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Research Article

Formulation, Characterization and *In-vitro* Evaluation of Aceclofenac Solid Dispersion in Corporated Gels

Pathak Prashant*[1], Ghelani Tejas[1], Seth A. K.[1], Shah Chainesh[1], Bhalala Chirag[1], Dhamat Khushal[1], Ramani vinod[2]
[1] Sumandeep Vidyapeeth, Piparia, Waghodiya, Vadodara. Gujarat.
[2] C.K. Pithawalla Institute of Pharmaceutical Science & Research, Surat. Gujarat.
Corresponding author Email: prashant_pathak2005@yahoo.com
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ABSTRACT
Aceclofenac, an analgesic and anti inflammatory drug is used in treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis. Various batches of Aceclofenac solid dispersions were prepared by physical mixing, fusion and solvent evaporation methods using PVP as carrier to enhance the solubility of drug. The formulations evaluated for drug content, *in-vitro* dissolution study and also characterized by IR study. There is no interaction between drug and carrier. The general trend indicated that there was an increase in *in-vitro* drug release for solid dispersion prepared in PVP. Based on *in-vtiro* drug release pattern, 1:3 drug carrier ratio was selected as ideal dispersion for gels prepared by solvent evaporation technique. HPMC selected as ideal gel base for preparation of gels and dispersions are incorporated to gel bases by trituration. Formulations were characterized for rheological studies, drug content estimation and *in-vitro* diffusion study, IR spectroscopy. All these properties were found to be ideal. The in vitro release of Aceclofenac solid dispersion incorporated gel is significantly improved when compared to pure drug in corporated gel.

Key words: Aceclofenac, solid dispersion incorporated gels, *in-vitro* dissolution, IR spectroscopy.

INTRODUCTION [1,2,3]

Aceclofenac is an analgesic, anti pyretic and antiflammatory drug. The major drawback of Aceclofenac is its poor aqeous solubility. The continuous use of Aceclofenac through oral route cuases ulcerogenic effect. Solid dispersion is an effective technique which can easily enhance the dissolution rate of drugs. Subcutaneous absorption of Aceclofenac with solid dispersion was significantly greater than that obtained with an intact drug. The present study was performed to investigate the dissolution behavior and topical absorption characteristics of Aceclofenac from solid dispersion incorporated gels, tend to avoid typical side effect of NSAIDS associated with oral and systemic administration. To improve the permeability of Aceclofenac, the use of gel bases is a logical approach to increase the drug flux across the epithelium. To determine the diffusion properties of drugs in semisolid vehicles especially when the release of drug is at the application site is likely to be rate limited by the diffusion of the drug. The ability of vehicle to release the drug at the local site is limited by numerous factors such as drug-vehicle, drug-skin and vehicle-skin interaction. In this paper the influence of Aceclofenac solid dispersion on diffusion from HPMC gel base was investigated in order to develop the effective semisolid formulation of Aceclofenac for treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis.

Materials and Methods

Materials

Aceclofenac was a gift sample from Unix Biotech Pvt. Ltd., Baddi (Solan). Polyvinyl pyrrolidone, HPMC was purchased from Loba Chem Pvt. Ltd (Mumbai). All the chemicals used in the present study were of AR Grade.

Compatibility Study:[1,4]

Infrared spectra of pure drug, polymer, as well as for combination of drug-polymer were taken by KBr pellet technique and were recorded in the range of 4000- 400cm^{-1} by using FT-IR Spectrophotometer Shimadzu.

Formulation of solid dispersion

Preparation of physical mixture [5,6]

The physical mixture of Aceclofenac prepared using PVP in 1:1, 1:2 and 1:3 ratios were obtained by mixing pulverized powders of drugs and various carriers with the help of a spatula.

Preparation by solvent evaporation method [5,6]

The required amount of Aceclofenac and carrier in 1:1, 1:2 & 1:3 ratio were dissolved in sufficient volume of methanol with continuous stirring. The solvent from the solution was removed at 45° with continuous stirring to obtain dry mass. The dried mass was pulverized passed through 44 mesh sieve and stored in desiccator until used for further studies.

Preparation by fusion method [5,6]

Solid dispersion of Aceclofenac & carriers in ratios of 1:1, 1:2 & 1:3 were obtained by melting carrier in a porcelain dish at 80 – 85° and to this Aceclofenac added with thorough mixing for 1-2 minutes followed by quick cooling. The dumped mass was the pulverized passed through 44 mesh sieve and stored in a desiccator until used for further studies.

