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# *Journal of Chemical and Pharmaceutical Research*

*J. Chem. Pharm. Res., 2011, 3(4):882-892*

**ISSN No: 0975-7384**
**CODEN(USA): JCPRC5**

## Design and evaluation of orodispersible taste masked valdecoxib tablets

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**ABSTRACT**

*Orodispersible tablets of Valdecoxib, to disintegrate rapidly in the oral cavity upon contact with saliva by formation of easy to swallow suspension without the aid of water were prepared. Mass extrusion technique and sublimation methods were employed in designing of orodispersible formulations. In the present study, bitter taste of Valdecoxib was masked by using previously optimized ratio of Valdecoxib: Eudragit E -100. Orodispersible tablets were developed using the prepared taste masked granules and a mixture of excipients consisting of MCC and L-HPC by mass extrusion technique. Sublimation method also employed to formulate orodispersible tablets using camphor as subliming material and water-soluble materials like mannitol. Pre-compression parameters like angle of repose, % compressibility index results showed better flow properties. Hardness, friability, wetting time, water absorption ratio, in vitro disintegration were found to be well within the specification. The disintegration was achieved within 30 seconds from all the formulations prepared by both methods when observed in the saliva of healthy volunteers. The in vitro dissolution was almost 90% within 15 min for all formulations. Formulations of sublimation method were subjected for SEM study to evidence formation of porous cavities within the tablets, which were responsible for fast disintegration in the oral cavity. Selected formulations were subjected for stability studies for 30 days at different temperatures. Tablet properties were evaluated at different intervals. It is confirmed that Orodispersible tablets can be developed by mass extrusion technique and sublimation method.*

**Keywords:** Orodispersible tablets; Mass extrusion method; Sublimation method; Valdecoxib; Eudragit E-100; Camphor.

## INTRODUCTION

In recent decades, a variety of pharmaceutical research has been conducted to develop new dosage forms. Considering quality of life, most of these efforts have been focused on ease of

medication. Among the dosage forms developed to facilitate ease of medication, the orodispersible tablet is one of the most widely employed commercial products. The orodispersible has remarkable disintegration properties; it can rapidly disintegrate without water in the mouth within a few seconds. When an orodispersible is placed in the oral cavity, saliva quickly penetrates into the pores causing rapid disintegration. Orodispersible are useful in patients, such as paediatric, geriatric, bedridden, or developmentally disabled, who may face difficulty in swallowing conventional tablets or capsules and liquid orals or syrup, leading to ineffective therapy, with persistent nausea, sudden episodes of allergic attacks, or coughing for those who have an active life style. Orodispersible are also applicable when local action in the mouth is desirable such as local anaesthetic for toothaches, oral ulcers, cold sores, or teething, and to deliver sustained release multiparticulate system to those who cannot swallow intact sustained action tablets/capsules.

Valdecoxib, a selective COX-2 inhibitor (NSAID) and it is chemically designated as 4-(5-methyl-3-phenyl-4-isoxazolyl) benenesulfonamide and is diaryl substitutedisoxazole.

Valdecoxib is a novel COX-2 effective and selective inhibitor used in the treatment of oestroarthritis, rheumatoid arthritis, primary dysmenorrhoea and has also found to be effective analgesic in post-operative pain. Valdecoxib is preferred over conventional NSAIDs as they may lead to serious gastrointestinal complications such as ulcer, severe bleeding and perforation.

Pregastric absorption can result in improved bioavailability and as result of reduced dosage, improved clinical performance though a reduction of unwanted effects.

With the view to all the above data an attempt had been made to develop a rapidly disintegrating “Orodispersible tablets” which disintegrate in the oral cavity without the need of water within a matter of seconds. This will lead to the formation of suspension / solution form which can be easily swallowed, thereby improving dissolution rate and bioavailability of drug and onset of pharmacological actions.

Hence the present study was emphasized to formulate “Orodispersible Tablets” containing Valdecoxib, a COX-2 effective and selective inhibitor (NSAID) as made drug to evidence the absorption and bioavailability.

