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FORMULATION AND EVALUATION OF TENOXICAM ORALLY DISINTEGRATING TABLET

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ABSTRACT

Orally Disintegrating Tablets (ODTs) have become a very popular dosage form as they disintegrate rapidly (< one minute) in the mouth and don't require water for administration. This is due to the increased patient compliance, pleasant mouth feel, ease of administration & swallowing and rapid disintegration and dissolution. There are three main manufacturing methods used for the production of ODTs, namely, freeze drying, molding and compression method. Also, different technologies are routinely used for manufacturing ODTs as Orasolv®, Durasolv®, WOWTAB®, Flash tab®, Zydis®, Quicksolv® and Lyoc® technologies. Some methods of manufacturing ODTs are complex, require multiple processes and don't provide all ODTs ideal properties. For example, freeze drying and molding provide very light and porous products which disintegrate very rapidly, but they are expensive and produce fragile products. On the other hand, compression method is the easiest and cost effective method for the production of ODTs. It has several advantages as simple equipment, commonly available excipients, high doses can be used and limited number of manufacturing steps. Orally disintegrating tablets containing 10 mg of Tenoxicam were manufactured using direct compression method. Experiments were evaluated for effects of formulation parameters like type & concentration of diluents, concentration of disintegrating agent and their interactions on Tenoxicam ODTs properties and Dicalcium phosphate were used as diluents of different properties, in addition to croscarmellose sodium (CCS), sodium starch glycolate, crosspovidone and the treated agar which was used as a natural superdisintegrant in combination with the synthetic. The obtained results revealed that disintegration time of the optimized ODTs formula (12.5 sec. ± 40 sec). ODTs composed of crosspovidone in combination with natural superdisintegrants

5% level was chosen as optimized formula, as it showed the lowest disintegration time with the highest drug release up to 93%. Furthermore, hardness of the manufactured tablets was not significantly affected by the use of Crosspoidone and sodium starch glycolate instead of CCS. Finally, it was concluded that Tenoxicam oral disintegrating tablets were developed using crosspovidone and Treated agar. These tablets provided low disintegration time and high hardness that are acceptable for ODTs.

KEYWORDS: Fast dissolving tablet, Superdisintegrants (synthetic, natural), Tenoxicam.

INTRODUCTION

Tenoxicam is 4-hydroxy-2-methyl-N(2-pyridyl)-2Hthieno[2,3e][1,2] thiazine -3-carboxamide-1,1-dioxide.[1] It is used in the treatment of rheumatoid arthritis and osteoarthritis and employed in the short term management of musculoskeletal disorders. It is administered in dose 20mg daily for 7 days.[2] It is a crystalline BCS class II drug and is very slightly soluble in water (0.045mg/ml).[1] Although it has excellent oral bioavailability, its poor aqueous solubility limits its dissolution rate and thus delays its onset of action.

The present work was aimed to increasing the dissolution rate of Tenoxicam, thus providing faster rate of absorption by adding potential Superdisintegrants like Crosspoidone, sodium starch glycolate, treated agar, cross carmellose sodium in the formulation. Mannitol was used as sweetening agent to mask bitter taste of Tenoxicam. The FDT of Tenoxicam may overcome problems such as difficulty in swallowing, inconvenience in administration while travelling and patient's acceptability.[3]

Characteristics of Fast Dissolving Tablets[4,5]

- Not require water to swallow, but it should dissolve or disintegrate in the mouth in a matter of seconds.
- Be compatible with other excipients used.
- Be portable without fragility concern.
- Have a pleasant mouth feel.
- Leave minimum or no residue in the mouth after oral administration.
- Exhibit low sensitive to environmental condition as temperature and humidity.
- Allow the manufacture of the tablet using conventional processing and packaging equipments at low cost.

