

In Nilgiris, the ethnic tribe Kurumbas use the plant *B. tinctoria* root and root bark for stomach ache and the aqueous root paste for skin diseases. Results of preliminary antifungal and antibacterial screening of methanol and chloroform extracts of *B. tinctoria* (Table 1 and 2) revealed that the extracts were active against all the organisms, except the chloroform root extract against the fungi tested. The root bark extracts showed better activity against the organisms than that of the extracts of the root. The methanol extract showed higher activity than the chloroform extract.

#### ACKNOWLEDGEMENTS

The authors are grateful to Jagadguru Sri Sri Shivarathreeshwara Deshikendra Mahaswamigalavaru of Sri Suttur Mut, Mysore for providing facilities for the successful completion of this work.

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## Development of Dissolution Medium for a Poorly Water Soluble Drug, Celecoxib

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Accepted 20 June 2002

Revised 14 May 2002

Received 5 July 2001

**Celecoxib, a non-steroidal antiinflammatory drug is poorly water soluble. In the present study a new dissolution medium was developed, as there is no official dissolution medium. The composition of the medium was selected on the basis of solubility data of celecoxib at 37°. Solubility data revealed that water consisting of 2% w/v sodium lauryl sulphate could be a suitable dissolution medium. The discriminating power of the selected dissolution medium (2% w/v sodium lauryl sulphate in water) relative to other dissolution mediums was evaluated and the results further justified the usage of 2% w/v sodium lauryl sulphate in water as dissolution medium for celecoxib.**

Celecoxib (CB), N-(4-sulphonamide),3-trifluoromethane,5-(4-tolyl) pyrazole, is a new non-steroidal antiinflammatory drug (NSAID)<sup>1</sup>. It is a selective inhibitor of the cyclooxygenase-2 (COX-2) and exhibits many of the pharmacological actions of prototypical NSAIDs, including

antiinflammatory, analgesic and antipyretic activity<sup>2</sup>. It is not official in any pharmacopoeia.

The testing of pharmaceutical dosage forms for *in vitro* drug release and dissolution characteristics is very important for ensuring batch to batch quality control and to optimize formulations during product development. Drugs that are practically insoluble (less than 0.01%) are of increasing

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therapeutic interest, but it is well recognized that they may present particular problems of bioavailability when administered orally. Since their dissolution rate can be the rate limiting step in the *in vivo* absorption process, there is a definite need for the development of an appropriate dissolution test<sup>3</sup>.

Approaches usually used in the design of dissolution media for poorly water soluble drugs include, a) bringing about drug solubility by increasing the volume of the aqueous sink or removing the dissolved drug, b) solubilization of the drug by co-solvents, upto 40% and by anionic or non-ionic surfactants added to the dissolution medium in post micellar concentrations, c) alteration of pH to enhance the solubility of insoluble drug molecules<sup>4,5</sup>. The last two approaches seem less cumbersome and have been more widely employed in pharmacopoeial dissolution tests<sup>6</sup>.

In the present investigation, aqueous solubility of CB containing co-solvent or surfactants was assessed to prepare dissolution system, which satisfies sink conditions, for testing CB formulations. The discriminating power of selected dissolution medium was evaluated using prepared and commercial formulations.

Celecoxib was a gift sample from M/s Unichem Laboratories Ltd., Mumbai. Two brands of celecoxib capsules, Celib (M/s Unichem Laboratories Ltd., Mumbai) and Celact (M/s Sun Pharmaceutical Industries Ltd., Ahmedabad) were purchased from local market. Sodium lauryl sulphate, Tween 80, ethanol purchased from Qualigens Fine Chemicals, Mumbai. All other materials were of analytical reagent grade.

The apparent solubility of CB in water and presence of co-solvent or surfactant in water was determined at 37°. CB (50 mg) was added to 50 ml of water in a conical flask with Teflon-lined screw caps. The conical flasks were kept on a shaker incubator maintained at 37±0.5° for 24 h. After shaking, the flasks were kept in an incubator at 37±0.5° for equilibration for 12 h. Then solution was filtered through 0.45 µm millipore filter and the filtrate was assayed spectrophotometrically at 254 nm against to respective blank solutions.

Dissolution experiments were performed using USP standard dissolution apparatus II (M/s Campbell Electronics, India) at 37±0.5° at a paddle speed of 50 rpm. The dissolution medium was 900 ml of either water or a mixture of water and sodium lauryl sulphate (SLS) solution, selected on the basis of solubility data obtained in the experiment (0.25% w/v SLS in water, 0.5% w/v SLS in water, 1% w/v SLS in water, 1.5% w/v SLS in water, and 2% w/v SLS in

water). This procedure was used to test the dissolution of bulk powder samples (100 mg, particle size <200 µm) of CB. Samples (5 ml) of dissolution medium were withdrawn at different time intervals and filtered through 0.22 µm millipore filter. Same volume of fresh dissolution medium, maintained at 37±0.5° was added to maintain constant volume. The dissolution medium was analyzed for CB using UV method as described above. Results presented are the average of three experiments.