## EXPERIMENTAL SECTION

Valdecoxib was a gift sample obtained from Cipla Limited, Mumbai, Eudragit E-100 was obtained from Degussa Bombay, Avicel pH 102 was purchased from Medikon Galenicals, Hyderabad and other chemicals used were of analytical grade.

### Preparation of granules

The granules were prepared by Mass Extrusion Technique and sublimation method using different proportions of super disintegrants and compressed by direct compression technique.. The composition of different formulation were given in Table.No:1.

### Mass Extrusion Technique

The drug is mixed with powdered Eudragit E100 in a suitable ratio. Then 10% ethanol was added to the mixture of each drug with Eudragit E-100 in a glass beaker. The consistency of the above solution is reduced to get gel type of preparation, and it is extruded through a syringe on clean glass slab. After extrusion of the gel dried overnight till ethanol is evaporated and

solidified material (gel) crushed into granules using a mortar and pestle. The granules passed through a sieve and collected. The taste-masked tablets were prepared using the taste-masked granules, excipient mixture for orodispersible tablet, Avicel pH 102 and L-HPC, at mixing ratio by weigh of avicel pH 102: L-HPC = 4 : 1, magnesium state (1%). Lactose, aspartame and talc are blended and subjected for compression using Hydraulic press (500-1500 kgf).

**Sublimation Method:**

The basic principle involved in preparing orodispersible tablets by sublimation technique is addition of a volatile salt to the tabletting components. Four formulations were developed by varying concentration of subliming agent i.e. Camphor (0-30% w/w).

Accurately weighed ingredients are sifted through sieve no.44 and thoroughly mixed in a cone blender for 10 min. Magnesium stearate, talc were sifted through sieve no.44 and added to the blend and thoroughly mixed. The tables were compressed using Hydraulic press. The compressed tablets were than subjected to sublimation of 80° for 30 min.

**Pre-compression Parameters:**

***1. Micromeritic Properties:***

***a. Angle of Repose (θ)***

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and horizontal plane. The frictional force in a loose powder or granules can be measured by angle of repose.

$$\tan \theta = h / r$$

$$\theta = \tan^{-1} (h/r)$$

Where, θ is the angle of repose

h is height of pile

r is radius of the base of pile

**2. Bulk Density:**

Bulk density is defined as the mass of a powder divided by the bulk volume. The bulk density of a powder depends primarily on particle size distribution, particle shape, and the tendency of the particles to adhere to one another.

$$LBD = \frac{\text{Weight of the powder}}{\text{Volume of the packing}} \quad \text{--------- (a)}$$

$$TBD = \frac{\text{Weight of the powder}}{\text{Tapped volume of packing}} \quad \text{---------- (b)}$$

***Carr's Compressibility Index:***

The compressibility index of the granules was determined by Carr's compressibility index.

$$\text{Carr's Index (\%)} = \frac{TBD - LBD}{TBD} \times 100 \quad \text{----- (c)}$$

***Post-Compression Parameters*:**

***Shape and colour of tablets:***

Uncoated tablets were examined under a lens for the shape of the tablet and colour was observed by keeping the tablets in light.

**Uniformity of thickness:**
Three tablets were picked from each formulation randomly and thickness was measured individually. It is expressed in mm and standard deviation was also calculated. The tablet thickness was measured using dial-caliper (Mitutoyo, Japan).

**Hardness test:**
Hardness indicates the ability of a tablet to withstand mechanical strength while handling. The hardness of the tablets were determined using Monsanto Hardness tester. It is expressed in Kg/cm2. Three tablets were randomly picked from each formulation and the mean and standard deviation values were calculated.

**Friability test:**
It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition. The friability of tablets was determined by using Roche Friabilator. It is expressed in percentage (%). Ten tables were initially weighed ($W_{initial}$) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again ($W_{final}$). The percentage friability was then calculated by,

$$F = \frac{W_{initial} - W_{final} \times 100}{W_{initial}} \quad \text{---------- (d)}$$

% Friability of tablets less than 1% are considered acceptable.

