (RDT) was very important in the evaluation and the development of new formulation.

***In Vitro* Disintegration Study**

The disintegration test for Rapid Disintegrating Tablet was performed by using modified disintegration apparatus. In this modified disintegration apparatus, first 900 ml of simulated salivary fluid was taken in a beaker. Basket was positioned in a beaker. The beaker was placed at 25 rpm and 37.5˚C temperature. Then the tablet was dropped in the basket and the time required for complete disintegration of tablet was recorded using a stopwatch.

Taste evaluation of tablets[91]

1 In-vitro taste evaluation of tablets

Any substance, which is soluble in saliva will interact with taste buds, and can impart its taste. Therefore dissolution study of tablets was conducted in Phosphate buffer pH 6.8 for approximate estimation of release in human saliva before doing actual volunteer study. Tablet containing 60 mg of Etoricoxib was taken in a 25ml volumetric flask. To this, 10ml of Phosphate buffer pH 6.8 was added and was shaken for 60 seconds on mechanical shaker. The amount of drug released was analyzed spectrophotometrically at 234 nm.

2 In- vivo taste evaluation of tablets

Taste masking was evaluated using the stages and using time intensity method. For this study a panel of eleven healthy human volunteers was chosen, from whom informed consent was first obtained. The tablet containing 60 mg of Etoricoxib was held in the mouth for 10 sec. Bitterness was recorded immediately according to the bitterness intensity scale from 0 to 3, 3 being strongest, 2 being moderate, 1 being slight, 0.5 being threshold and 0 for no bitter taste. The readings were taken immediately and at several intervals over the period of 15 min. After study the mouth was rinsed well with water and waited for 1 hour before administering the next sample.

Dissolution study of tablets

In vitro dissolution studies for rapid disintegrating tablets of different batches and marketed tablet were carried out in 900 ml 0.1 N HCL using USP type II (paddle) apparatus at 50 rpm and 37± 0.5°C temperature. Dissolution study of marketed tablet of Etoricoxib was done in a same way as that of the formulated tablet

Stability studies of tablet formulations[75]

The tablets were studied for stability at 40°C and 75% RH conditions for the period of three months. Each tablet was individually weighed and wrapped in an aluminum foil and packed in black PVC bottle and put at above specified conditioned in a heating humidity chamber for 3 months. After each month tablet samples were analyzed for the weight gain, drug content, disintegration time and in vitro drug release study.

Table no. 3 Absorbance of Etoricoxib Solutions of Different Concentrations in 0.1N HCL

Sr. No.	Concentration (µg/ml)	Absorbance at 234nm	S.D. (Standard deviation)
1	0	0	0
2	2	0.151	0.01
3	4	0.319	0.016
4	6	0.489	0.009
5	8	0.656	0.011
6	10	0.82	0.019
7	12	0.996	0.003

Each value represents mean (n=3) ±S.D. (Standard deviation)

RESULTS AND DISSCUSSION

Construction of calibration curve of Etoricoxib

Concentration and their absorbances represent in table no. 3, graph plot concentration versus absorption which show that linear curve was developed which indicate that Etoricoxib follows Beers Lambert's law. From above result it can conclude that sample of Etoricoxib was authentic one (Figure 1).

