Formulation and evaluation of orodispersible tablet containing piroxicam by sublimation method

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Abstract

The most preferred route of administration is oral administration of any dosage form because of its self-medication, exact dose of drug and easily administration but difficulty in swallowing in geriatric patients is one important drawback of this route and mentally disturb patients. To solved this problem disintigration time of oral disintegration tablet is within 30 sec. which is disintegrate in mouth. Piroxicam with camphor as subliming agent combined to form fast dissolving tablet.wet granulation technique is used for preparation of Orodispersible tablets of Piroxicam drug. Camphor was removed from the granules by using vaccum. Then tablet were prepared and expose to vaccum. The tablet formulations were evaluated for Disintegration time, dissolution, hardness, friability, weight variation and thickness.

Keywords: Orodispersible tablet (ODTs), Piroxicam, Subliming agent, Camphor.

Introduction

Oral dispersible tablets (ODTs): Difficulty in swallowing or Dysphagia is common in all age groups. Dysphagia is seen in about 35% of the general population. The preparation of Orally Disintegrating tablets (ODTs) emerged with an objective to improve patient's compliance. These tablet rapidly disintegrate and/or dissolve to release the drug fastly and they come in contact with saliva in mouth, thus avoid the need for water during administration, an attribute that makes them highly accepted for pediatric and geriatric patients. Difficulty in swallowing conventional tablets and capsules is usually seen in all age groups, mostly in elderly and dysphasic patient.

Ideal properties of ODTs

- Not necessary water to swallow and should dissolve or disintegrate in the mouth within a few seconds.
- Allow high drug capacity.
- Be acceptable with taste masking and other excipients.
- Have a good mouth feel.
- Have good strength to withstand the rigors of the formulation process and post manufacturing handling.
- Useful in cases such as motion sickness, sudden episodes of allergic attack or cough, where an rapid onset of action required.
- An increased bioavailability, mostly in situation of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.

Advantages of ODTs

- Fast drug therapy intervention.
- Beneficial for administration and patient compliant for disabled, bedridden patients and for travelers and busy people, who do not always have access to water.
- Great mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patients.
- Apart from it the drug secured from degradation due to pH and GIT enzymes
- It improves patient compliance due to the remove pain with injections.
- Correct dosing as compared to liquids.

Disadvantages of ODTs

- ODT is water loving in nature so must be stored in dry place.
- It is also shows the fragile, effervescence granules characteristics.
- ODT always need special packaging for properly stabilization & safety of stable product

Conventional Technique

Sublimation

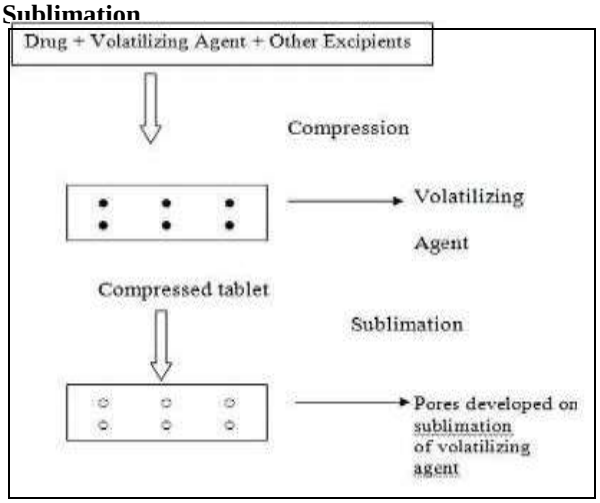


Fig. 1: Steps Involved in Sublimation

Materials and Method

Drug profile

PIROXICAM: Piroxicam is a non-steroidal anti-inflammatory agent of the oxicam class indicated to relieve the symptoms of rheumatoid and osteoarthritis, and used as an analgesic, mostly where there is an inflammatory component. Piroxicam is structurally unrelated to other NSAIDs. It has a long half-life and may be administered as a single daily dose, which can be an advantage over other NSAIDs. The anti-inflammatory potential of it has been equated with that of indomethacin, and its analgesic activity has been shown to be greater than that of aspirin. Piroxicam is used in the treatment of osteoarthritis and rheumatoid arthritis. It was approved by the FDA in 1982. The anti-inflammatory effects of it may result from the peripheral inhibition of prostaglandin synthesis due to the inhibition of the enzyme cyclooxygenase. It also can inhibit the activation of neutrophils, which may contribute to anti-inflammatory effects as well. Prostaglandins sensitize pain receptors, and their inhibition is believed to be responsible for the analgesic effects of it.