**Tensile strength:**
The tablet crushing load which is the force required to break a tablet by compression in the radial direction, was measured using a tablet hardness tester (Monsanto Hardness Tester). The plunger was driven down at a speed of 20 mm/min. Tensile strength for crushing (T) was calculated using the following equation.

$$T = 2F / (\pi dt) \quad \text{-------- (e)}$$

Where, F is crushing load
d is diameter of tablet
t is thickness of tablet

**Weight variation test:**
The tablets were selected randomly from each formulation and weighed individually to check for weight variation. The U.S Pharmacopoeia allows a little variation in the weight of a tablet. The following percentage deviation in weight variation is allowed.

**Drug Content Uniformity:**
Ten tablets were randomly selected, accurately weighed and average weight per tablet calculated. The tablets were ground individually to fine powder. Accurately weighed tablet powder, equivalent to 10 mg of valdecoxib was transferred to 100 ml volumetric flask. Add 0.1N HCl up to the mark. After few minutes the solution was filtered; rejecting first few ml of the filtrate. 2 ml of filtrate was taken in a 25 ml volumetric flask and diluted up to the mark with 0.1NHCl and analyzed spectrophotometrically at 245 nm. The concentration of Valdecoxib (in μg/ml) was calculated by using standard calibration curve of Valdecoxib.
Drug content in mg was calculated by using formula

$$= \frac{\text{Concentration in } \mu g/ml \times 100 \times 25}{2 \times 1000} \quad \text{---------- (f)}$$

Drug content claim was 10 mg per tablet. This procedure was followed for 5 tablets from each formulation. The mean and standard deviation value were also calculated.

**Wetting time**

The method was applied to measure tablet wetting time. A piece of tissue paper folded twice was placed in a small petridish (i.d. = 6.5 cm) containing 6 ml of water, a tablet was put on the paper, and the time for complete wetting was measured. Three trials for each batch was performed and standard deviation was also determined. The method was reported by Yunxia Bi.

**Water absorption ratio:**

A piece of tissue paper folded twice was placed in a small petridish containing 6 ml of water. A tablet was put on the paper and time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R was determined using following equation.

$R = 100 (W_a - W_b)/ W_b$ ------- (g)

Where, $W_b$ – weight of tablet before absorption
$W_a$ – weight of tablet after absorption

Three tablets from each formulation were performed and standard deviation was also determined.

**In vitro dispersion time:**

In vitro dispersion time was measured by dropping a tablet in a measuring cylinder containing 6 ml of pH 6.8 (simulated saliva pH). Three tablets from each formulation were randomly selected and in vitro dispersion time is expressed in seconds.

**In vitro disintegration time:**

The process of breakdown of a tablet into smaller particles is called as disintegration. The in-vitro disintegration time of a tablet was determined using disintegration apparatus as per I.P. specifications.

**In vitro dissolution studies:**

In vitro release studies were carried out using tablet dissolution test apparatus USP XXIII. Two objectives in the development of in vitro dissolution tests are to show,

The various parameters related to dissolution which are evaluated in the present work are as follows:

1. Drug release
2. Cumulative percentage drug release
3. Cumulative percentage drug retained
4. Model fitting of the release profiles using the different models viz. Zero order, First order, Higuchi matrix, Peppas model and Hixson-Crowell equation.

## RESULTS AND DISCUSSION

The present study was undertaken to design and evaluate Orodispersible tablets which will disintegrate in the oral cavity using COX-2 selective inhibitor Valdecoxib as a model active medicament, aiming to enhance the solubility, absorption, bioavailability and efficacy.

**Evaluation of tablets:**

**Pre-compression Parameters:**

Blend ready for compression containing drug and various excipients was subjected for pre-compression parameters (Micromeritic properties) to study the flow properties of granules, to achieve uniformity of tablet weight. The values of angle of repose were found to be in the range of 25°65' to 31°08'. The loose bulk density and tapped bulk density for all the formulation blend varied from 0.553 gm/cm$^3$ to 0.575 gm/cm$^3$ and 0.632 gm/cm$^3$ to 0.667 gm/cm$^3$ respectively. The results of Carr's consolidation index or compressibility index (%) for all the formulation blend ranged from 12.42 to 16.10. The results for all the formulations were recorded in Table No.2.