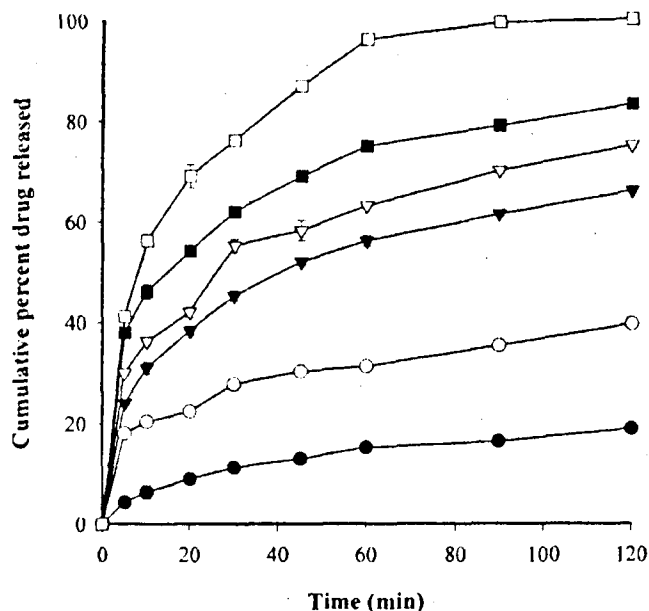
A batch of 100 capsules of CB were prepared for comparative studies by filling 100 mg of CB, which is lubricated with 0.5% w/w magnesium stearate and 0.5% w/w talc. The dissolution experiments for prepared and commercial formulations of CB were performed using above *in vitro* dissolution conditions by selecting 2% w/v SLS in water as dissolution medium.

In this study solubility data was used as a basis for the development of a dissolution medium for the CB. Since CB

TABLE 1: SOLUBILITY STUDIES OF CELECOXIB.

Solvent	Saturation Solubility (µg/ml)
Water	6.18±0.23
0.1 N HCl (pH 1.2)	4.45±0.11
Phosphate buffer (pH 7.4)	3.94±0.20
Phosphate buffer (pH 8.0)	3.41±0.16
5% v/v Methanol in water	6.63±0.56
10% v/v Methanol in water	16.10±0.69
0.25% v/v Tween 80 in water	84.31±1.78
0.5% v/v Tween 80 in water	211.04±1.56
1% v/v Tween 80 in water	334.82±1.23
0.1% w/v SLS in water	11.78±0.45
0.25% w/v SLS in water	76.49±1.02
0.5% w/v SLS in water	209.99±2.03
1% w/v SLS in water	407.14±1.89
1.5% w/v SLS in water	596.35±2.66
2% w/v SLS in water	956.32±1.89

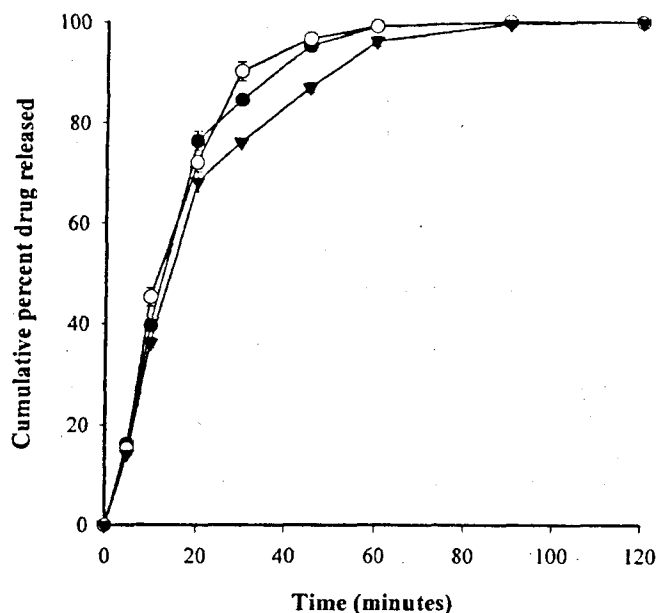
Solubility studies of celecoxib done in various media at 37° are given. SLS is sodium lauryl sulphate, HCl is hydrochloric acid.