Formulation development

1. **Preliminary screening for ODTs**

A. **Trails for selecting superdisintegrants**

- Tablets were formulated by setting various concentrations of super disintegrantie, Cross carmellose Sodium (Ac-Di-Sol) along with drug, mannitol, (with different concentrations) and magnesium stearate respectively.
- Powder blend for every batch was then compressed to get fast disintegrating tablets.
- 8, 12, 16, 20, 24 and 28% of Ac-Di-Sol was taken in F1 to F6 batch respectively.

Table 1: Trials for Disintegrants

Batch No	Drug (mg)	Ac-Di-Sol (mg)	Mannitol (mg)	Mg. Stearate (mg)	Total weight (mg)
F1	20	8	168	4	200
F2	20	12	164	4	200
F3	20	16	160	4	200
F4	20	20	156	4	200
F5	20	24	152	4	200
F6	20	28	148	4	200

Table 2: Trails for screening sublimating agents

Batch No.	Drug (mg)	Subliming Agent			Ac-Di-Sol (mg)	Xylitol (mg)	Mannitol (mg)	Mg.Stearate (mg)	Total Wt. (mg)
		Camphor (mg)	Menthol (mg)	Thymol (mg)					
F1	20	10			20	2	144	4	200
F2	20	20			20	2	134	4	200
F3	20	30			20	2	124	4	200
F4	20		10		20	2	144	4	200
F5	20		20		20	2	134	4	200
F6	20		30		20	2	124	4	200
F7	20			10	20	2	144	4	200
F8	20			20	20	2	134	4	200
F9	20			30	20	2	124	4	200

B. **Trails for subliming agents**

- Tablets were formulated by adding subliming agents such as camphor, menthol and Thymol in different concentrations with drug, Ac-Di-Sol, mannitol, Xylitol, and magnesium stearate.
- After formulation, tablets of each batch were exposed for sublimation in oven at 40^0c for 1 hour.
- Thereafter all the batches were evaluated for friability, DT and hardness.

Preparation of Piroxicam ODTs Tablets: Piroxicam and all other ingredients were passed through the sieve no. 60 and the tablets were prepared by adding drug, Mannitol, Camphor, Menthol, Thymol, Xylitol, Super disintegrant Ac-Di-sol and magnesium stearate in different concentrations. The directly compressible blend was then compressed by means of 8 stations tablet compression machine (Jaguar).After compression, the tablets were collected and were subjected for sublimation at a temperature of 40^0c to facilitate the volatilization of sublimely components.

Evaluation of tablet

Evaluation parameter

1. Appearance of tablet
2. Size of tablet and Shape of tablet
3. Tablet Uniformity of weight

4. Thickness of tablet and diameter
5. Hardness (Crushing strength).
6. Friability test
7. Water absorption ratio
8. Wetting time
9. Disintegration time
10. Dissolution test

Results and Discussion

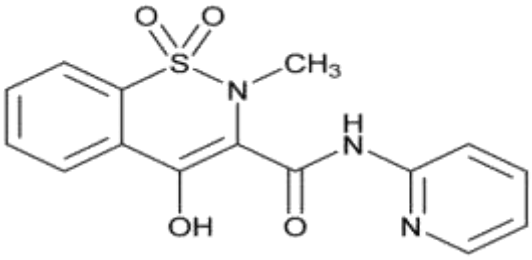
Characterization of drug (Piroxicam): The characterization of drug is necessary for identification and purity of drug. In characterization of drug different physical, chemical and spectroscopic tests were performed which are given below.