- Ease of administration to the patient who cannot swallow, such as the elderly, stroke victims, bedridden patients, patient affected by renal failure and patient who refuse to swallow such as pediatric, geriatric and psychiatric patients.
- No need of water to swallow the dosage form, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
- Rapid dissolution and absorption of the drug, which will produce quick onset of action.
- Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patient.

- **MATERIAL AND METHOD**

Materials

Sr.no.	Name	Category	Company
1.	Tenoxicam	API	Ramdev Chemicals, Palghar
2.	Treated agar	Natural superdisintigrants.	.Research-lab Fine che. Industries, Mumbai.
3.	Microcrystalline cellulose	Adsorbent, diluent	Thomas Baker, Mumbai.
4.	Magnesium stearate	Gliadent, diluent	S.D. Fine Ltd, Mumbai
5.	Talc	Therapeutic agent	Meher Chemie, Mumbai.
6.	Mannitol	Lubricant	Monarch labs, Hyderabad.
7.	Cross povidone	Disintegrant	Research-lab fine che. industries Mumbai,
8.	Cross carmellose sodium	Disintegrant	Research-lab fine che. industries Mumbai
9.	Aspartame	Artificial sweetener	Research-lab fine che. industries Mumbai
10.	Sodium starch glycolate	Disintegrant	Meher chemie, mumbai
11.	Menthol	Carminative	Meher chemie, Mumbai

- **Precompression parameter study**

Evaluation of flow properties of powder blends of factorial batches

The characterization of flow properties of powder blends is important in tablet compression. The powder blends with good flow properties gives uniform die fill and consequently it gives the uniform tablet weight.

- **Bulk density**

The bulk density of powder is important parameter in the compressibility of the powder. The bulk density was between 0.33±0.02 to 0.38±0.07gm/cm^3.

- **Tapped density**

The tapped density of powder is important parameters in the compressibility of the powder. The tapped density was found to 0.37±0.06 to 0.45 ± 0.01 gm/cm^3.

- **Carr's index**

The Carr's index is indicator of compressibility. The value below 21% shows fair to passable compressibility. It was found to be 11.62±0.17 to 22.2±0.18 indicating passable compressibility.

- **Hausner's ratio**

The hausner ratio is another parameter indicating the flow properties. The value of ratio below 1.25 indicates good flow while above 1.25 indicates the poor flow. It was found to be1.13±0.03 to 1.28±0.07 indicating good to passable flow ability.

- **Angle of repose**

The angle of repose can be correlated with type of flow of powder. The angle of repose 31 to 35 indicates the good flow while the angle of repose more 30 indicates poor flow properties and angle of repose below 30 indicates excellent flow properties. The angle of repose was found to be within the range of 26.56±0.70 to 30.00±0.45 indicating good flowability.

Table no 2. Precompression parameter study

Formulation code	Angle of repose	Bulk density (wt/ml)	Taped density (wt/ml)	Hausner's ratio (%)	Compressibility index (%)
F1	27.47±0.56	0.33±0.02	0.38±0.05	1.15±0.06	13.15±0.23
F2	26.56±0.70	0.35±0.04	0.41±0.04	1.17±0.01	14.63±0.34
F3	30±0.45	0.32±0.01	0.37±0.06	1.15±0.06	13.51±0.42
F4	28.81±0.63	0.38±0.07	0.43±0.03	1.13±0.03	11.62±0.17
F5	29.24±0.69	0.38±0.07	0.43±0.03	1.13±0.03	11.62±0.17
F6	27.92±0.14	0.35±0.04	0.41±0.04	1.17±0.01	14.63±0.34
F7	27.92±0.14	0.34±0.03	0.41±0.04	1.20±0.04	17.03±0.46
F8	28.81±0.63	0.35±0.04	0.41±0.04	1.17±0.02	14.63±0.34
F9	29.68±0.60	0.38±0.07	0.43±0.03	1.13±0.03	11.62±0.17
F10	28.36±0.85	0.35±0.04	0.45±0.01	1.28±0.07	22.2±0.18
F11	28.81±0.63	0.38±0.07	0.45±0.01	1.18±0.05	15.5±0.22

The values represents Mean ±SD, n=3

METHODOLOGY

Preparation of Treated Agar[6]

Suitable quantity of agar powder (5-10gm) weighed and added in distilled water(100ml). Agitation is continuously by stirrer for day to swell. The swollen contents were dried on a tray for 3 days at room temperature. The dry powder were grinded by pestle and mortar. Then grinded powder was passed through sieve no.100.