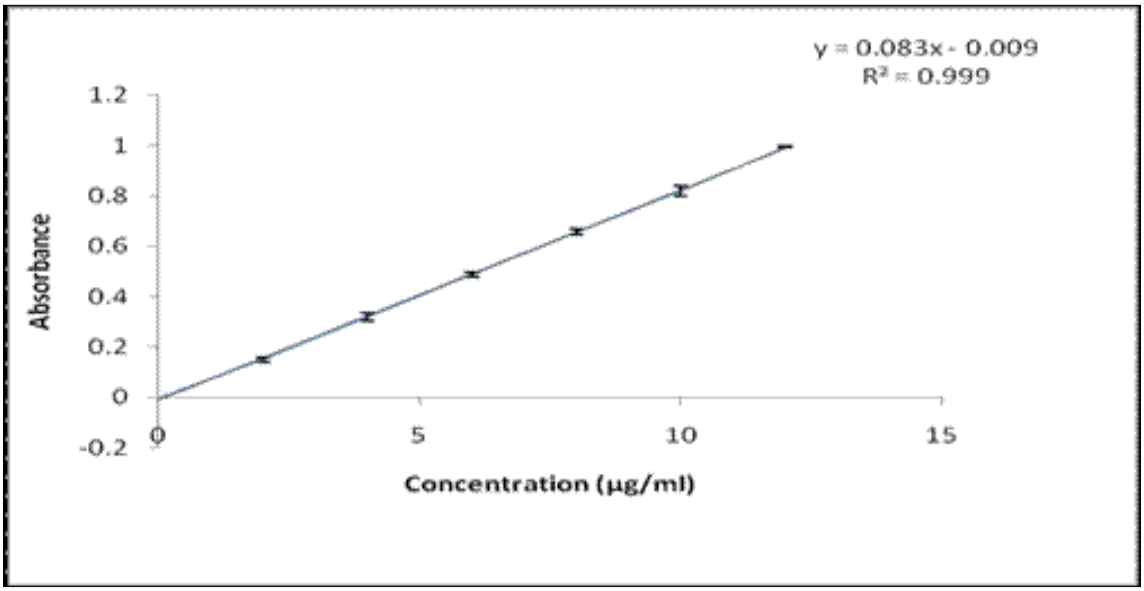


Figure 1 Standard Calibration curve of Etoricoxib

Drug- carrier interaction study

The possible interaction between the drug and the urea was studied by FT-IR spectroscopy. The FTIR spectra of Etoricoxib (Fig.2), Urea (Fig.3) and Etoricoxib + Urea (Fig. 4) were established by FTIR spectroscopy.