A. **Identification test**

IR spectroscopy: IR spectra interpretation study was performed for the identification of Piroxicam.

Wave numbers (cm^{-1})	Groups present
1700.04	C=o Stretch
3551.20	N-H Bending
3550.20	O-H Rocking
885.30	C-C Stretching
3610	O-H Stretch

Structure of Piroxicam



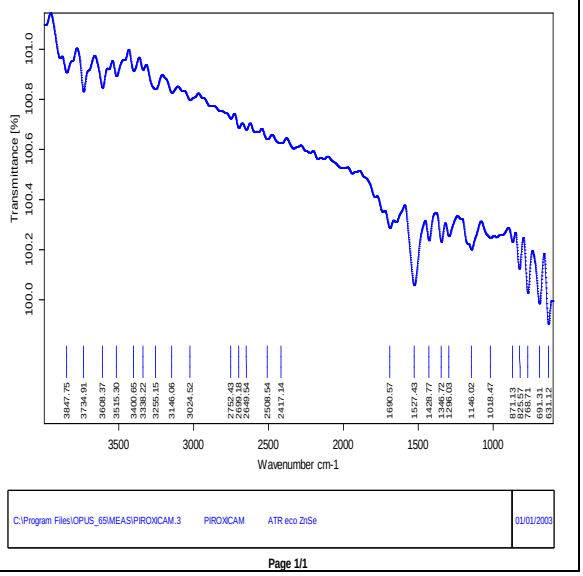


Fig. 2: IR spectra interpretation of Piroxicam

FT-IR study is important for determination of functional groups present in structure of sample. The IR spectrum of the pure Piroxicam sample was recorded by FT-IR spectrometer as shown Fig. 2. The major peaks observed and corresponding functional groups are also given in Fig 2.

UV spectroscopy

A. **Determination of absorption maxima:** The absorption maxima of Piroxicaminwater was determined using double beam UV spectrophotometer. The λ_{max} of Piroxicam in buffer pH6.8 was found to be 354 nm. The λ_{max} for Piroxicam of 10 ppm solution is shown in following figure. (Fig. 2)

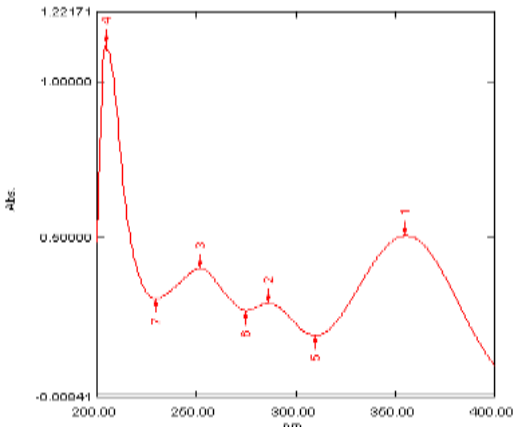


Fig. 3: UV spectrum of Piroxicam

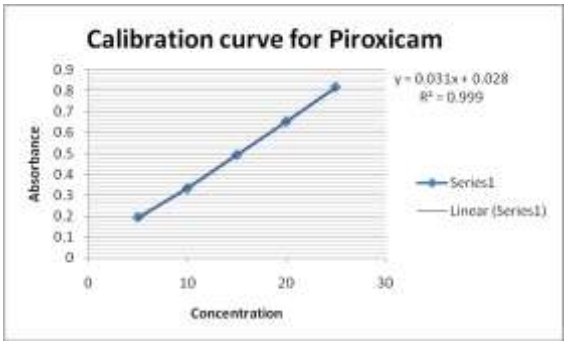


Fig. 4: Calibration curve of Piroxicam

Calibration curve of Piroxicam

Table 3: Absorbance at different concentrations

Sr. no.	Concentration (µg/ml)	Absorbance (354 nm)
1	5	0.195
2	10	0.333
3	15	0.492
4	20	0.652
5	25	0.817

The standard calibration curve of Piroxicam was estimated in buffer pH 6.8 andit was shown that linear in the concentration range of 5-25 µg/ml. The observed absorbance showed in the above figure. (Fig.4) and regression coefficient was 0.999.

