Section: Research paper

STUDY OF PHYSIOCHEMICAL & SOLUBILITY PROPERTIES OF ACELOFENAC USING FTIR

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1. ABSTRACT

The aim of this study was to improve the dissolution and release rate of Aceclofenac drug in controlled manner over a period of 24 h. Matrix tablets were prepared by direct compression method, using hydrophilic polymers (HPMC/ guar gum). Matrix tablets were prepared by wet granulation method using different concentration of hydrophilic polymers (HPMC/ guar gum).Tablets were evaluated for *in-vitro* drug release profile in phosphate buffer, pH 6.8, (without enzymes).Drug release was retarded with an increased in polymer concentration due to the gelling property of polymers. The *in-vitro* drug release from proposed system was best explained by the Higuchi's model indicating that the release of drug from tablets displayed diffusion controlled mechanism. Aceclofenac is used in the management of pain and inflammation. The drawback encountered with the conventional tablet dosage forms of aceclofenac are poor aqueous solubility, extensive first pass metabolism. Hence to overcome these issues, the dosage form may be designed in form sustained release formulation to improve its dissolution and bypassing hepatic first-pass effect. Hence the aim of the present study was to prepare and evaluate sustained release matrix tablet of Aceclofenac, tablets were prepared by direct compression by using hydrophilic polymers (HPMC/ guar gum).

2.INTRODUCTION

Oral medication conveyance is the most broadly appropriate route among every single other route, for example, nasal, ophthalmic, rectal, transdermal and parenteral routes. It has been

investigated for systemic transport of drug through different pharmaceutical products of a dissimilar dosage form. The oral course is viewed as most regular, uncomplicated, advantageous and safe because of its simplicity of administration, and patient consistence. Dominant part of the pharmaceutical items intended for oral conveyance is prompt discharge or conventional release system for fast medicine captivation. An ideal dosage regimen in drug therapy of any disease is the one which immediately attains the desired therapeutic concentration of drug in plasma (or at the site of action) and maintains it constant for the entire duration of treatment. This is possible through administration of a conventional dosage form in a particular dose and at a particular frequency. The frequency of administration or the dosing interval depends upon its half-life or mean residence time and its therapeutic index. In most cases, the dosing interval is much shorter than the half-life of the drug resulting in number of limitations associated with such a conventional dosage form. These limitations can be overcome by controlled release dosage forms. Oral route was the most convenient route for the drug delivery. It received more attention in the pharmaceutical field because of more flexibility in designing of dosage form than the drug delivery design for other routes. The design for oral route depends up on various factors such as type of delivery system, the disease being targeted, the patient, the length of therapy and the properties of drug. Most of the oral controlled drug delivery systems release the drug by diffusion, dissolution or combination of both mechanisms to release the drug in a controlled manner to the gastrointestinal tract. The physicochemical properties and biological properties of drugs the drug profile must be determined for the desired release rate of the drug from controlled release dosage form.

Key words-: Drug Delivery, Tablets, Acelofenac Tablets

3.METHODOLOGY

Pre-formulation studies

To understand physiochemical properties of the compounds which affect performance and development of an efficacious dosage form ultimately provide a rationale for formulation design. Drug identification test and drug excipient compatibility studies were done in this phase to provide a useful support in development of dosage forms.

Physiochemical characterization

The drug was examined for various physicochemical properties such as physical appearance, melting point and solubility in different solvents and compared with the literature.

Physical appearance

The powdered drug was poured on light and dark backgrounds and observed for its physical appearance. The results were compared with the reported literature.

Determination of melting point

By Capillary fusion method melting point of the Aceclofenac was determined. One sided closed capillary was filled with drug and placed into the Remi's melting point apparatus [69].The temperature at which first molecule of drug converted into liquid was recorded and compared with literature.

Determination of solubility

The solubility of Aceclofenac was tested in different solvents, drug (50 mg) was dissolved in 10 ml of solvent in a 10 ml solubility bottle. The bottle was properly covered with lid and placed on the water bath shaker maintained at 37ºC for 24 h. Samples were withdrawn manually and filtered through 0.45µm filter paper, using UV spectrophotometer (LabIndia 3000+, Mumbai, India) absorbance of the solution was recorded after suitable dilutions at 273.5 nm [70].

Fourier transforms infrared analysis (FTIR)

The FTIR analysis is the most powerful technique for qualitative identification of compound, main application of FTIR spectrophotometry is determination of drug identity by means of spectral comparison with that of an authentic sample and verification of the presence of functional groups in an unknown sample. Briefly, the sample was subjected to FTIR spectroscopy and spectra taken by an FTIR spectrophotometer (IR affinity-1, Shimadzu,Japan). The sampl was mixed with suitable amount of KBr and converted into pellets by using KBr press at 15 tons hydraulic pressure. The IR scanning of samples was done in between 4000 and 400 cm-1 and spectrum observed for any occurrence and disappearance of characteristic drug peak and compared with the literature.