**II. Post-compression Parameters:**

The tablets prepared by both Mass extrusion technique and sublimation methods were subjected for evaluation according to various official specifications and other parameters. Shape, thickness, hardness, friability, weight variation, *in vitro* disintegration time, *in vivo* disintegration, wetting time, water absorption ratio, drug content, mouth feel, *in vitro* dissolution studies, model fitting of release profile were performed.

Tablets showed flat, circular shape in white colour. The mean thickness was (n=3) almost uniform in all the formulations and values ranged from 2.93±0.12 mm to 3.10±0.09 mm. The hardness values ranged from 2.67±0.77 kg/cm$^2$ to 4.00±0.50 kg/cm$^2$ for formulations were almost uniform and was found to be well within the approved range (<1%) in all designed formulations. The friability of the formulations EM-1 and SM-4 showed slightly higher than the other. Tensile strength for formulations of mass extrusion technique and sublimation technique were ranged from 7.26±0.19 kg/cm$^2$ to 8.18±0.66 kg/cm$^2$ and 5.48±1.63 kg/cm$^2$ to 8.66±0.87 kg/cm$^2$ respectively. The average percentage weight variation was found to be 298.69±2.05 mg to 300.21±1.60 mg. The results of all the physical parameters were tabulated in Table No.3.

Wetting time is closely related to the inner structure of the tablet. The results of wetting time are shown in Table No.4, which showed that wetting process was very rapid in almost all formulations. This may be due to ability of swelling and also capacity of water absorption and cause swelling. Water absorption ratio, which is important criteria for understanding the capacity of disintegrants to swell in presence of little amount of water, was calculated. It was found to be in the range of 13.68±0.54 to 39.28±1.06.

In the formulations prepared mass extrusion technique as L-HPC quantity decreases, the water absorption also decreases due to less swelling property. In the formulations prepared by sublimation method as the quantity of mannitol decreases the water absorption also decreases wetting characteristic of the tablet is shown in Table No.4.

The drugs content of the tablets were found to be between 9.773±0.02 mg to 9.154±0.004 mg of valdecoxib. The *in vitro* dispersion time is measured by the time taken to undergo uniform dispersion. Rapid dispersion within seconds was observed in all the formulations. The results showed that L-HPC and Avicel PH 102 in formulations EM-1, EM-2, EM-3 and EM-4 were best

disintegrants in the prepared tablets. In sublimation method formation of pores due to sublimation of camphor will decrease the *in vitro* dispersion time. All the formulations showed disintegration time less than 30 sec except for formulation SM-1 where no disintegrants was used or there were no sufficient pores within the tablets to enter the water or saliva. Formulations EM-4 and SM-3 showed rapid disintegration compared to other formulations. The formulated preparations were subjected for mouth feel. The volunteers felt good taste in all the formulations.

**Table 1 Composition of Orodispersible Tablets of Valdecoxib**

| Ingredients (mgs) | FORMULATION CODE | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | EM-1 | EM-2 | EM-3 | EM-4 | SM-1 | SM-2 | SM-3 | SM-4 |
| Valdecoxib | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Eudragit E-100 | 30 | 30 | 30 | 30 | -- | -- | -- | -- |
| Avicel PH 102 | 132 | 118 | 106 | 94 | -- | -- | -- | -- |
| Low hydroxy propyl cellulose | 30 | 29 | 26 | 23 | -- | -- | -- | -- |
| Mannitol | -- | -- | -- | -- | 274 | 244 | 214 | 184 |
| Camphor | -- | -- | -- | -- | 00 | 30 | 60 | 90 |
| Asparatame | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Lactose | 82 | 97 | 112 | 127 | -- | -- | -- | -- |
| Magnesium stearate | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| Talc | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |

**Table 2 Angle of Repose, Loose Bulk Density, Tapped Bulk Density, Carr's Compressibility Index**

| Formulations | Angle of Repose (θ) | Loose Bulk Density ($gm/cm^3$) | Tapped Bulk Density ($gm/cm^3$) | % Compressibility |
|---|---|---|---|---|
| EM-1 | $28^o$ 82’ | 0.569 | 0.662 | 14.05 |
| EM-2 | $28^o$ 18’ | 0.571 | 0.997 | 14.39 |
| EM-3 | $26^o$ 19’ | 0.575 | 0.674 | 14.69 |
| EM-4 | $25^o$ 65’ | 0.569 | 0..662 | 14.05 |
| SM-1 | $28^o$ 41’ | 0.568 | 0.677 | 16.10 |
| SM-2 | $28^o$ 24’ | 0.559 | 0.650 | 14.00 |
| SM-3 | $26^o$ 60’ | 0.557 | 0.636 | 12.42 |
| SM-4 | $31^o$ 08’ | 0.553 | 0.632 | 12.50 |