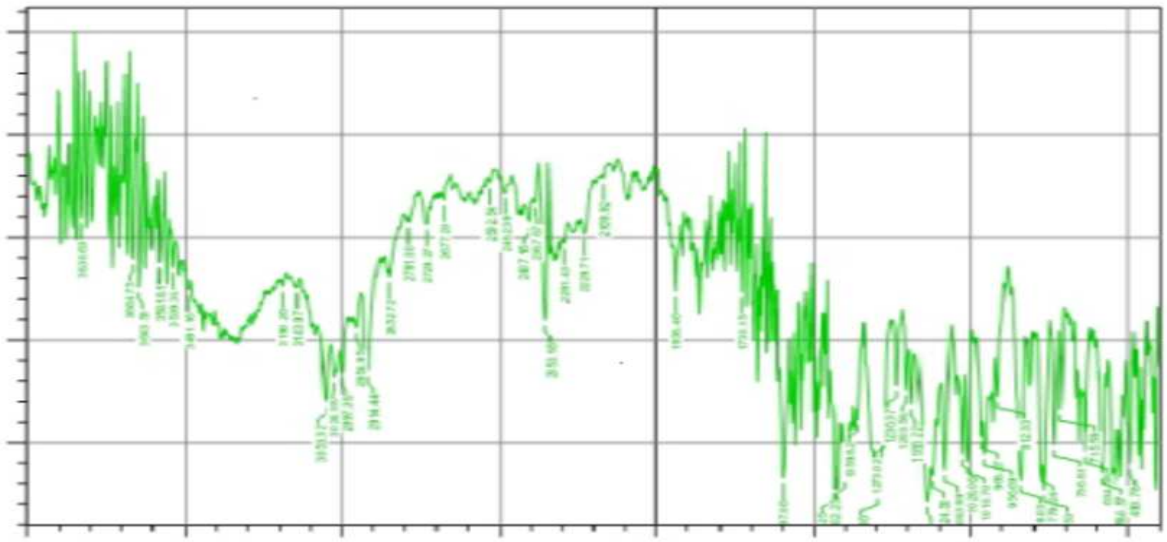


Figure 2 FTIR of Etoricoxib

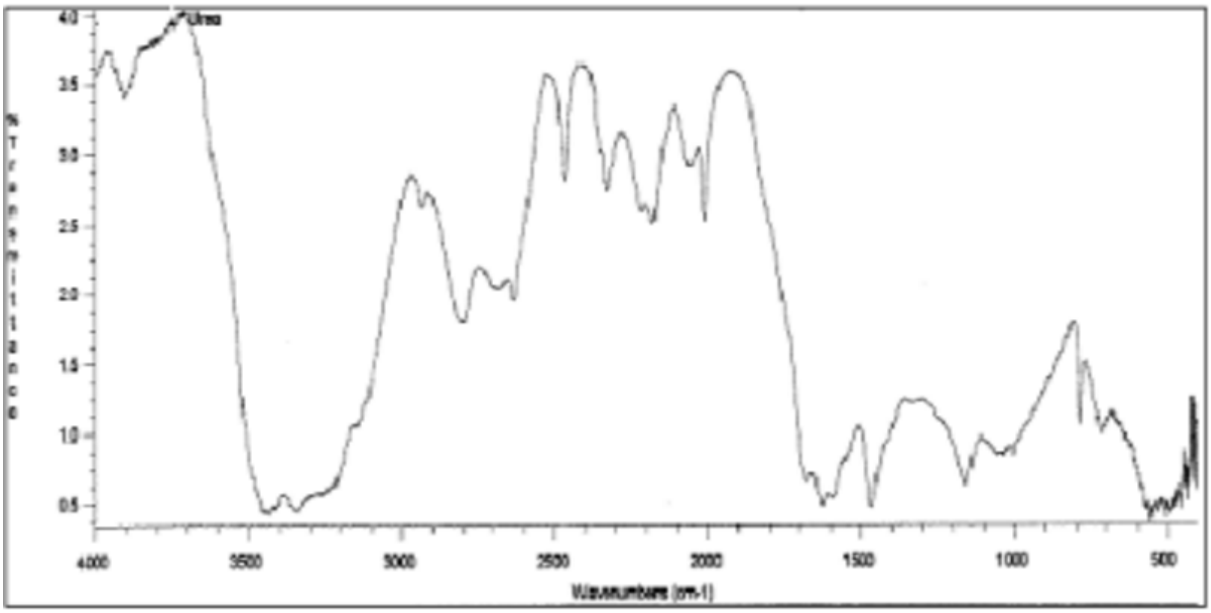


Figure 3 FTIR of Urea

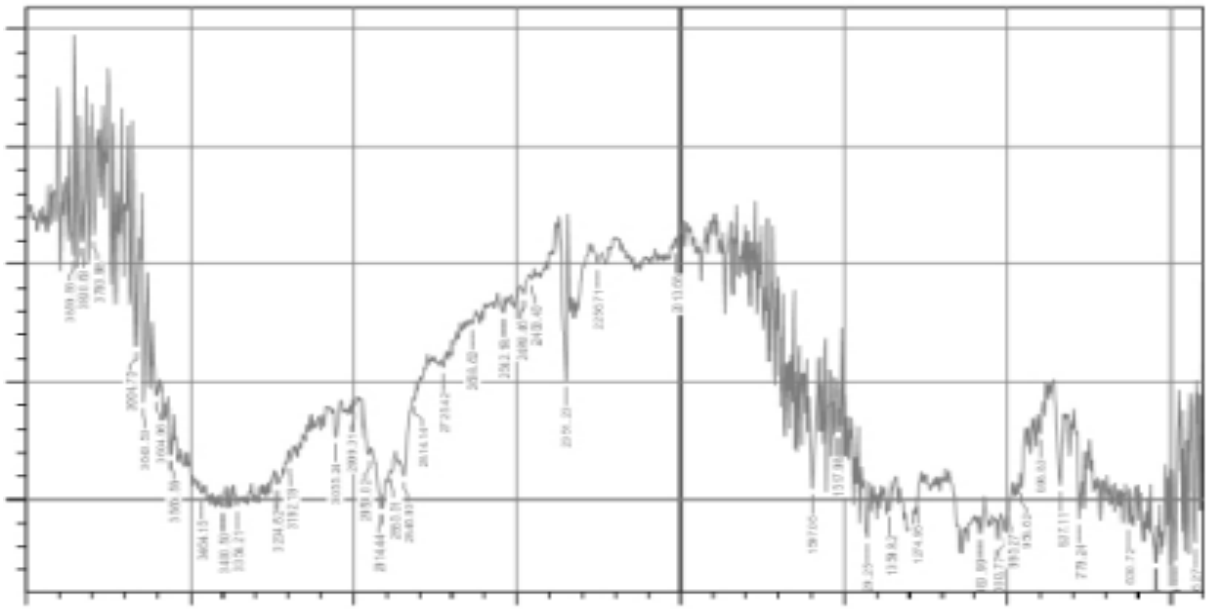


Fig.4 FTIR of Etoricoxib + Urea

The result shows that there is no incompatibility/ interaction was seen in between the drug Etoricoxib and Urea used, as there is no significant change in the pattern of peaks of pure Etoricoxib and physical mixture Etoricoxib + Urea.

Evaluation of tablet

All Fast Dissolving Tablets from batches PM1 to FM3 were evaluated for tablet properties like friability, weight variation and drug content. Tablets passed all the tests. Friability, Weight variation and Content uniformity of all formulations were within acceptable limits. Results were represented in table no. 4

Table no.4: Tablet Evaluation parameters

Sr.No	Parameters / Batches	Drug content (%)	Hardness	Friability (%)	Thickness (cm)	Diameter (cm)	Wetting time (sec)	Water absorption ratio (%)
1	PM1	97.63± (0.02)	3.83± (0.26)	0.66± (0.01)	0.42± (0.01)	0.81± (0.01)	11± (0.031)	170.27± (0.04)
2	PM2	99.3± (0.067)	3.66± (0.288)	0.65± (0.01)	0.51± (0.011)	0.82± (0.011)	13.2± (0.044)	166.46± (0.003)
3	PM3	99.99± (0.006)	3.66± (0.288)	0.61± (0.01)	0.52± (0.012)	0.82± (0.01)	12.4± (0.031)	165.74± (0.03)
4	KM1	100.69± (0.076)	3.83± (0.26)	0.54± (0.01)	0.42± (0.01)	0.81± (0.01)	14.21± (0.053)	166.17± (0.1)
5	KM2	99.3± (0.056)	3.66± (0.288)	0.56± (0.005)	0.52± (0.01)	0.81± (0.01)	15.32± (0.062)	167.06± (0.005)
6	KM3	101.38± (0.066)	3.66± (0.288)	0.56± (0.01)	0.52± (0.011)	0.81± (0.009)	17.3± (0.058)	157.32± (0.04)
7	FM1	98.61± (0.036)	3.83± (0.26)	0.59± (0.01)	0.42± (0.01)	0.82± (0.01)	16.23± (0.027)	160.62± (0.12)
8	FM2	100.69± (0.1)	3.83± (0.26)	0.60± (0.005)	0.52± (0.01)	0.82± (0.01)	18.4± (0.002)	154.11± (0.007)
9	FM3	99.99± (0.4)	3.83± (0.26)	0.60± (0.005)	0.51± (0.013)	0.81± (0.01)	17.2± (0.01)	163.06± (0.033)

Each value represents mean (n=3) ±S.D.