Preparation of calibration curve of pure drug

Aceclofenac (100 mg) was precisely weighed and dissolved in phosphate buffer (pH 6.8) in a 100 ml of volumetric flask. The drug was not completely soluble in phosphate buffer (pH 6.8) so

methanol was used as co-solvent to dissolve the drug and volume was made up to 100 ml using phosphate buffer (pH 6.8). Stock solution of 100 µg/ml was prepared by diluting solution (10 ml) to 100 ml with phosphate buffer (pH 6.8). From stock solution, aliquots of 0.5 ml, 1.0 ml, 1.5 ml, 2.0 ml to 4.0 ml were transferred to 10 ml volumetric flasks and the volume was made up to 10 ml with phosphate buffer (pH 6.8). The absorbance of these solutions was measured using UV spectrophotometer (LabIndia 3000+, Mumbai, India) at 273.5 nm .

4.RESULT & DISCUSSION

4.1. Physiochemical properties

As kind gift pure drug was received. It is white to off white crystalline powder as mentioned in Table 4.1. The results of physical identification of drug sample were identical to the literature which gives a preliminarily confirmation of drug.

Table 4.1 Results of physical characterisation of the drug.

Colour	White to off white
State	Crystalline Powder

Melting point

The melting point was determined by the capillary fused method. The observed melting point was matched with literature, which confirms that the drug used in the present study was in its pure form.

Table 4.2 Results of melting point study.

Method applied	Observed	Reported
Capillary fusion method	148ºC	149-150ºC

Quantitative and qualitative estimation of solubility of Aceclofenac

Solubility of drug was determined results were presented in Table 4.3. Aceclofenac having better solubility in phosphate buffer (pH 6.8) and it does not have good solubility in distilled water and 0.1N HCl (pH 1.2).

Table 4.3 Results ofsolubility study of aceclofenac.

Solvent	**Solubility (mg/ml)**	**Remark**
Distilled water	0.187	-
0.1N HCl (pH 1.2)	0.283	-
Phosphate buffer pH 6.8	0.841	++

- practically insoluble, ++ slightlysoluble

4.2 Fourier transforms infrared (FTIR) spectroscopy

FTIR spectrum of aceclofenac shows peaks at 3319 $cm^{-1}$and 3267 cm^{-1} are attributed to the OH hydrogen bonding. Peak at 2970 cm^{-1} is due to the NH aromatic stretching, characteristic peak near 2937 cm^{-1}may be due to CH stretching of CH_2 groups while peak at 1750 cm^{-1} indicating presence of carboxylic acid. Peaks at 1589 cm^{-1}, 1577 cm^{-1}, and 1508 cm^{-1} indicate the presence of C=C ring stretching (Figure 4.1 and Table 4.4).

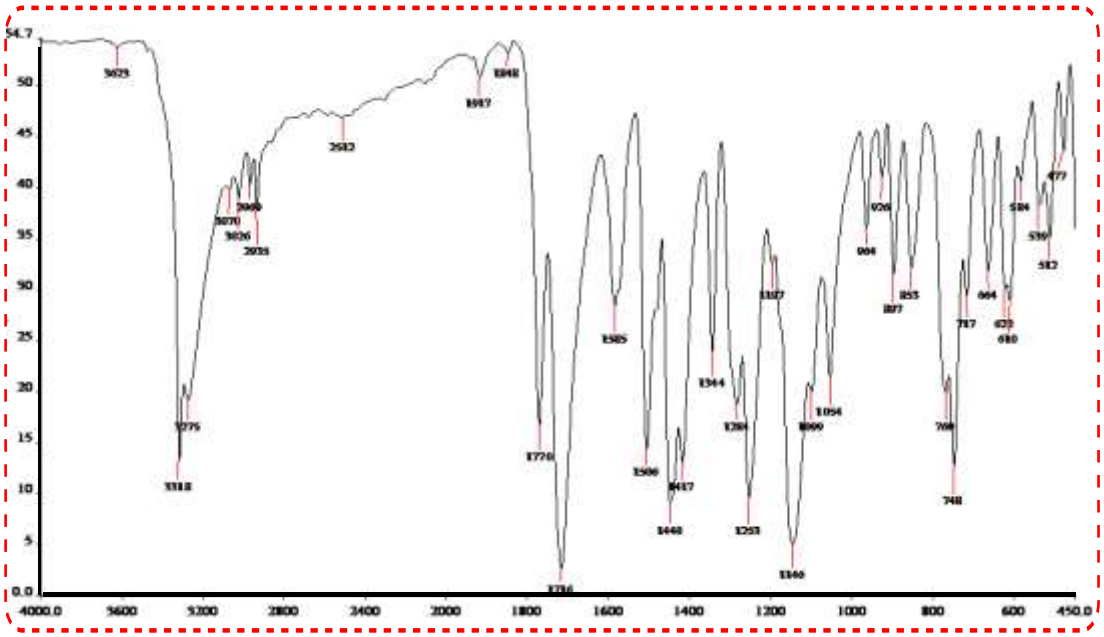

Figure 4.1 FTIR spectrum of aceclofenac.