Preparation of Mixed Blend of Drug and Excipient

The formulations of FDTs of Tenoxicam were prepared by direct compression method. A total of 11 formulations (F1 to F11) of fast dissolving tablets of Tenoxicam using different Superdisintegrants namely Crosspoidone, sodium starch glycolate and treated agar, Crosscarmallose sodium. All the ingredients were passed through mesh no.60 and collected separately. The drug, superdisintegrant mannitol and microcrystalline cellulose were mixed uniformly with gentle trituration using mortar and pestle to get a uniform mixture. Finally magnesium stearate and talc were added to the mixture and mixed well. The tablets were compressed using 10 mm flat- face surface punch tablet compression machine to get tablet of 200 mg weight (Table-1). Before tablet preparation, the mixture blend of all the formulations were subjected to precompression parameters like bulk density, tapped density, compressibility index and Hausner's ratio.

Table No.1 Formulation table of Fast dissolving tablet of Tenoxicam

Sr. No	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
1.	Tenoxicam	20	20	20	20	20	20	20	20	20	20	20
2.	Sodium Starch Glycolate	6	10	_	_	_	_	_	_	_	_	_
3.	Crosspovidone	_	_	6	10	_	_	_	_	_	_	_
4.	Cross carmellose Sodium	_	_	_	_	_	18	12	6	_	_	_
5.	Treated Agar	_	_	_	_	_	_	_	_	18	12	6
6.	Microcrystalline Cellulose	110	106	110	106	116	98	104	110	98	104	110
7.	Mannitol	54	54	54	54	54	54	54	54	54	54	54
8.	Aspartame	8	8	8	8	8	8	8	8	8	8	8
9.	Magnesium Sterate	2	2	2	2	2	2	2	2	2	2	2
10.	Menthol	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
	Total	200	200	200	200	200	200	200	200	200	200	200

Post compression parameter

- **Tablet hardness**

The resistance of tablets to shipping or breakage, under conditions of storage, transportation and handling before usage, depends on its hardness. The hardness of tablet of each

formulation was measured by Pfizer hardness tester. The hardness was measured in terms of kg/cm2. the hardness of tablet was found in between 2.40±0.09 to 3.00±0.12.

- **Weight variation**

Twenty tablets were selected at random and the average weight was calculated. Weight variation was calculated and was compared with I. P. standards. The weight variation of Tenoxicam tablet was found to be 200.0±0.01 to202.3±0.05.

- **Friability**

Friability is the measure of tablet strength. Roche type friabilator was used for testing the friability using the following procedure. Twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 min, the tablets were weighed and the percentage loss in tablet weight was determined. The percent friability was found to be 0.35±0.06 to 0.8±0.08.

- **Content uniformity**

Twenty tablets were crushed and powder equivalent to weight of one tablet was dissolved in phosphate buffer 6.8. Then suitable dilutions were made and absorbance at 263 nm wavelength was taken by using a UV visible spectrophotometer. the content uniformity of Tenoxicam were found to be 96.11±0.33 to 99.26±0.22.

- **Disintegration time**

For Fast Disintegrating tablets apply the tests observe the tablets within the time limit all of the tablets have disintegrated. If 1 or 2 tablets fail to disintegrate completely repeat the test on 12 additional tablets, not less than 16 of the total of 18 tablets tested disintegrate completely. The Tenoxicam tablets were found in between the 15sec to 30 sec.