**Table 3 Evaluation of Tablet Parameters**

| Formulation Code | Uniformity of Thickness (n=3) (mm) | Hardness (n=3) ($kg/cm^3$) | Friability % | Tensile strength $Kg/cm^2$ | Weight Variation (n=10) (mg) |
|---|---|---|---|---|---|
| EM-1 | 2.98 ± 0.03 | 3.83 ± 0.29 | 0.8319 | 8.18± 0.66 | 299.82 ± 2.05 |
| EM-2 | 3.07 ± 3.00 | 3.50 ± 0.50 | 0.7363 | 7.26 ± 0.19 | 299.2 ± 2.17 |
| EM-3 | 3.10 ± 0.09 | 3.50 ± 0.50 | 0.4654 | 7.37 ± 0.94 | 299.86 ± 1.78 |
| EM-4 | 3.02 ± 0.06 | 3.83 ± 0.29 | 0.6627 | 7.86 ± 0.38 | 300.06 ± 2.44 |
| SM-1 | 2.95 ± 0.08 | 4.00 ± 0.50 | 0.4305 | 8.66 ± 0.87 | 300.56 ± 2.11 |
| SM-2 | 2.93 ± 0.12 | 3.50 ± 0.50 | 0.7314 | 7.34 ± 0.96 | 298.69 ± 2.05 |
| SM-3 | 3.03 ± 0.13 | 3.67 ± 0.29 | 0.5670 | 7.71 ± 0.92 | 300.21 ± 1.60 |
| SM-4 | 3.10 ± 0.09 | 2.67 ± 0.77 | 0.8624 | 5.48± 1.63 | 299.49 ± 1.82 |

In the oral disintegration test all the formulations showed rapid disintegration, except formulation SM-1, which disintegrates after more than 69 seconds in the oral cavity, because it does not included any disintegrants or there is no formation of pores. Formulations EM-1 to EM-4 which are prepared by mass extrusion technique disintegrates rapidly mainly due to the use of superdisintegrants like Microcrystalline cellulose and low hydroxyl propyl cellulose. The ratio of MCC : L-HPC = 4:1 was used for the development of Orodispersible tablets which was

previously optimized. Formulations SM-1 to SM-4, which were prepared by sublimation method, disintegrates rapidly except SM-1 because lack of formation of pores within the tablet due to sublimation of camphor. The formulation containing mannitol without camphor (SM-1) did not dissolve rapidly in the saliva or oral cavity. The data obtained from above parameters are shown in the Table No.5.

**Table 4 Wetting Time, Water Absorption Ratio**

| Formulation Code | Wetting Time (n=3) | Water Absorption Ratio (n=3) |
|---|---|---|
| | ***Mean ± SD*** | ***Mean ± SD*** |
| EM-1 | 22.00 ± 2.65 | 39.28 ± 0.99 |
| EM-2 | 20.67 ± 1.53 | 38.77 ± 1.06 |
| EM-3 | 20.33 ± 2.52 | 33.93 ± 1.30 |
| EM-4 | 15.67 ± 2.53 | 29.11 ± 1.47 |
| SM-1 | 31.00 ± 4.36 | 24.11 ± 0.80 |
| SM-2 | 21.00 ± 2.65 | 23.67 ± 0.60 |
| SM-3 | 20.67 ± 1.53 | 13.86 ± 0.54 |
| SM-4 | 16.67 ± 1.53 | 21.44 ± 0.73 |

