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SOLUBILITY ENHANCEMENT OF ACECLOFENAC BY SOLVENT DEPOSITION METHOD

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ABSTRACT: Aceclofenac is a nonsteriodal anti-inflammatory, analgesic and antipyretic drug used in the treatment of rheumatoid arthritis, post-traumatic pain, masculo-skeletal and joint disorders. Problem with this drug is its poor solubility in water and hence poor bioavailability after oral administration. Solvent deposition system has been developed for solubility enhancement by adsorbing poorly water soluble drug over lactose particles exposing fine particles of drug in dissolution media. This solvent deposition system was formulated as orodispersible tablet through wet granulation, using camphor as subliming agent and sodium starch glycolate as superdisintegrant. The formulations were evaluated for weight variation, hardness, friability, drug content, wetting time, in vitro dispersion time and in vitro dissolution. All the formulations showed low weight variation with in vitro dispersion time less than 40 seconds and rapid in vitro dissolution. Fine particles of drug adsorbed over lactose and porous nature of tablet gave higher drug dissolution and hence rapid drug release. The formulation F4 showed good release profile with maximum drug being released at all time intervals (99% drug release within 35 min). The present study demonstrated potentials for rapid absorption, improved bioavailability, effective therapy and patient compliance.

KEYWORDS: Mouth dissolving tablets, Aceclofenac, Solvent deposition system

INTRODUCTION

Fast dissolving tablets are gaining prominence as new drug delivery systems. These dosage forms disintegrate or dissolve in oral cavity within a minute without need of water or chewing. These are not only useful in administration of drugs in pediatric or geriatric patients but also in patients suffering from dysphagia, leading to better patient compliance.[1-2] Aceclofenac is nonsteriodal anti-inflammatory, analgesic and antipyretic drug used in rheumatoid arthritis, post-traumatic pain, masculo-skeletal and joint disorders [3] The present drug is chosen as a suitable candidate for the formulation of mouth dissolving tablet. Selected drug is poorly water-soluble having poor bioavailability, which gives rise to difficulties in the formulation of dosage form leading to variable dissolution rates. Dissolution of tablet can be improved by forming porous structure in it. Vacuum drying and freeze drying have been used for that purpose. Freeze drying is time consuming, expensive and it gives hygroscopic and friable product. Therefore vacuum drying is adopted in this effert with use of camphor as subliming agent. The dissolution rate and bioavailability of poorly water soluble drugs from solid dosage forms depends much on formulation additives, hence the present study firstly aims at improving solubility of aceclofenac by adsorbing it on lactose employing solvent deposition technique[4-7] and then formulating it into mouth dissolving tablet by sublimation technique. The principle of solvent deposition technique is deposition of the drug in "minuscular form" from an organic solvent on to the surface of an inert excipient. Due to micronization the surface area of drug increases which in turn improves dissolution rate.[4]

MATERIAL AND METHODS

Materials:

Aceclofenac was obtained as a gift sample from torrent pharmaceuticals, gandhinagar. Sodium Starch Glycolate (SSG), mannitol, calcium stearate and

lactose were obtained as gift samples from IPCA Laboratories, Mumbai.

Methods:

I. Preparation of solvent deposition system:

Aceclofenacs solvent deposition system (SDS) was prepared by adsorbing drug over lactose particles. For SDS preparation, proportion of aceclofenac: lactose were selected as 1:0.5, 1:1, 1:1.5, and 1:2. Required amount of aceclofenac powder was dissolved in methanol to form a clear solution. A known amount of lactose was dispersed in the drug solution. The solvent was evaporated at room temperature with constant stirring. Products thus obtained were kept in vacuum oven at 37 °C for 24 hrs to allow complete evaporation of methanol. The SDS thus formed was passed through 60-mesh sieve to get dry free flowing powder.

II. Mouth dissolving tablets preparation:

Four mouth dissolving formulations of aceclofenac SDS has been developed as mentioned in Table 1. The tablets were prepared by wet granulation method using SDS of the ratio 1:1.5 containing aceclofenac equivalent to 100 mg. In these formulations, camphor was used as subliming agent, sodium starch glycolate as superdisintegrant, mannitol as diluent and calcium stearate as lubricant. The granules were compressed by using Rimek tableting machine, Minipress-1 and then tablets sublimed at 40 ºC in vacuum oven for 10 hrs.

III. Evaluation of formulated tablets:

Tablets so prepared were analyzed for hardness, friability, weight variation, wetting time, in vitro dispersion time, % drug content and % drug released.[8-9] The hardness was tested using Pfizer hardness tester whereas the friability by Roche friabilator.

IV. Wetting time[10]:

For estimation of wetting time, circular tissue paper of 10 cm diameter was placed in petriplate of 10 cm diameter containing 10 ml of simulated salivary fluid (pH 6.8). A tablet was placed on the paper and time required for complete wetting was measured.

V. In vitro dispersion time[11]:

In vitro dispersion time of prepared tablet was done by dropping the tablet in 10ml measuring cylinder containing 6ml of simulated salivary fluid (pH 6.8). Time required for complete dispersion of tablet was measured.