- **Thickness**

The Thickness of tablet was measured by Monsanto hardness tester & the Tenoxicam tablet of thickness were found in between the 2.29 to 2.76.

Table no 3. Postcompression parameter study

Formulation code	Hardness (kg/cm^2)	Friability (%)	Weight variation (mg)	Thickness (mm)	Disintegration time	Content Uniformity(%)
F1	2.6±0.08	0.8±0.08	201.2±0.05	2.52	15 sec.	96.21±0.09
F2	2.75±0.06	0.65±0.04	200.1±0.06	2.33	22 sec.	96.26±0.19
F3	3.00±0.10	0.75±0.03	200.1±0.03	2.57	24 sec.	97.11±0.11
F4	2.9±0.02	0.85±0.08	200.0±0.01	2.28	30 sec.	95.29±0.10
F5	2.8±0.05	0.70±0.03	200.3±0.02	2.58	16 sec.	98.11±0.23
F6	2.8±0.05	0.45±0.02	202.0±0.03	2.76	21 sec.	96.17±0.11
F7	2.40±0.09	0.5±0.05	202.1±0.08	2.65	17 sec.	98.15±0.11
F8	2.50±0.05	0.35±0.06	200.3±0.03	2.28	23 sec.	97.32±0.19
F9	3.00±0.12	0.75±0.04	200.0±0.03	2.35	30sec	96.11±0.33
F10	2.70±0.08	0.6±0.06	201.1±0.05	2.29	20sec	99.26±0.22
F11	2.80±0.06	0.55±0.05	202.3±0.05	2.35	15sec	99.15±0.33

All values are represented as mean ± standard deviation (n=3)

- **Drug- Excipients Compatibility Study**

FTIR studies were conducted and the spectrum was recorded in the range of 4000-400cm-1. No significant interaction between drug and Excipients was observed. All the spectrum i.e. drug and Excipients were concordant with that of standard IR spectra of pure drug Tenoxicam.