**Table 5 *In vitro* Disintegration Time, *In vitro* Dispersion Time, *In vivo* Disintegration Time, Drug Content Uniformity, and Mouth Feel**

| Formulation Code | *In vitro* Disintegration Time | *In vitro* Dispersion Time | *In vivo* Disintegration Time | Drug Content Uniformity (n=5) (mg) | Mouth Feel |
|---|---|---|---|---|---|
| EM-1 | 21.33 ± 1.53 | 20.67 ± 2.08 | 28.67 ± 5.51 | 9.6126 ± 0.01 | + |
| EM-2 | 17.67 ± 1.55 | 19.67 ± 2.08 | 27.67 ± 2.52 | 9.773 ± 0.02 | + |
| EM-3 | 12.67 ± 1.54 | 14.33 ± 1.53 | 22.67 ± 3.21 | 9.8402 ± 0.06 | + |
| EM-4 | 10.67 ± 1.54 | 11.67 ± 0.58 | 16.33 ± 1.53 | 9.9072 ± 0.03 | + |
| SM-1 | 59.33 ± 3.51 | 72.67 ± 5.51 | 69.33 ± 1.53 | 9.8528 ± 0.04 | + |
| SM-2 | 29.67 ± 2.89 | 23.67 ± 2.08 | 27.66 ± 1.53 | 9.8752 ± 0.01 | + |
| SM-3 | 12.33 ± 1.53 | 14.33 ± 0.58 | 17.33 ± 2.08 | 9.9154 ± 0.004 | + |
| SM-4 | 12.67 ± 0.58 | 14.33 ± 0.58 | 18.66 ± 2.08 | 9.7392 ± 0.05 | + |

*'+' good palatable mouth feel*
*'-' poor palatable mouth feel*

### *In vitro* dissolution studies*:*

All the eight formulations were subjected for *in-vitro* dissolution studies using tablet dissolution tester USP XXIII. The dissolution medium 0.1N HCl was used to study the drug release at 245nm using UV spectrophotometer. Cumulative percentage drug release and cumulative percentage drug retained were calculated on the basis of average amount of valdecoxib present in the respective formulations.

The plots of cumulative percentage of valdecoxib released as a function of time (t) for formulations prepared by Mass extrusion technique (EM-1 to EM-4) are shown in Figure No. 1 and formulations developed by sublimation method (SM-1 to SM-4) are shown in Figure No. 2.

All the formulations showed rapid drug release (87.49% - 97.04%) due to fast disintegration of tablets. Formulations EM-1, EM-2, EM-3, SM-1 and SM-2 showed drug release 93.85%, 93.01%, 93.88%, 88.25% and 87.49% respectively. But the rapid drug dissolution was noticed in EM-4, SM-3, and SM-4 formulations compared to other formulations, which releases 97.04%, 95.86% and 94.25% respectively at the end of the 15 minutes. The fast dissolution might be due to quick disintegration of the tablets to form particles and rapid absorption will take place.

