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# Formulation and Evaluation of Sublimed Mouth Dissolving Tablets of Aceclofenac

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## ABSTRACT

Aceclofenac is a non-steroidal anti-inflammatory, analgesic and antipyretic drug used in the treatment of rheumatic arthritis, post-traumatic pain, masculo-skeletal and joint disorder. Problem with this drug is poor solubility in water hence poor bioavailability after oral administration. The objective of the research work was to develop and evaluate mouth dissolving tablets of Aceclofenac by using sublimation technique. The sublimation technique is used to increase the porosity of the tablets in which camphor was used as subliming agents which in turn forms the porous structure on the surface of tablets after sublimation. Aspartame was used as sweetening agent. The formulated tablets were evaluated for different parameters like weight variation, hardness, friability, drug content, disintegration time, wetting time, water absorption ratio, and *In-vitro* dissolution studies. Based on the results, formulation F-3 & F-6 containing Crosprovidon and Kyron T-314 10% concentration as superdisintegrants showed the least wetting time of about 17 & 13 sec, disintegration time of 25 & 18 sec and drug release of about 89.13 & 99.14% within 180 sec respectively and was found to be promising and selected as the optimized formulations. From the results, it was concluded that mouth dissolving tablets with improved Aceclofenac dissolution could be prepared by sublimation of tablets containing suitable subliming agent.

**Key words:** Aceclofenac, mouth dissolving tablets, *in-vitro*, sublimation technique.

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# INTRODUCTION

Mouth dissolving tablets disintegrates or dissolves in saliva and is sallowed without the use of water. Pediatric and geriatric patient have difficulty in swallowing the conventional dosage forms. Mouth dissolving drug delivery system may offer a solution to these problems. Various technologies have been used in the manufacture of mouth dissolving tablets includes Freeze drying or Lyophilization, Tablet Molding, Direct compression, Spray drying, Sublimation, Taste masking, Mass extraction, and Addition of superdisintegrants. Among the number of NSAIDs available, Aceclofenac is considered as one of the emerging NSAID. It is a newer derivative of Diclofenac and has less gastrointestinal complications[1, 2]. However, the problems of side effects after long term administration of these drugs, such as irritation and ulceration of the GI mucosa, have arisen in clinical trials. These gastroenteropathies are generally believed to be resulted from the direct contact effect, which can be attributed to the combination of local irritation produced by the free carboxylic group in the molecular structure and by local blockage of prostaglandin biosynthesis in the GI tract[3]. The use of conjugates to provisionally hide the acidic group of NSAIDs has been proposed as an approach to reduce or suppress the GI toxicity due to the direct contact effect. Therefore, the development of new NSAIDs without these side effects has long been awaited. In the present study, an attempt has been made to develop mouth dissolving tablets of Aceclofenac using novel superdisintegrants and to investigate the effect of subliming agent on the release profile of the drug. The fundamental principle used in the development of the mouth dissolving tablet is to maximize its pore structure. A sublimation technique was adopted in the present investigation after addition of a subliming agent to increase porosity of the tablets. It is likely that a porous hydrophilic will easily pick up the disintegrating medium and break quickly.

# MATERIALS AND METHODS:

Aceclofenac and Camphor were obtained from Yarrow chemicals Pvt. Ltd., Mumbai, India. Crosprovidon was obtained from Colorcon Asia Pvt. Ltd., Goa, India and Kyron T-314 was obtained from Corel pharma. Ahmedabad, India. All other ingredients used throughout the study were of analytical grade and were used as received.