Disintegration taste

The results of drug content, hardness, and % Friability, thickness, diameter, wetting time, water absorption ratio are given in table no. 5. The hardness of all these batches was in the range of 3.5-4 Kg/cm^2. Such hardness range is enough to give mechanical indicates good Compressibility of blends. The value of friability for all these formulations was less than the limits of 1.0% which is given in the U.S.P. The friability found in these formulations shows a good strength of tablets to withstand abrasion during transportation and general handling.

Table no. 5: Comparative Study of Disintegration Time with Different Methods and weight variation for individual batches

Sr. No.	Batch	*In vitro* disintegration time(sec.)	Weight variation(mg) (n=3)
0	**0**	0	------
1	**PM1**	**14.5**± (1.02)	**197.63** ± (0.26)
2	**PM2**	**16**± (0.1)	**248.63** ± (0.21)
3	**PM3**	**12.73**± (1.88)	**319.63** ± (0.26)
4	**KM1**	**17.32**± (1.45)	**98.63** ± (0.45)
5	**KM2**	**16.42**± (1.22)	**249.73** ± (0.36)
6	**KM3**	**13.14**± (0.76)	**319.63** ± (0.26)
7	**FM1**	**14.5**± (1.02)	**199.63** ± (0.26)
8	**FM2**	**17**± (0.1)	**249.63** ± (0.26)
9	**FM3**	**17.73**± (1.88)	**319.63** ± (0.31)
10	**M** *	**18.4**± (0.077)	------

**M-Marketed Tablet, Each value represents mean (n=3) ±S.D.*

TASTE EVALUATION OF TABLETS

Table no.6: *In vitro* taste evaluation of tablet (Release in Phosphate Buffer pH 6.8)

SR NO.	BATCH	% RELEASE OF DRUG
1	**PM1**	**22.1**± (0.002)
2	**PM2**	**23.2**±. (011)
3	**PM3**	**23.6**± (0.02)
4	**KM1**	**25.1**± **n** (0.1)
5	**KM2**	**23.2**± (0.003)
6	**KM3**	**19.3**± (0.02)
7	**FM1**	**20.1**± (0.01)
8	**FM2**	**24.3**± (0.03)
9	**FM**	**23.6**± (0.1)

Each value represents mean (n=3) ±S.D.

Table no. 7: *In Vivo* Taste Evaluation of Tablets

Etoricoxib Tablet	Degree of bitterness after time					
	10 sec	1 min	2 min	5 min	10 min	15 min
Pure drug	3	2	2	2	2.5	2.5
KM3 Optimize Batch	0	0.1	0.15	0.11	0	0

The bitterness intensity scale from 0 to 3, 3 being strongest, 2 being moderate, 1 being slight, 0.5 being threshold and 0 for no bitter taste.

Any substance which is soluble in saliva will interact with taste buds, and can impart its taste. Therefore *in-vitro* taste evaluation study of the Fast Dissolving Tablet was done in the Phosphate Buffer PH 6.8 for approximate estimation of drug release in human saliva before doing actual volunteer study. This study shows that optimum batch KM3 having 1:3 (drug: Urea) ratio shows 19.3±0.02% of the drug release from the tablet in Phosphate Buffer PH6.8. [Table no. 6] The amount released was less than the amount that can induce bitterness. Result of *in-Vivo* taste evaluation study represented in table no. 7.