**Fig No 1 Invitro drug release studies for the tablets prepared by mass extrusion technique**

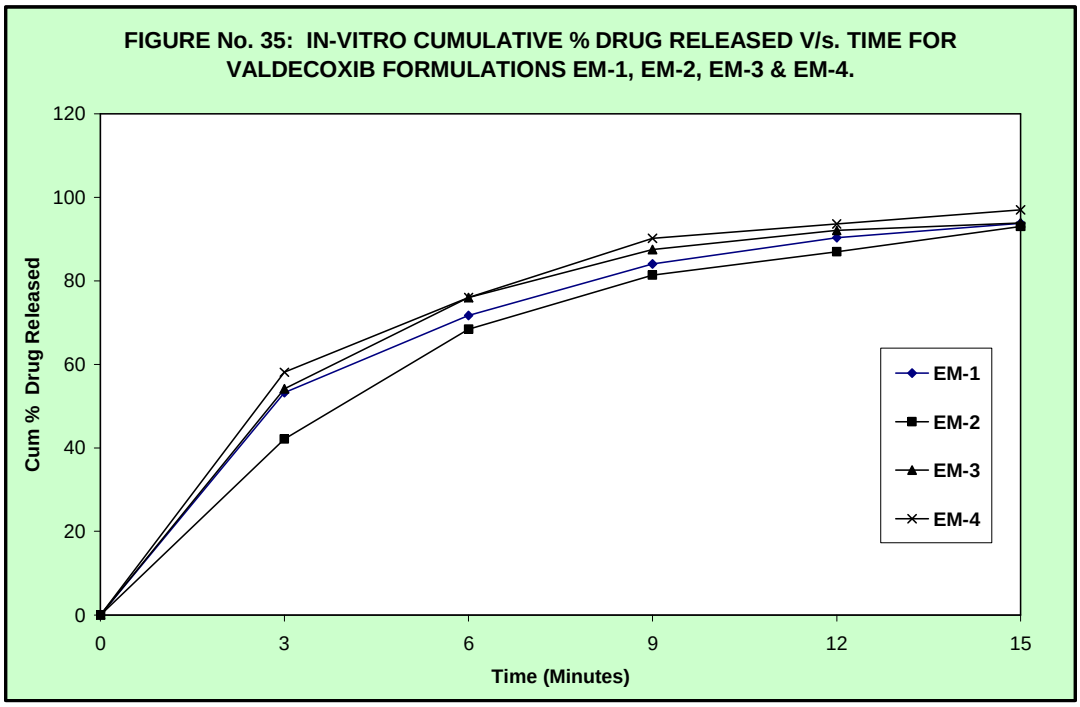
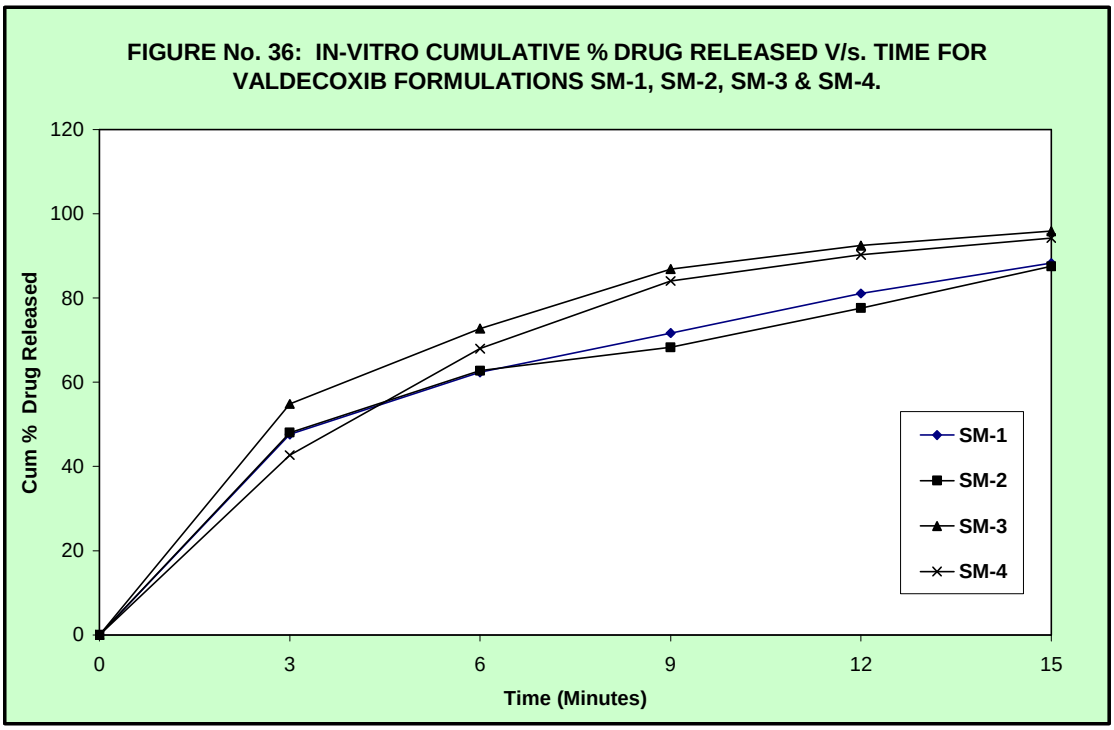



**Fig No 2 Invitro drug release studies for the tablets prepared by mass sublimation technique**




In the formulations prepared by mass extrusion method Eudragit E-100 shows high solubility, which is mainly used as taste masking agent. It is also acts as superdisintegrants. EM-4 formulation showed maximum drug release about 97.04% because of rapid disintegration.