**Fig. 1: Comparative dissolution profiles of celecoxib.** Dissolution studies of celecoxib (100 mg) were performed in water (-●-) or 0.25% w/v SLS in water (-○-) or 0.5% w/v SLS in water (-▼-) or 1.0% w/v SLS in water (-▽-) or 1.5% w/v SLS in water (-■-) or 2.0% w/v SLS in water (-□-) as dissolution medium at 37°.

is poorly soluble in water, 0.1 N HCl and phosphate buffers as indicated from solubility data given in Table 1. Co-solvent (methanol) and surfactants (SLS and Tween 80) were added to water. It was found that the maximum solubility was obtained with 2% w/v SLS in water (956.32 µg/ml). From the above results, it was calculated that the solubility of CB in 900 ml of 2% w/v SLS in water and found to be approximately 10 times of the solubility to the original dose of CB (100 mg). As 900 ml of 2% w/v SLS in water was satisfying the sink conditions<sup>7</sup>, it was considered to be a suitable dissolution medium for absolute dissolution studies.

The comparative study of the dissolution rate of pure drug in water and in different ratios of SLS (0.25, 0.5, 1, 1.5, 2% w/v) containing water was carried out to justify the inclusion of SLS in the dissolution medium and the results are shown in fig. 1. The results indicated that the dissolution rate of CB increased with increase in SLS content in dissolution medium and maximum dissolution was found in water containing 2% w/v SLS. Addition of surfactant to the dissolution medium improves the dissolution of pure drug by facilitating the drug release process at the solid/liquid interface and micelle solubilisation in the bulk<sup>8</sup>. The usage of water containing 2% w/v SLS as the dissolution medium was



**Fig. 2: Dissolution profiles of celecoxib from commercial formulations in comparison with prepared formulation.** Dissolution profiles of celecoxib from commercial formulation (100 mg) such as Celib (-●-) or Celact (-○-) and prepared formulation (-▼-) in 2.0% w/v SLS aqueous solution as dissolution medium were performed to assess the effectiveness of dissolution medium.

further justified by this data.

The performance of selected dissolution medium (900 ml of 2% w/v SLS in water) was confirmed by conducting the dissolution experiments of commercial formulations and the results are shown in fig 2. Though the release rate of CB from commercial formulations higher than prepared formulation, it was found that more than 85% of CB was released from all the formulations with in 45 min under test conditions. Commercial formulations may contain solubilizers, which resulted in higher release rate of CB from these formulations. The results of present study clearly indicating that 2% w/v SLS in water, as dissolution medium was suitable for routine *in vitro* dissolution testing of conventional CB formulations.

**ACKNOWLEDGEMENTS**

Authors are grateful to Unichem Laboratories Ltd. Mumbai, for providing gift sample of celecoxib. One of the authors, GVMMB thanks M/s Andhra Sugars Ltd., Tanuku (India) for awarding a research fellowship.

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## Design and Fabrication of a Special Punch for Buccoadhesive Core-in-Cup Tablets

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Accepted 27 June 2002

Revised 20 May 2002

Received 21 August 2001

**A special punch was designed and fabricated to prepare buccoadhesive core-in-cup tablets by making protrusion in the 11 mm upper flat-faced punch. The buccoadhesive cups were prepared by direct compression method using polymers like carbopol 934P and hydroxy propyl methylcellulose on a Cadmach single station tableting machine. The cups were evaluated for uniformity of weight, depth and thickness.**

Absorption of therapeutic agents from the oral mucosa overcomes premature drug degradation within the gastrointestinal tract, as well as active drug loss due to first-pass hepatic metabolism that may be associated with other route of administration. The oral cavity has a number of features that make it a desirable site for drug delivery, including a rich blood supply that drains directly into the jugular vein bypassing the liver and thereby sparing the drug from first-pass metabolism. Successful buccal delivery requires atleast three things, (a) a bioadhesive to retain the drug in the oral cavity and maximize the intimacy of contact with mucosa, (b) a vehicle that releases the drug at an appropriate rate under the conditions prevailing in the mouth and (c) strategies for overcoming the low permeability of the oral mucosa<sup>1</sup>.

Buccoadhesive tablets consist of three layers, the core layer, the peripheral layer, and a backing layer, usually prepared by direct compression method as follows. The core layer is first compressed and is placed in a die cavity of higher diameter, then the peripheral layer material is added and compressed. Next the upper punch is raised; the backing layer material is added and compressed to get a buccoadhesive tablet<sup>2</sup>. The tablets prepared by this method have certain drawbacks like more number of compressions (three times), non-uniformity in peripheral layer thickness and multidirectional release of the drug.

Agarwal and Mishra have prepared buccoadhesive compacts of pentazocine using 7 mm and 11 mm flat faced punches to prepare core layer and peripheral layer, respectively by compressing three times<sup>2</sup>. Dinsheet *et al.* have prepared mucoadhesive buccal tablets of hydralazine hydrochloride using 9.6 mm and 13.6 mm flat faced punches to

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