Preparation of solid dispersion incorporated gels [7]

Hydroxypropyl methyl cellulose (HPMC) Gel

Weighed quantity of HPMC and soaked in 100ml water was added with stirring. Keep above for 24 hours.

Weigh the solid dispersions containing 1% drug. This dry dispersion was added to above gel with continuous stirring.

Table 1 Composition of Solid Dispersion of Aceclofenac

Formulation Code	Drug-Polymer Ration	Method of Preparation
AS1	1:1	
AS2	1:2	Physical mixture
AS3	1:3	
AS4	1:1	
AS5	1:2	Fusion method
AS6	1:3	
AS7	1:1	
AS8	1:2	Solvent Evaporation
AS9	1:3	

Table 2 Composition of Aceclofenac Solid Dispersion in corporated Gels

Ingredients	ASG1	ASG2	ASG3
SD equivalent to 1gm of Aceclofenac	4	4	4
HPMC K4M (gm)	4	5	6
Dist. water (ml)	100	100	100

Characterization of solid dispersions

***In-vitro* dissolution studies for solid dispersions [8]**

The USP dissolution apparatus (Type-II) was used for evaluation of *in vitro* release profile of solid dispersions. The dissolution medium was 900ml phosphate buffer of pH 7.4 kept at 37 ± 0.1°C. The drug or physical mixture or solid dispersion was filled in capsule and then kept in the basket of dissolution apparatus, which was then rotated at 50 rpm. Samples of 5ml were withdrawn at specified time intervals and analyzed spectrophotometrically at 275 nm. Withdrawn samples were replaced by fresh buffer solution.

Physical characterization of Gels

Physical characterization such as spreadability, extrudability, viscosity, PH, drug content was measured.

Determination of spreadibility [9]

The spreadibility of the formulations was determined by an apparatus suggested by Mutimer et al, which was suitable modified in the laboratory and used for the study. It consists of a wooden block which was provided by a pulley at one end. A rectangular ground glass plate was fixed on the block. An excess of gels (about 2 g) under study was placed on this ground plate. The gel was then sandwiched between this plate and another glass plate having the dimensions of the ground plate and provided with the hook. A 300gm weight was placed on the top of two plates for five minutes to expel air and provide a uniform film of the gel between the plates. Excess of gel was scrapped off from the edges. The top plate was then subjected to a pull of 30g. with the help of a string attached to the hook and the time (in sec) required by the top plate to cover a distance of 10cms was noted. The spreadibility was calculated using the formula.

$$\text{Spreadibility} = M\,L/t$$

where,

M = weight tied to the upper glass slide,

L = length of the glass side and

t = time taken in seconds.

Determination of Extrudability [10,11]

The apparatus used for extrudability was suitably fabricated in the laboratory. It consist of a wooden block inclined at an angle of 45° fitted with a thin, ling metal strip (tin) at one end. While the other end was free. The aluminium tube containing 10gm of gel was positioned on inclined surface of wooden block 30gm weight was placed on free end of the aluminium strip and was just touched for 10 seconds. The quantity of gel extruded from each tube was noted.

Determination of viscosity [12]

Viscosity of prepared gels was determined by Brook field programmable DV-II viscometer by spindle no. 52 at 20-25 RPM.

Determination of pH [13]

pH of formulation determined by dispersing 0.5 gm of gel in 50 ml of water. It was checked using digital pH meter at constant temperature. Prior to this, the pH meter was calibrated using buffer solution of pH 4.0 and 9.2, and then electrode was washed with demineralised water. The electrode was then directly dipped in to gel formulation and constant reading as noted.

Determination of drug content [14]

One gm of solid dispersion incorporated gel was mixed with methanol, diluted to 100ml then after filtering the stock solution, filtrate was diluted suitably and absorbance was measured against blank at 275nm.