In the formulations prepared by sublimation method SM-3 and SM-4 showed better drug release than the SM-1 and SM-2 because of fast disintegration time. SM-2 and SM-4 formulations

containing 20% and 30% camphor respectively as subliming material showed the maximum drug release. As the concentration of camphor increases, there will be more number of pores formation in the tablet, ultimately water/ saliva can enter and absorbs more quantity, which will lead to rapid disintegration. Another ingredient which is included in the formulations of this technique is mannitol, which is also responsible for disintegration of tablet and is highly soluble in water. The variation of drug release from the formulations EM-1, EM-2, EM-3, SM-1 and SM-2 may be due to slow breakdown of particles from the tablet.

**Table 6 Model Fitting of the Release Profile using Five Different Model (r-value)**

| Formulation Code | Mathematical Models (Kinetics) | | | | | | |
|---|---|---|---|---|---|---|---|
| | ***Zero Order*** | ***First Order*** | ***Higuchi Matrix*** | ***Peppas*** | ***Hixson Crowell*** | ***'n' values*** | ***Best fit Model*** |
| EM-1 | 0.9562 | -0.9992 | 0.9830 | 0.9909 | -0.9575 | 0.1153 | ***First Order*** |
| EM-2 | 0.9420 | -0.9966 | 0.9735 | 0.9776 | -0.9441 | 0.1552 | First Order |
| EM-3 | 0.9207 | -0.9864 | 0.9590 | 0.9742 | -0.9223 | 0.1104 | First Order |
| EM-4 | 0.9406 | -0.9958 | 0.9720 | 0.9846 | -0.9419 | 0.1046 | First Order |
| SM-1 | 0.9911 | -0.948 | 0.9995 | 0.9997 | -0.9919 | 0.1243 | Peppas |
| SM-2 | 0.9912 | -0.9778 | 0.9930 | 0.9931 | -0.9916 | 0.1165 | Peppas |
| SM-3 | 0.9538 | -0.9988 | 0.9810 | 0.9899 | -0.9552 | 0.1146 | First Order |
| SM-4 | 0.94713 | -0.9982 | 0.9733 | 0.97978 | -0.9432 | 0.1591 | First Order |

The values of the drug release were attempted to fit into various mathematical models to observe the mechanism. The correlation coefficient values obtained for all the five models are tabulated in Table No.6. The formulations SM-1 and SM-2 showed Peppas model and other formulations EM-1, EM-2, EM-3, EM-4, SM-3 and SM-4 showed first order kinetic model.

From the obtained data, it can be proved that formulations EM-1, EM-2, EM-3, EM-4, SM-3 and SM-4 drug release follows first order, which may be due to rapid diffusion or the porous nature of the formulations.

The values of diffusion coefficient (n) for formulations SM-1 and SM-2 are shown to be 0.1243 and 0.1165 respectively which suggest that the release of drug occurs by diffusion following Fickian transport mechanism as all diffusion co-efficient values were less than 0.5.

## CONCLUSION

The results of the evaluation parameters demonstrate that it is possible to design and develop Orodispersible tablets of Valdecoxib by using Mass extrusion technique and sublimation method. As the drug Valdecoxib is bitter in taste, the primary approach is to mask the bitter taste, by using polymers like Eudragit E-100. In the sublimation method Mannitol was used along with sweeteners like aspartame to impart the mouth feel and as diluent due to its negative heat of solubilization. Camphor was used as subliming material in developing orodispersible tablets. The tablets disintegrated rapidly in oral cavity and had acceptable hardness and friability. *In vitro* drug release from the tablets shows significantly improved drug dissolution. Hence it could be concluded that the superdisintegrant based oro dispersible tablets of valdecoxib would be quite effective as COX-2 selective NSAID, providing quick onset of action without need for water for swallowing or administration.

**Acknowledgement**
The authors are thankful to the Management, Trinity College of Pharmaceutical Sciences, for providing necessary facilities to carry out this work. We are grateful to my friends and parents for their great support and encouragement.

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