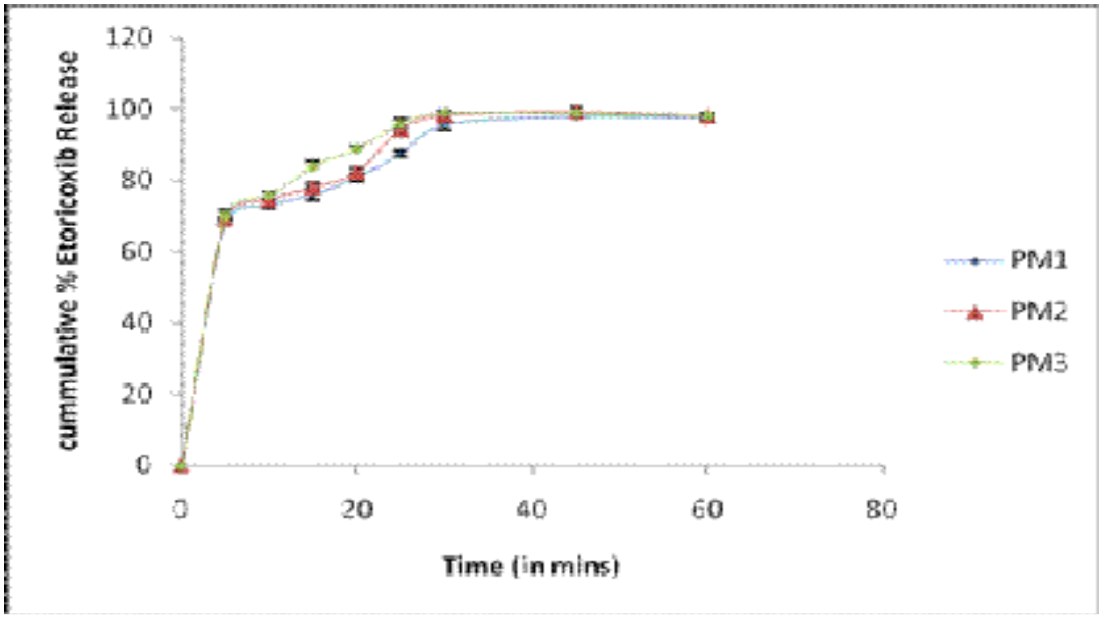
IN-VITRO DISSOLUTION STUDIES

Physical mixture, Kneading, Fusion method were used for the preparation of Fast Dissolving Tablet it is well known fact that superdisintegrant and Hydrophilic Carrier i.e., Urea are the main constituents in the preparation of Fast Dissolving Tablet. Hence Urea was used in different ratios and superdisintegrant was used in fixed proportion. Mannitol was added in the sufficient quantity to maintain rapid disintegration. It offers and provides synergistic effect to improve hardness and disintegration. Percent drug release is highest in KM3 batch of kneading method i.e. 99.96 at 20 min. Its show highest drug release in less time i.e. 20 min compared other batch hence its disintegration time was very less. (Table no. 8 b, fig. 7) Results of KM3 batch for other parameter were within official limit. Wetting time for KM3 batch was 17.3±0.058 sec. and 13.14±0.76 sec. respectively. Dissolution studies of the optimized tablet of batch KM3 reveled rapid release of drug (t_{90} for batch KM3 is 15 mins.) as compared to marketed tablet wherein t_{90} around 20 mins. (Table no. 9, fig. 8)

The tablet having the sufficient hardness and the minimum disintegrating time the batch KM3 was selected as the optimized batches amongst all the 9 batches. These dosage forms include of water dispersible carrier material, which is impregnated with a unit dose of the pharmaceutical active agent. These formulations show significant difference in disintegration time as compared to marketed formulation. Hence these batches were selected as optimized batches. Sensory evaluation of optimized tablet proves better palatability. Also the tablet creates modern roughness in the mouth which gets vanished within a short span without affecting compliance of the tablet.

Table no. 8(a): Cumulative % Drug Released from Fast Disintegrating Tablet by Physical Mixture method at Different Time Interval

Sr. No.	Time (min)	Cumulative % drug released		
		PM1	PM2	PM3
1	**0**	0	0	0
2	**5**	**68.38**± (0.97)	**69.09**± (0.49)	**70.18**± (1.47)
3	**10**	**73.09**± (1.12)	**74.5**± (0.21)	**75.75**± (0.98)
4	**15**	**76.15**± (1.89)	**78.05**± (1.13)	**83.97**± (1.36)
5	**20**	**80.94**± (1.18)	**82.25**± (1.25)	**88.9**± (0.64)
6	**25**	**87.48**± (1.1)	**94.26**± (0.65)	**96.05**± (1.22)
7	**30**	**95.68**± (1.35)	**98.11**± (1.2)	**98.92**± (0.45)
8	**45**	**97.99**± (0.31)	**99.2**± (1.6)	**98.84**± (0.22)
9	**60**	**97.63**± (0.65)	**97.87**± (0.69)	**98.15**± (0.01)



Each value represents mean (n=3) ±S.D.

Fig. 5: Cumulative % Drug Released from Fast Disintegrating Tablet by Physical Mixture method.

Table 8 (b): Cumulative % Drug Released from Fast Disintegrating Tablet by Kneading method at Different Time Interval

Sr. No.	Time (min)	Cumulative % drug released		
		KM1	KM2	KM3
1	0	0	0	0
2	5	**69.59**± (0.41)	**69.76**± (0.52)	**75.5**± (0.54)
3	10	**75.25**± (0.47)	**75.37**± (0.53)	**80.05**± (0.31)
4	15	**79.04**± (0.89)	**79.46**± (0.31)	**89.76**± (0.94)
5	20	**85.95**± (0.15)	**89.15**± (0.93)	**99.96**± (0.51)
6	25	**94.91**± (0.62)	**96.79**±. (1.82)	**99.77**± (0.29)
7	30	**98.39**± (1.57)	**99.08**± (0.29)	**99.49**± (0.93)
8	45	**99.2**± (1.6)	**98.8**± (0.92)	**98.56**± (0.69)
9	60	**97.57**± (0.6)	**97.25**± (0.65)	**97.87**± (0.69)

Each value represents mean (n=3) ±S.D.