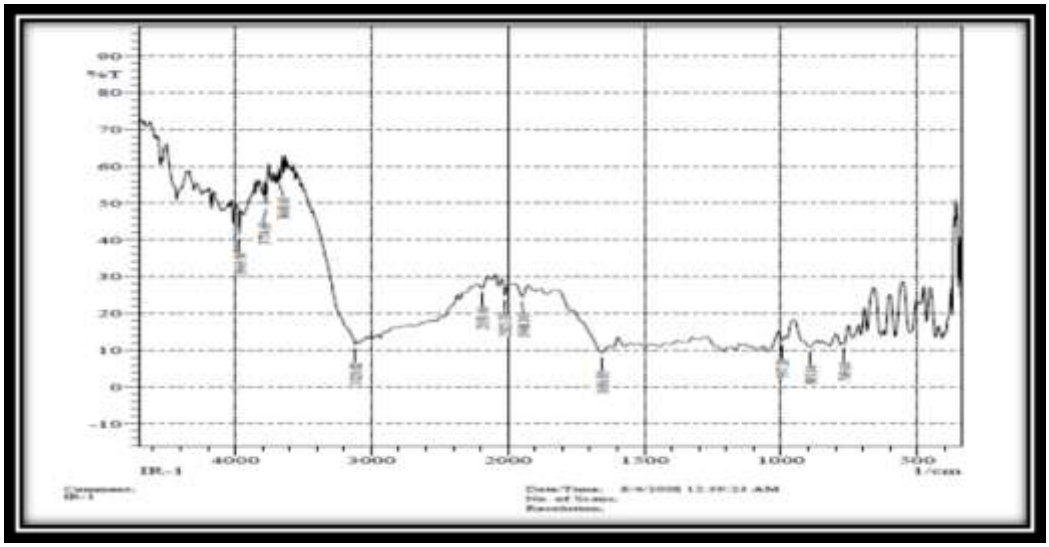

Fig.no.1. FT-IR Spectrum of Tenoxicam

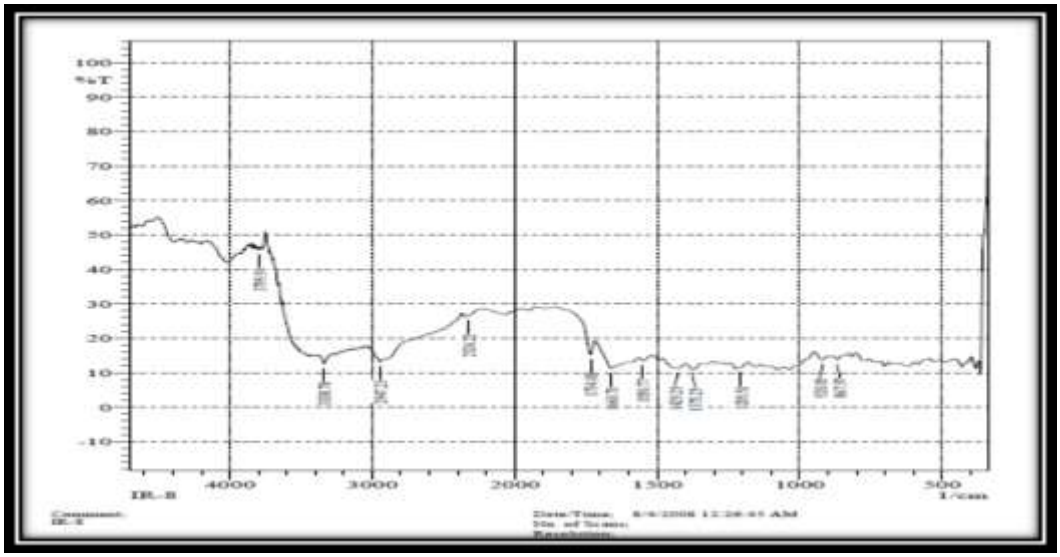

Fig.no.2. FT-IR Spectrum of mixture

Dissolution Study

Table No.4 Percentage drugs release Vs time of formulation f1to f4.

Time (min)	F1	F2	F3	F4
0	0	0	0	0
1	9.825	8.11	10.74	8.17
3	20.74	13.73	24.68	19.72
5	24.36	23.205	31.67	25.64
7	30.79	29.2	38.581	32.645
10	45.41	39.993	46.58	40.381
15	52.82	43.05	56.866	49.388
20	68.208	56.13	74.37	70.07
25	74.204	67.981	82.172	81.65
30	84.87	68.73	89.13	93.33