B. **Physicochemical study**

1. **Organoleptic characterization**
2. **Solubility study of drug**
3. **Melting point determination of drug**
4. **Loss on drying of drug**

Post compression characterizations (Prepared ODT)

For the five batches the evaluation parameters as follow before and after sublimation.

Table 4: Post compression before sublimation characteristics of formulations

Formulation of tablet dosage form	Hardness of tablet (Kg / cm)	Friability of tablet (%)	Thickness of tablet (mm)	Disintegration time(sec) of tablet	Weight variation(average weight)(mg)	Wetting time(sec)
F1	3.6	0.40	2.8	42	204 ± 0.5	3.5
F2	3.9	0.44	2.9	37	203 ± 1.10	3.1
F3	3.9	0.46	2.7	30	200 ± 0.7	2.7
F4	4.3	0.40	2.8	35	201 ± 1.15	2.6
F5	4.0	0.47	2.6	27	198 ± 1.5	2.2
F6	3.7	0.43	2.7	38	200 ± 1.22	1.7
F7	3.6	0.42	2.7	69	199 ± 0.65	4.2
F8	3.8	0.43	2.9	53	201 ± 0.50	3.9
F9	3.8	0.45	2.7	46	199 ± 0.80	3.4

Table 5: Post compression after sublimation characteristics of formulations

Formulation	Hardness (Kg / cm^2)	Friability (%)	Thickness (mm)	Disintegration time(sec)	Weight variation(average weight)(mg)	Wetting time(sec)
F1	3.5	0.41	2.7	32	202 ± 0.5	2.3
F2	3.8	0.46	2.8	29	201 ± 1.10	2.2
F3	3.6	0.48	2.5	24	198 ± 0.7	1.9
F4	4.1	0.42	2.6	29	199 ± 1.15	1.5
F5	3.8	0.49	2.5	33	196 ± 1.5	1.4
F6	3.5	0.45	2.6	40	198± 1.22	1.1
F7	3.5	0.44	2.6	55	200 ± 0.65	3.6

F8	3.6	0.47	2.8	40	202 ± 0.50	3.2
F9	3.8	0.49	2.6	31	199 ± 0.80	2.9

Discussion

- It was seen that hardness of formulation was reduced little a bit after sublimation but it is maintained so far. Hardness for the ODT's should be in range of 3.6- 4.3 k g/cm^2 and it has result found in between 3.5 - 4.1kg/cm^2 and it was conclude that it has good hardness to pass friability test.
- Friability shown after sublimation in between the range of 0.41-0.49% for all the preparation and for the selected batch it was 0.48% it means that it passes friability test with good margin.
- Before sublimation DT of the preparation were in between 27-69 sec after sublimation it changed to the range of 11-55 sec. hence, DT was reduced after performing sublimation to formulations.
- Disintegrating time of the formulation is directly related to hardness and friability of formulation. It is always seen that disintegration time of a formulation increases with increase in hardness. But the formulation doesn't show the effect on disintegrating time with increase in hardness hence.

Summaries and Conclusion

- IR spectra revealed that, the drug sample was pure.
- If the amount of subliming material was increased then the DT was decreased, but at the same time the hardness of tablet preparation was increased.
- The hardness of tablet and DT of the heated tablets high with an high concentration of the xylitol content. These conclude that the heating process and xylitol content change the properties of MDTs.
- Next step heating, in that increase pore size of tablet i.e. disintegration of tablet shown fastly and tablet hardness was also high.
- Post compression study was carried out for each and every formulation amongst all the batches, batch F3 showed good results with hardness 3.6kg/cm^2 and disintegrating time 30 sec. and selected as an optimised batch.

Finally it was concluded that using Xylitol compressibility of the tablet to with stand its mechanical strength and incorporation of Camphor as a subliming agent formed porous structure in the tablet aid to easy penetration of fluid reducing disintegrating time.

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