Physical mixture, Kneading, Fusion method were used for the preparation of Fast Dissolving Tablet it is well known fact that superdisintegrant and Hydrophilic Carrier i.e., Urea are the main constituents in the preparation of Fast Dissolving Tablet. Hence Urea was used in different ratios and superdisintegrant was used in fixed proportion. Mannitol was added in the sufficient quantity to maintain rapid disintegration. It offers and provides synergistic effect to improve hardness and disintegration. Percent drug release is highest in KM3 batch of kneading method i.e. 99.96 at 20 min. Its show highest drug release in less time i.e. 20 min compared other batch hence its disintegration time was very less. (Table no. 8 b, fig. 7) Result of KM3 batch for other parameter were within official limit. Wetting time for KM3 batch was 17.3±0.058 sec. and 13.14±0.76 sec. respectively. Dissolution studies of the optimized tablet of batch KM3 reveled rapid release of drug (t_{90} for batch KM3 is 15 mins.) as compared to marketed tablet wherein t_{90} around 20 mins. (Table no. 9, fig. 8)

The tablet having the sufficient hardness and the minimum disintegrating time the batch KM3 was selected as the optimized batches amongst all the 9 batches. These dosage forms include of water dispersible carrier material, which is impregnated with a unit dose of the pharmaceutical active agent. These formulations show significant difference in disintegration time as compared to marketed formulation. Hence these batches were selected as optimized batches. Sensory evaluation of optimized tablet proves better palatability. Also the tablet creates modern roughness in the mouth which gets vanished within a short span without affecting compliance of the tablet.

Similarity analysis

Similarity factor were calculated from the *in-vitro* release profiles of both the formulation. The calculated value of KM3 was **65.01** (above 50) which clearly indicate indicated that the in-vitro release of KM3 were closely similar to that of marketed tablet release profiles. (Table no. 10)

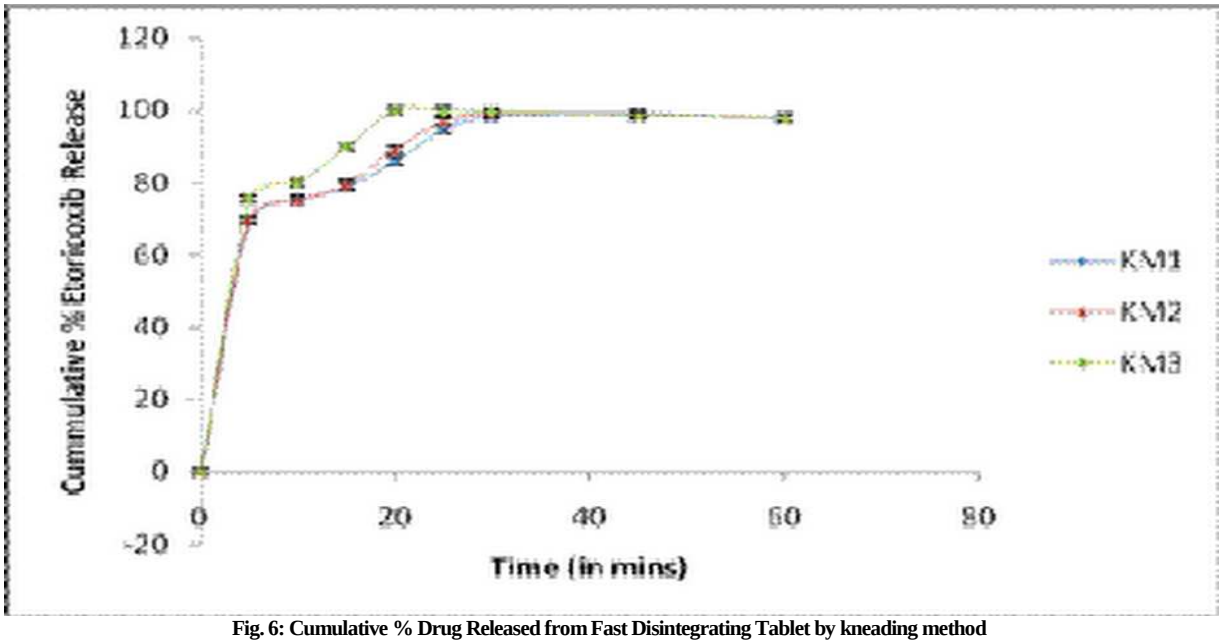


Fig. 6: Cumulative % Drug Released from Fast Disintegrating Tablet by kneading method

Table 8 (c): Cumulative % Drug Released from Fast Disintegrating Tablet by Fusion method at Different Time Interval