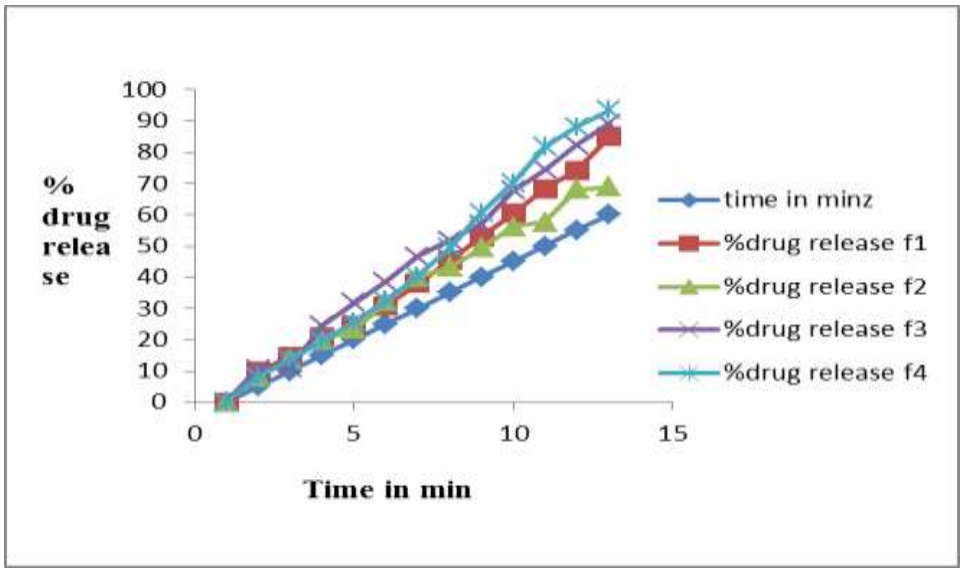

Figure No.3 Percentage drugs release Vs time of formulation f1to f4

Table No. 5 Percentage drugs release Vs time of formulation f5 to f8.

Time (min)	F5	F6	F7	F8
0	0	0	0	0
1	15.41	11.4	17.82	12.98
3	22.702	21.26	25.37	21.82
5	31.53	30.98	30.99	28.15
7	39.02	32.56	42.18	33.66
10	41.230	32.56	49.88	41.28
15	48.34	39.245	57.66	48.98
20	66.93	46.58	63.88	64.60
25	75.22	64.12	74.47	75.54
30	85.09	76.71	88.12	85.17

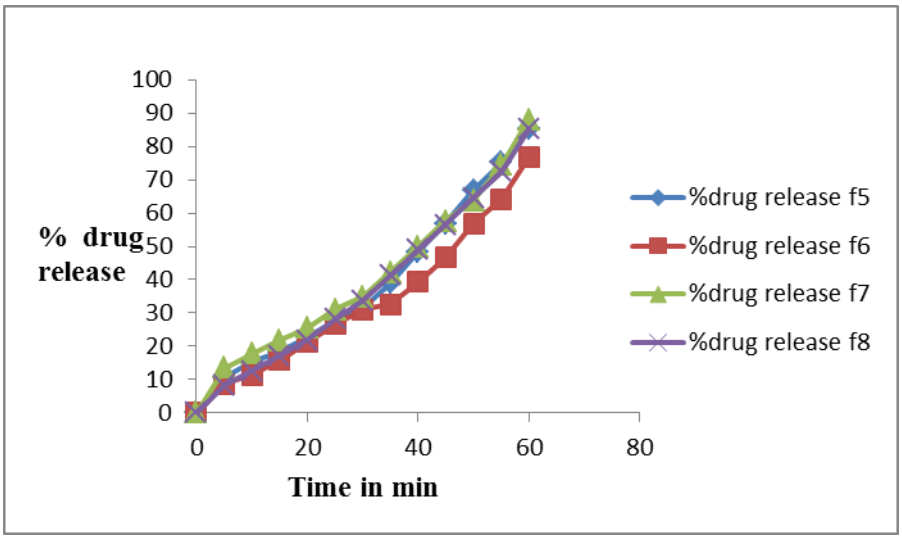

Fig.no. 4 Percentage drugs release Vs time of formulation f5to f8.

Table No. 6 Percentage drugs release Vs time of formulation f9 to f11

Time (min)	F9	F10	F11
0	0	0	0
1	13.48	14.20	13.11
3	22.18	19.35	18.44
5	30.15	24.49	23.25
7	34.55	29.69	27.55
10	38.99	33.19	29.11
15	42.60	40.55	38.44
20	60.19	52.95	46.55
25	75.67	70.91	62.70
30	84.90	80.95	70.90