VI. In vitro drug release[12,13]:

In vitro drug release was studied using USP Apparatus II (DISSO 2000, Lab India, Chennai, India) in 900 ml pH 7.5 phosphate buffer containing 1% sodium lauryl sulphate was at 37.5± 0.1 °C and 50 rpm. Five ml of sample was withdrawn after every 5 min, and was replaced with an equal volume of fresh dissolution medium. Collected samples were analyzed at 273 nm using same as the blank on UV spectrophotometer (UV-2501 PC, Shimadzu, Japan). The study was performed in triplicate. Dissolution study was conducted for compressed plain drug and formulated (F1, F2, F3, F4) mouth dissolving tablets.

RESULT AND DISCUSSION

Prepared mouth dissolving formulations were evaluated for hardness, friability, weight variation, wetting time, in vitro dispersion time, % drug content and % drug released. All quality control parameters of orodispersible tablets were found to be following within limits of IP 2007. It was found that 45.80% of drug was dissolved in 40 min from plain drug formulation where as 99% of drug was dissolved from formulation F4 within 35 min. As the formulation (F1) contained low level of superdisintegrant and subliming agent its dissolution is less (84% drug release in 40 min)as compared to others whereas as the level of superdisintegrant and subliming agent is higher in formulation (F4), more than 14% increase in percent dissolution was observed. Increased dissolution may be due to increased porosity of tablet as well as use of high amount of superdisintegrant.

CONCLUSIONS

From dissolution data of all formulations developed, solubility of aceclofenac, a poorly water-soluble drug was enhanced by solvent deposition technique using lactose as a adsorbent. It may be due to fine particles of aceclofenac adsorbed over lactose and hence higher surface area of drug is exposed towards dissolution media. Sublimation of tablet has increased porosity of tablet matrix and hence wetting and in vitro dispersion was best. Solvent deposition system of aceclofenac can be successfully formulated into mouth dissolving tablet in order to improve disintegration/dissolution of the drug in oral cavity and hence better patient compliance and effective therapy.

Table I: VARIOUS MOUTH DISSOLVING FORMULATIONS CONTAINING ACECLOFENAC

Formulation	**F1**	**F2**	**F3**	**F4**
SDS (mg)	250	250	250	250
SSG (mg)	7	14	7	14
Camphor (mg)	15	15	25	25
Ca-stearate (mg)	5	5	5	5
Mannitol (mg)	23	16	13	06
Total (mg)	300	300	300	300

Table II: EVALUATION OF FORMULATED MOUTH DISSOLVING TABLETS

Formulation	**F1**	**F2**	**F3**	**F4**
Hardness (Kg/Sq.cm)	3.4±0.4	3.25±0.12	3.3±0.6	3.3±0.4
Friability (%)	0.64±0.1	0.54±0.2	0.52±0.04	0.56±0.043
Weight Variation (%)	2.4±0.042	1.4±0.066	3.8±0.022	1.4±0.088
Wetting Time (sec)	35.0±1.67	31.8±0.80	29.4±1.38	26.8±0.44
In vitro dispersion time (sec)	31.4±0.092	27.4±1.48	28.2±0.78	22.6±0.46
% Drug content	98.86±0.56	99.66±0.6	99.44±0.40	99.58±0.40
% Drug released	84.40±0.17	95.44±2.20	90.6±0.38	99.00±0.52

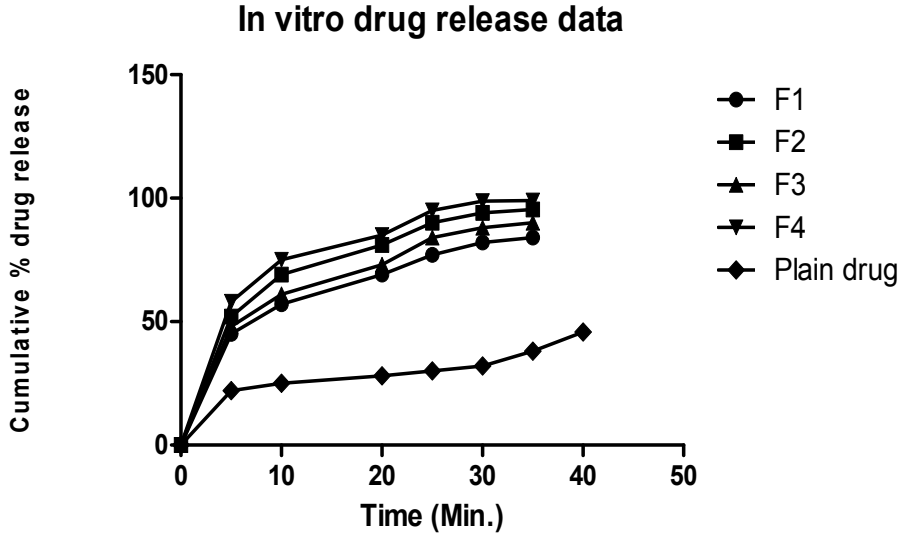

Fig 1. IN VITRO DRUG RELEASE PROFILE OF VARIOUS ACECLOFENAC FORMULATIONS

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