**Preparation of mouth dissolving tablets**

Aceclofenac and all other ingredients were passed through the sieve no. 60 and then the tablets were formulated by mixing drug, camphor, superdisintegrants (Crosprovidon and Kyron T-314) in different concentrations and other ingredients in a plastic container. The directly compressible blend was compressed to get hardness in the range of 4-5 kg/cm$^2$. After compression the tablets

were collected and were subjected for drying at a temperature of 60 °C to facilitate the volatilization of sublimable components added. The tablets were weighed at regular intervals until constant weight was achieved ensuring complete removal of the sublimable ingredients. The compositions of various batches are shown in **Table 1.**

**Table 1: Composition of sublimed mouth dissolving tablets of Aceclofenac.**

| Ingredients (mg) | Formulation code | | | | | | |
|---|---|---|---|---|---|---|---|
| | F0 | F1 | F2 | F3 | F4 | F5 | F6 |
| Aceclofenac | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Camphor | 15 | 15 | 15 | 15 | 15 | 15 | 15 |
| Crosspovidon | --- | 10 | 15 | 20 | --- | --- | --- |
| Kyron T-314 | --- | --- | --- | --- | 10 | 15 | 20 |
| Aspartame | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Directly compressible mannitol | 72 | 62 | 57 | 52 | 62 | 57 | 52 |
| Magnesium stearate | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Aerosil | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Total weight | 200 | 200 | 200 | 200 | 200 | 200 | 200 |

**FTIR Studies**

Pure drug and optimized formulations (F-3 & F-6) were subjected for FTIR analysis using Fourier transformer infrared spectrophotometer (4100, Jasco Corporation, Tokyo, Japan). The samples were prepared on KBr-press (Himedia chemicals, Mumbai, India) and scanned over wave number range of 4000 to 400 $cm^{-1}$. Spectra were analysed for drug polymer interactions and functional groups.

**Weight Variation**

The weight variation test was done by (Shimadzu digital balance) weighing 20 tablets individually, calculating the average weight and comparing the individual tablet weights to the average. The percentage weight deviation was calculated and then compared with USP specifications.

**Hardness**[4]

The hardness of prepared tablets were determined by using Monsanto hardness tester and measured in terms of $kg/cm^2$. Test was done in triplicate.

**Friability**[5]

The test was performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche Friabilator was used for testing the friability of prepared fast dissolving tablets. 20 tablets were accurately weighed and placed in the Friabilator and operated for 100 revolutions. The tablets were re-dusted and reweighed. Friability (F) was calculated using the following formula.

$$F = (1- W_0 / W) \times 100$$

Where, $W_0$ and W are the weight of the tablets before after the test respectively. The test was done in triplicate. The tablets that loose less than 1% weight were considered to be compliant.

**Drug Content**[6]

Weighed tablets (5) were powdered using a glass mortar and pestle. An accurately weighed quantity of powder equivalent to 100 mg of Aceclofenac was taken into 50 ml volumetric flask, dissolved in phosphate buffer of pH 6.8 and the solution was filtered through whatman filter paper no.41. The filtrate was collected and suitably diluted with phosphate buffer of pH 6.8. The drug content was determined at 276 nm by UV-spectrophotometer (UV-1700 Shimadzu Corporation, Japan) against blank. The test was done in triplicate.

**Disintegration test**[6]

Six tablets along disc were introduced in each tube of basket of disintegration test apparatus (Lab care instruments). The basket was positioned into a beaker containing 900 ml of distilled water and operated at 37 ± 0.5$^o$ C. The time of disintegration of tablets were recorded. The average time and standard deviation were calculated. Three trails were performed.

**Wetting time**[7]

A piece of tissue paper folded twice was placed in a small Petri dish (internal diameter = 6.5 cm) containing 6 ml of simulated saliva pH 6.8. A tablet having amaranth powder on the upper surface was placed on the filter paper. Time required to develop red color on the upper surface of tablet was recorded as wetting time. Test was repeated thrice.

***In-vitro* drug release studies**[8]

*In-vitro* dissolution studies for all the fabricated tablets was carried out using USP XXII paddle method (Model TDL-08, Electrolab, Mumbai) at 50 rpm in 900 ml of phosphate buffer pH 6.8 as dissolution media, maintained at 37±0.5°C. 5 ml aliquot was withdrawn at the specified time intervals, an equal volume of fresh medium, which was pre-warmed at 37°C was replaced into the dissolution media after each sampling to maintain the constant volume throughout the test. Withdrawn sample was filtered through a 0.45 micron membrane filter, and assayed spectrophotometrically at 275 nm using a Shimadzu-1700 UV-Visible double beam spectrophotometer. The percentage drug dissolved at different time intervals were calculated.