Sr. No.	Time (sec)	Cumulative % drug released		
		FM1	FM2	FM3
1	**0**	0	0	0
2	**5**	**66.91**± (1.72)	**69.26**± (1.28)	**70.18**± (1.47)
3	**10**	**71.83**± (1.24)	**75.37**± (0.46)	**75.42**± (0.91)
4	**15**	**74.37**± (1.65)	**79.92**± (0.71)	**85.21**± (1.09)
5	**20**	**81.39**± (1.85)	**90.38**± (1.22)	**89.07**± (0.46)
6	**25**	**88.06**± (1.3)	**97.56**± (1.09)	**96.05**± (1.22)
7	**30**	**95.68**± (1.35)	**99.08**± (0.29)	**98.92**± (0.45)
8	**45**	**97.99**± (0.31)	**98.8**± (0.92)	**98.84**± (0.22)
9	**60**	**97.63**± (0.65)	**97.87**± (0.69)	**98.15**± (0.01)

Each value represents mean (n=3) ±S.D

Table no.9: Dissolution Profile of Marketed Etoricoxib Tablet

Time in min	Cumulative % release
0	0
5	**68.38**± (0.97)
10	**76.88**± (0.084)
15	**83.68**± (0.65)
20	**90.22**± (1.38)
25	**99.34**± (0.9)

Each value represents mean (n=3) ±S.D.

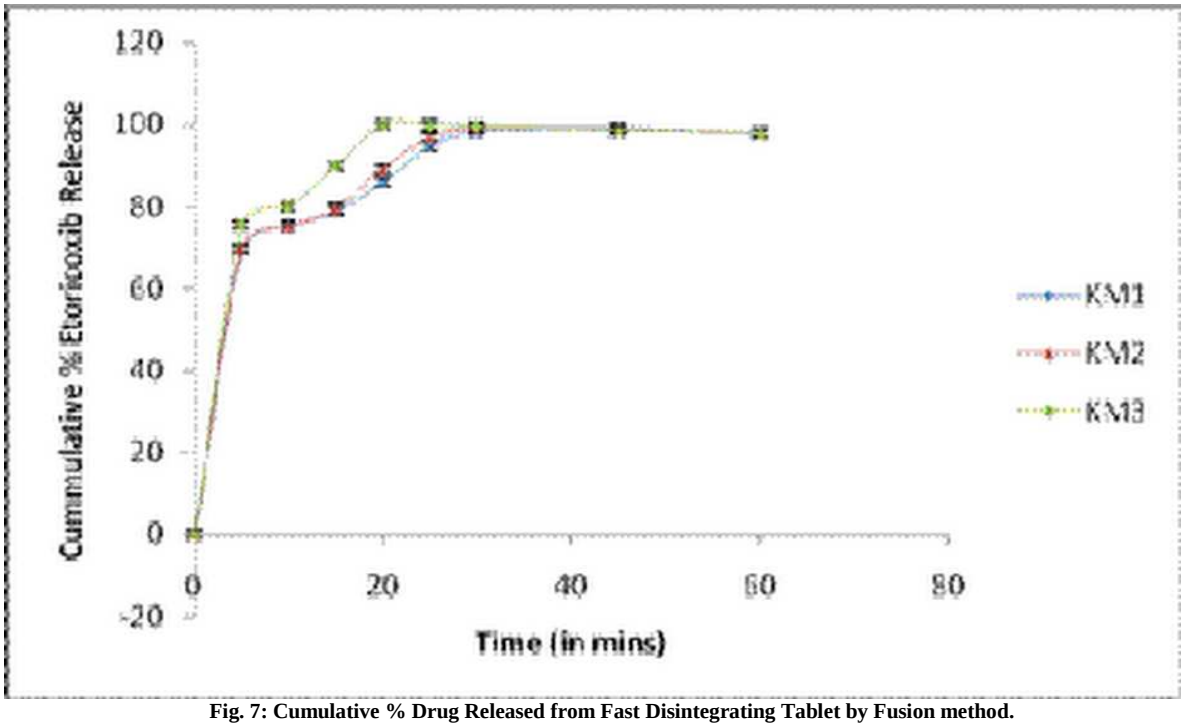


Fig. 7: Cumulative % Drug Released from Fast Disintegrating Tablet by Fusion method.