***In-vitro* diffusion studies for solid dispersion incorporated gels [14]**

The in-vitro diffusion studies for the gels were carried out by apparatus consist of cylindrical glass tube which was opened at both the ends 1gm of gel formulation equivalent to 10gm of Aceclofenac was spread uniformly on the surface of cellophane membrane (previously soaked in water for overnight). Whole assembly was fixed in such a way that the lower end of tube containing gel was just touched the surface of diffusion medium i.e. 100ml PH 7.4 phosphate buffer contained in 150ml beaker which was placed in water bath and maintained at 37 ± 2°C, the contents were stirred using magnetic stirrer at 5 rpm. The sampling was done at different time intervals over a period of 6 hours and absorbance was measured at 275 nm using shimadzu UV-visible spectrophotometer.

RESULT AND DISCUSSION

The present study was an attempt to formulation, characterization and invitro evaluation of aceclofenac solid dispersion in corporated gels by different technique like physical mixture, fusion method, and solvent evaporation technique. Among the solid dispersions prepared 1:3 ratio showed greater solubility than the others. Because of enhanced greater release with 98% solid dispersion prepared by solvent evaporation technique with 1:3 drug carrier ratios was selected as ideal batch for incorporation into gels. FT-IR results shows there were no drug-polymer interaction. The influences of drug – polymer ratio on the physical characteristics of solid dispersion were investigated.

Table 3 Physical characteristics of Aceclofenac Solid Dispersion in corporated Gels

Batch Code	pH	Drug Content (%)	Viscosity (Cp)	Spreadibility (gcm/s)	Extrudability
ASG1	6.5	95.45	384.4	11.40	Satisfactory
ASG2	6.9	98.62	582.5	15.53	Good
ASG3	7.1	96.30	290.8	13.65	Satisfactory

From the various characterization studies like drug content 98.62%, viscosity 582.5 cp, spreadibility 15.53 gcm/s, good extrudability & in vitro diffusion 72%, batch AS9 by Solvent evaporation method was selected as optimised batch. In vitro release of Aceclofenac from prepared solid dispersion was found to be satisfactory. From in-vitro drug release profile of optimized batch ASG2, release pattern could be better expressed by higuchi model as they showed good linearity with "R" value. The analysis of variance was performed. The optimized batch ASG2 formulation was subjected to accelerated stability studies by storing at various ICH storage conditions for 60 days. The samples were analyzed for its drug content and physical appearance at an interval of 15 days. It shows better storage at 25° C ± 2°C/60% RH and 30° C ± 2°C/65% RH.

Thus, from the obtain data it can be concluded that ASG2 formulation shows better drug content hence, Aceclofenac anti-inflammatory can be successfully formulated as solid dispersion in corporated gel.

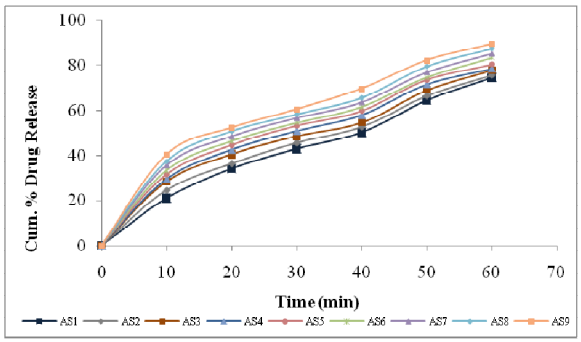

Figure 1 Dissolution profile of batch AS1 to AS9.

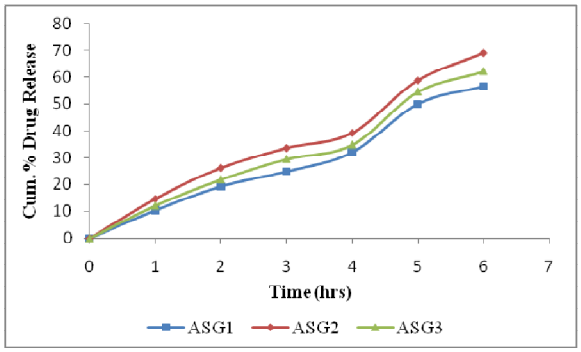

Figure 2 Diffusion study of Aceclofenac Solid Dispersion in corporated Gels ASG1, ASG2 and ASG3.

Conclusion:

The *in vitro* diffusion study of Aceclofenac solid dispersion incorporated gels was greatly improved when compared with those of intact Aceclofenac incorporated gels. From overall formulations ASG2 was found to be the best formulations. From the above results, it may be concluded that solid dispersion incorporated Gels were better for improvement of dissolution and diffusion of Aceclofenac and also to overcome gastric side effect of the drug.

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