Table 4.4 Result of FTIR study showing different functional groups present within the drug Aceclofenac.

Observed (cm^{-1})	**Remark**
3319	OH hydrogen bonding
3267	OH hydrogen bonding
2970	NH aromatic stretching
2937	CH stretching
1750	C=O stretching

4.3 Calibration curve for the drug in phosphate buffer (pH 6.8)

Calibration curve of Aceclofenac was prepared in phosphate buffer (pH 6.8), from curve is shows that drug obeys Beer-Lambert law in a concentration range from 0 – 40 µg/ml at 273.5 nm (Table 4.5). The straight-line equation obtained was

$y = 0.025x + 0.0306 (R^2 = 0.9977)$ (Figure 4.2).

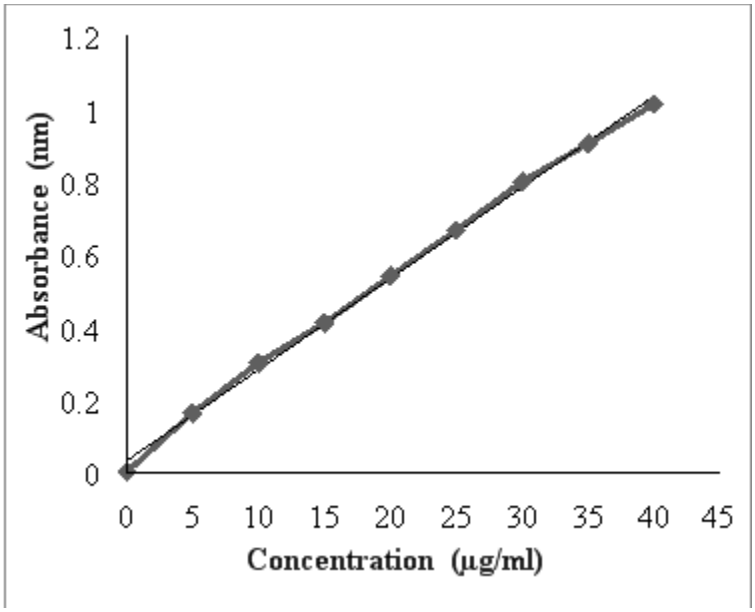

Figure 4.2 Calibration curve of aceclofenac in phosphate buffer (pH 6.8).

Table 4.5 Calibration curve data for aceclofenac in phosphate buffer (pH 6.8).

Concentration(µg/ml)	Absorbance(273.5nm)
0	0

5	0.162
10	0.300
15	0.409
20	0.538
25	0.664
30	0.798
35	0.902
40	1.0105

4.4 Compatibility study by Fourier transform infrared (FTIR) spectroscopy

FTIR spectrum of aceclofenac shows peaks at 3319 $cm^{-1}$and 3267 cm^{-1} are attributed to the OH hydrogen bonding. Peak at 2970 cm^{-1} is due to the NH aromatic stretching, characteristic peak near 2937 cm^{-1}may be due to CH stretching of CH_2 groups while peak at 1750 cm^{-1} indicating presence of carboxylic acid. Peaks at 1589 cm^{-1}, 1577 cm^{-1}, and 1508 cm^{-1} indicate the presence of C=C ring stretching. Further, the peak at 748 cm^{-1} is seen in all mixture is attributed to tri-substituted benzene, all the characteristic peaks of drug were present in the spectrum of the physical mixtures indicating no incompatibility between the drug and polymers selected.

5. CONCLUSION

In the Preformulation studies Aceclofenac was characterized based on its physiochemical properties by the determination of melting point, solubility, UV spectroscopy and FTIR studies. For quantitative assessment of Aceclofenac UV spectrophotometric method was established in the formulations. Linearity of calibration curve was observed in the range of 0-40 µg/ml. Drug polymer interaction studies were carried out for 4 weeks at 40±2ºC and 75±5% RH. Samples were evaluated after every week for their physical and chemical changes such as change in absorption maxima (λ_{max}) and FTIR studies. There were no physical changes after and also no significant interaction of drug with polymers was observed in the UV and FTIR analysis after four weeks. As the drug and polymer(s) were compatible and thus were finalized to use in formulation of sustained release tablets.

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