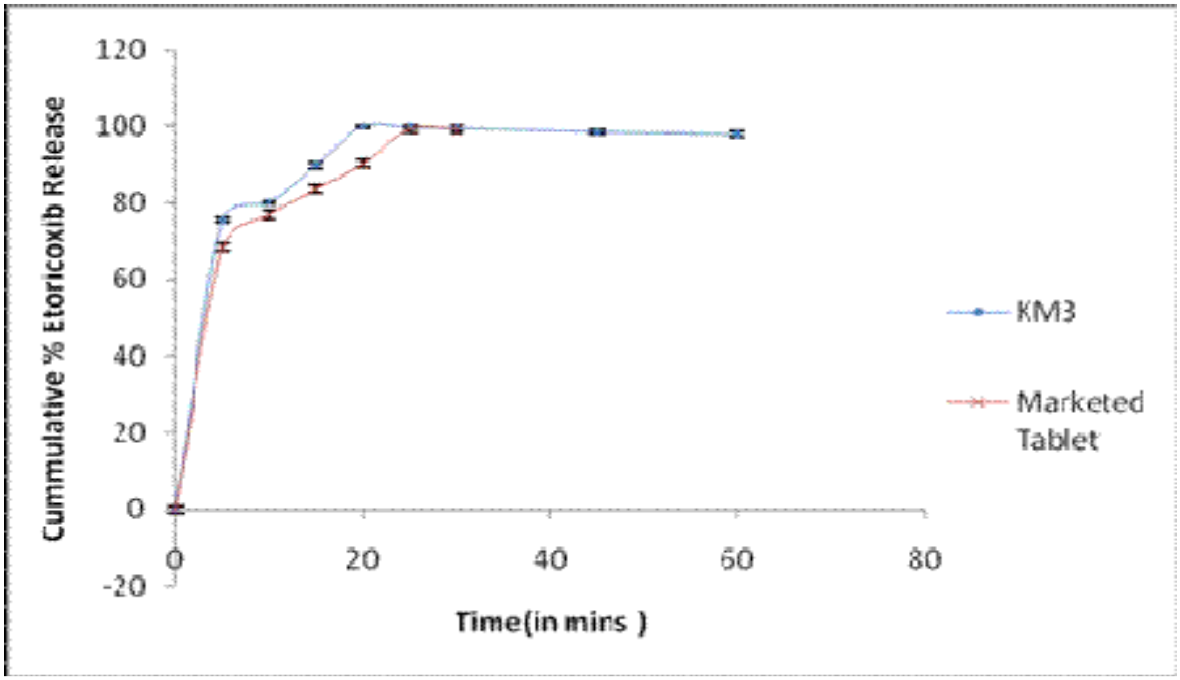


Fig 8: Dissolution profile of marketed Etoricoxib tablet

Table no. 10: Similarity Factor

Time (mins)	Innovator	Test	Rt-Tt	(Rt-Tt)^2
5	68.38	75.5	7.12	50.6944
10	76.88	80.05	3.17	10.0489
15	83.68	89.76	6.08	36.9664
20	90.22	99.96	9.74	94.8676
25	99.34	99.77	0.43	0.1849
∑	**418.5**	**445.04**	**26.54**	**192.7622**
Number of points		**8**		
F1	**6.34**			
F2	**65.01**			

Rt- Etoshine 60, Tt- KM3

Stability testing

Stability study was performed on optimized formulations KM3 results for weight gain, drug content, disintegration time and dissolution shows no appreciable change upto 3 months of accelerated stability studies. (Table no. 11 and 12)

Table 11: Parameters of Formulations at Time 0, 1, 2 and 3 Months of Stability Testing under 40°C and 75% RH.

Batch	Parameter	Months			
		0	1 month 1	2	3
KM3	Weight gain (%)	0	0.033	0.042	0.042
	Disintegration time(sec)	**13.73**± (1.88)	**13.70**± (1.03)	**13.75**± (1.06)	**13.75**± (1.01)
	Drug content (%)	**99.99**± (0.006)	**99.98**± (0.002)	**99.95**± (0.003)	**99.94**± (0.002)

Values shown in table are mean of three determinations

Table 12: Stability Study of KM3 Tablet for Dissolution Pattern

Time (sec)	Cumulative % drug release			
	0 month	1month	2month	3month
0	0	0	0	0
5	**75.5**± (0.54)	**74.2**± (0.052)	**74.3**± (0.32)	**74.2**± (0.25)
10	**80**± (0.31)	**80.4**± (0.22)	**79.5**± (0.42)	**79.6**± (0.35)
15	**89.76**± (0.94)	**89.2**± (0.012)	**89.4**± (0.14)	**89.2**± (0.1)
20	**99.96**± (0.51)	**99.9**± (0.1)	**99.5**± (0.1)	**99.5**± (0.1)
25	**99.77**± (0.29)	**99.7**± (0.02)	**99.7**± (0.1)	**99.6**± (0.1)
30	**99.49**±	**99.49**±	**99.49**±	**99.5**±

Values shown in table are mean of three determinations

CONCLUSION

In present investigation successfully Solubility and dissolution enhancement of Etoricoxib by kneading method of solid dispersion technique using Urea as carrier and taste masking of Etoricoxib by Aspartame. The KM3 batch having highest drug release and less disintegration time, which was optimized one. The prepared optimized tablet showed rapid disintegration as well as rapid dissolution as compared to marketed tablet. No changes occur in tablet during accerlated stability study. Taste masking of Bitter taste Etoricoxib by Aspartame and taste evaluation done successfully.

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