## RESULTS AND DISSCUSION:

IR spectra of Aceclofenac and Aceclofenac mouth dissolving tablets formulations F-3 and F-6 are shown in **Figure 1**.

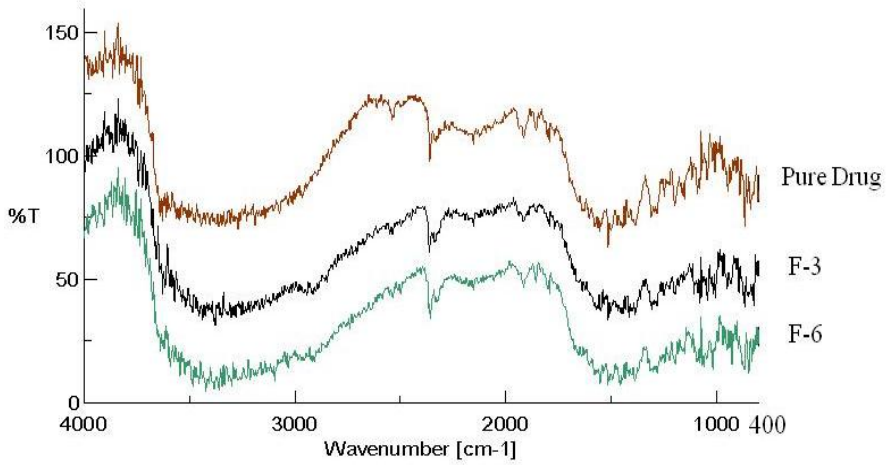


**Figure. 1: FTIR studies of pure drug and formulations (F-3 & F-6).**

In the formulations absorption peak of the drug and superdisintegrants (Crosprovidon and Kyron T-314) were observed and was found that there were no chemical reactions. Hence drug is present in Free State, not in the form of reaction product. Fast dissolving tablets were prepared by using superdisintegrants like Crosprovidon and Kyron T-314[9,10] in three different concentrations 5, 7.5 and 10% w/w of tablets. Directly compressible vehicle like mannitol was used as diluent. Besides the improvement of flow and compaction properties the directly compressible vehicles may aid optimum release of drug from the tablet. Magnesium stearate and aerosil were used as lubricants and antadherent to facilitate easy compression and ejection of tablets. Aspartame as sweetening agent was used. Camphor was used as sublimating agent which facilitates faster disintegration of tablets. The compositions of different fast dissolving tablets are shown in the Table 1. Further the tablets were subjected for physico-chemical evaluation. The results of physicochemical evaluation of tablets are given in **Table 2.**

**Table 2: Evaluation parameters of mouth dissolving tablets.**

| Formulation code | Thickness** (mm) | Hardness test* ($kg/cm^2$) | Weight variation*** (%) | Friability** | Drug content* (%) |
|---|---|---|---|---|---|
| **F0** | 4.32 ± 0.01 | 4.1 ± 0.27 | 201.25 ± 1.53 | 0.53 ± 0.02 | 99.18 ± 0.81 |
| **F1** | 4.27 ± 0.03 | 4.0 ± 0.30 | 199.62 ± 1.42 | 0.52 ± 0.03 | 98.73 ± 0.51 |
| **F2** | 4.29.± 0.01 | 3.9 ± 0.46 | 200.51 ± 1.36 | 0.50 ± 0.02 | 97.56 ± 0.68 |
| **F3** | 4.30 ± 0.02 | 3.9 ± 0.73 | 199.48 ± 1.38 | 0.47 ± 0.01 | 99.45± 0.44 |
| **F4** | 4.20 ± 0.02 | 4.0 ± 0.62 | 198.72 ± 1.37 | 0.44 ± 0.01 | 99.25 ± 0.55 |
| **F5** | 4.31 ± 0.03 | 4.0 ± 0.31 | 198.68 ± 1.51 | 0.41 ± 0.02 | 99.34 ± 0.76 |
| **F6** | 4.23 ± 0.01 | 3.8 ± 0.30 | 199.33 ± 1.48 | 0.35 ± 0.05 | 99.58 ± 0.51 |