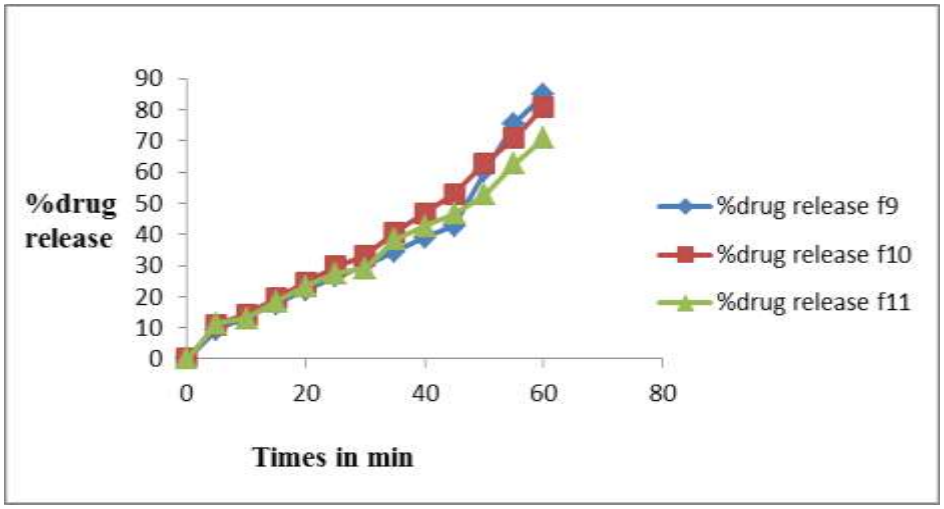

Fig.no. 5 Percentage drugs release Vs time of formulation f9to f11.

- **Stability studies**

Short term stability studies were performed at a temperature of 45 ^{0} c ±1^{0}c over a period of three weeks (21days) on the promising CGPS tablet formulation F4 sufficient number of tablets (10) were packed in amber colored screw capped bottles & kept in hot air oven maintained at 45^{0}c ±1^{0}c. samples were taken at weekly intervals for drug content estimation. at the end of three weeks period, dissolution test & *in-vitro* floating studies were performed to determine the drug release profiles.

Table no. 7. Stability studies

Sr.no.	Time (min.)	Cum. % drug released ± S.D. 1st day	Cum. % drug released ± S.D. 21st day
1	0	00	00
2	1	8.17	6.17
3	3	19.72	17.55
4	5	25.64	26.54
5	7	32.645	30.19
6	10	40.381	38.51
7	15	49.388	46.11
8	20	70.07	72.08
9	25	81.65	79.16
10	30	93.33	92.13

SUMMARY AND CONCLUSION

Summary: Tenoxicam is a member of class of agents called as oxicams. Tenoxicam is a potent, orally active cyclo-oxygenase 2 (COX-2) specific inhibitor within and significantly above the clinical dose range. Tenoxicam drug belongs to class II under BCS and exhibit low and variable oral bioavailability due to its poor aqueous solubility. The prepared tablets were

evaluated for micromeritic properties (like bulk density Tapped density, Angle of repose and compressibility index), hardness, friability, weight variation, drug content uniformity, wetting time, water absorption ratio, in-vitro disintegration. Time, in-vitro dissolution studies described in the result indicated that the significant effect was observed of increased polymer concentration on said parameters in each case.

CONCLUSION

In the present work, fast dissolving tablets of Tenoxicam were prepared by direct compression method using different Superdisintegrants. From the findings obtained, it can be concluded that:-

- The observed flow properties of polymer and drug good.
- FT-IR studies revealed that there is no chemical interaction between Tenoxicam and excipients used in the study.
- The tablets prepared were found to be good without any chipping, capping and sticking.
- Formulated tablets gives satisfactorily result for various physico-chemical evaluation of tablets like tablet dimension, hardness, friability, weight variation, *in vitro* dispersion time, wetting time, water absorption ratio and drug content.
- The low values of standard deviation for average weight and drug content of the prepared tablets indicate weight and drug content uniformity within the batches prepared.
- The promising formulation (4) have displayed good water absorption ratio of about 93.33% which indicate better and faster swelling ability of the disintegration in presence of little amount of water.
- From the present change study, it may be formulated that fast dissolving tablet of Tenoxicam can be prepared by direct compression method and Croscarmellose sodium, Treated agar; cross povidone as Superdisintegrants was found to be the best than other Superdisintegrants. F4 formulation showed the least and the highest release of more than 93.33% of the drug in just 40 seconds.

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