*All values are expressed as mean ± SD, n=5*/10**/20***

As the material was free flowing, tablets were obtained of uniform weight due to uniform die filling. Hardness of tablets was between 3.8-4.1 $kg/cm^2$ for all the formulations. The thickness

was found in range of 4.20-4.32 mm. Friability was found in between 0.35-0.53. The value below 1% was an indication of good mechanical resistance of the tablet. The drug content was found to be 97.56-99.58 % which was with in the acceptable limits. Disintegration time is very important for MDTs which is desired to be less than 43 sec. Wetting time is used as an indication from the ease of tablet disintegration in buccal cavity. There is a good relationship between wetting time and disintegration time. The wetting time decreases with increase in the concentration of superdisintegrants. It was observed that as the concentration of superdisintegrants increases water absorption ratio increases and disintegration time decreases. Sublimating agent enhances the wetting of tablet due to formation of pores. The porous structure is responsible for faster water uptake hence it facilitates wicking and swelling of superdisintegrants in bringing about faster disintegration. The results are shown in **Figure 2 and Table 3.**

**Table 3: Comparison of wetting time and *in-vitro* disintegration time of various formulations.**

| Formulation code | Wetting time* (sec) | Disintegration time* (sec) |
|---|---|---|
| F0 | 37.28 ± 1.3 | 43.12 ± 1.3 |
| F1 | 30.63 ± 1.2 | 38.18 ± 1.4 |
| F2 | 24.33 ± 1.4 | 31.05 ± 1.1 |
| F3 | 17.12 ± 1.3 | 25.15 ± 1.0 |
| F4 | 28.35 ± 1.2 | 35.24 ± 1.2 |
| F5 | 20.21 ± 1.5 | 27.31 ± 1.3 |
| F6 | 13.11 ± 1.2 | 18.10 ± 1.1 |

*All values are expressed as mean ± SD, n=5*

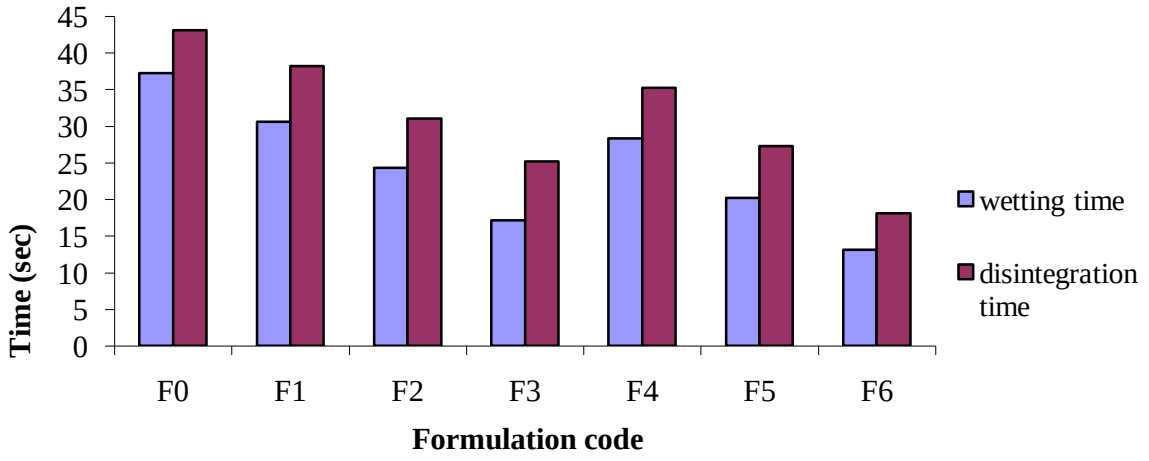


**Figure 2: Comparison of wetting time and *in-vitro* disintegration time of various formulations.**

The *in-vitro* dissolution of Aceclofenac mouth dissolving tablets were carried out by using USP XXIII paddle type dissolution test apparatus at 37 ± 0.5 $^0$C and at 50 rpm using 900 ml Phosphate Buffer (pH 6.8) as dissolution medium. Sublimation technique was adopted to enhance the dissolution of MDTs using camphor as sublimating agent with superdisintegrants like Crosprovidon and Kyron T-314 (F1-F6). The release profiles indicated the faster and maximum drug release due to easy breakdown of particles due to porous structure formation after sublimation of menthol. At 10% superdisintegrants level the drug release at the end of 180 sec were found to be 89.13 and 99.14% with Crosprovidon and Kyron T-314 respectively and the results are shown in **Figure 3** and **Table 4.** The release was also proportionate with superdisintegrant concentration. The results of dissolution profile of MDT were in accordance with that of disintegration data. Hence overall release data of MDT was proportionate with that of disintegration data irrespective of superdisintegrants.

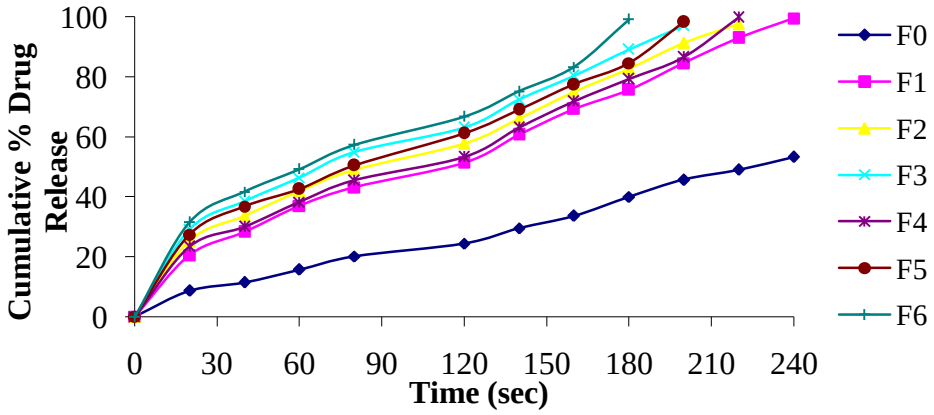


**Figure 3: *In-vitro* drug release studies of sublimed mouth dissolving tablets of Aceclofenac.**

**Table 4: *In-vitro* drug release studies of sublimed mouth dissolving tablets of Aceclofenac.**

| | Cumulative % Drug Release | | | | | | |
|---|---|---|---|---|---|---|---|
| **ime (sec)** | **F0** | **F1** | **F2** | **F3** | **F4** | **F5** | **F6** |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 20 | 8.64 | 20.48 | 25.31 | 29.01 | 23.41 | 27.32 | 31.45 |
| 40 | 11.45 | 28.31 | 33.64 | 38.41 | 30.01 | 36.73 | 41.67 |
| 60 | 15.66 | 36.96 | 41.83 | 46.38 | 38.23 | 42.61 | 49.18 |
| 80 | 20.11 | 43.17 | 49.05 | 54.92 | 45.46 | 50.45 | 57.28 |
| 120 | 24.34 | 51.36 | 57.72 | 63.12 | 53.30 | 61.16 | 66.67 |
| 140 | 29.46 | 60.71 | 66.12 | 72.38 | 63.13 | 69.04 | 75.13 |
| 160 | 33.63 | 69.33 | 74.96 | 80.34 | 71.89 | 77.46 | 83.31 |
| 180 | 39.94 | 75.66 | 82.78 | 89.13 | 79.31 | 84.54 | 99.14 |
| 200 | 45.67 | 84.58 | 91.33 | 97.08 | 86.56 | 98.36 | --- |
| 220 | 49.03 | 93.03 | 97.58 | --- | 99.78 | --- | --- |
| 240 | 53.26 | 99.54 | --- | --- | --- | --- | --- |

## CONCLUSION:

In the present research work, the effects of various superdisintegrants on MDTs of Aceclofenac were studied. It was concluded that Aceclofenac tablets passes for hardness, friability, wetting and disintegration time and *in-vitro* dissolution profile. The prepared tablets using Kyron T-314 (F-6) disintegrate within few seconds without need of water; thereby enhancing the absorption leading to its increased bioavailability.

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