PREPARATION AND CHARACTERISATION OF GRAFT BIOPOLYMER TO IMPROVE SUSTAINED RELEASE PROPERTY

P.Parida*, D.Dash, A.Behera, S.C.Mishra
University Department of Pharmaceutical Sciences,
Utkal University, Bhubaneswar-751004 Orissa, India*,
Department of Metallurgical & Materials Engineering,
National Institute of Technology, Rourkela-769008, Odisha, India.
*Corresponding Author, email id: patitapabana.pharma@gmail.com

Abstract

In the present piece of research work focuses on grafting Acrylic acid with HPMC to obtain copolymers with improved properties, biodegradable and biocompatible that will be used as hydrogel or water absorbing polymers. To develop a prolong release activity drug delivery system for the medication purpose to enhance drug activity and reduce the frequency of dose via this hydrogel. A novel HPMC-*g*- acrylic acid hydrogel was prepared by in-situ emulsifier free emulsion polymerization using benzyl peroxide as an initiator through 1-stage grafting. Acrylic Acid could intercalate into layers of HPMC and form graft composites through in situ graft-polymerization with acrylic acid and characterized by XRD, FTIR, Thermal spectra and SEM analysis. Swelling property and biodegradability study of the hydrogel graft polymer were investigated. A study of drug loading and drug release with taking the drug Ciprofloxacin is undertaken with this graft polymer using the dissolution apparatus and UV-visible spectrophotometer.

Keywords: Ciprofloxacin; grafting; Acrylic acid; biodegradability.

Introduction

In many years Ciprofloxacin had been available for the treatment of urinary tract infections for many years. It has broad antimicrobial activity and is effective after oral administration for the treatment of a wide variety of infectious diseases. Ciprofloxacin is used to treat a number of infections including: infections of bones and joints, endocarditis, gastroenteritis, malignant otitis externa, respiratory tract infections, cellulitis, urinary tract infections, gastrointestinal and abdominal infections prostatitis, anthrax, chancroid, among others. Ciprofloxacin belongs to fluoroquinolones are potent bactericidal agents against E. coli and various species of salmonella, shigella, enterobacter, campylobacter (Hooper, D.C., and Wolfson, J.S., eds.), and chlamydia, mycoplasma, legionella, brucella, and mycobacterium including mycobacterium tuberculosis (Leysen et al., 1989; Alangaden and Lerner, 1997). Ciprofloxacin has MIC_{90} values from 0.5 to 3 mg/ml for M. fortuitum, M. kansasii, and M. tuberculosis actives in animal [1]. Controlled drug release is to achieve more effective therapies

by eliminating the potential for both under- and overdosing with maintaining of drug concentration within a desired range, fewer administrations, optimal drug use and increased patient compliance [2]. Ciprofloxacin used to enhance the wound healing and cell adhesion as well as transparency through hydrogel [3]. Many novel hydrogel-based delivery matrices have been designed and fabricated to fulfill the ever-increasing needs of the pharmaceutical and medical fields. Mathematical modeling plays an important role in facilitating hydrogel network design by identifying key parameters and molecule release mechanisms [4]. Development of acute disease, after marrow transplantation in patients hematologic malignancies [5]. Pan et al. developed ophthalmic system of gatifloxacin using alginate in combination with HPMC which acted as a viscosity enhancing agents. In vivo precorneal retention studies indicated that the alginate-HPMC solution retained the drug better than the alginate or HPMC alone. Sol-to-gel system of ciprofloxacin hydrochloride was prepared by utilizing the phase transition properties of hydroxyl propylmethyl cellulose K15M and carbopol 934. Lui et al developed Alginate-HPMC based system for long acting delivery of gatifloxacin [6]. Polyacrylic acid was used as the gelling agent in combination with Methocel which acted as a viscosity enhancing agent. The developed formulation was therapeutically efficacious, stable, non-irritant and provided sustained release of the drug over an 8-h period. The developed system is thus a viable alternative to conventional eye drops [7].

Experimental

The chemical contents of HPMC solution, Acrylic Acid were taken in the vessel as for the mentioned 5% solution of HPMC 10 ml & Acrylic Acid-1ml crosslinked with the help of a magnetic bit and capped tightly in reaction vessel connected with nitrogen atmosphere for 20 minutes to make an inert atmosphere. Then the preloaded vessel was kept within a beaker of water on the magnetic stirrer to make the bit to mix homogeneously the contents and adjusted the temperature at 60^0c and 400 rpm. After 15 minutes of through mixing the initiator solution ie-benzoyl peroxide 1.5 ml is added with a syringe to initiate the reaction. Remove vapour from the vessel to avoid bursting. The reaction was carried out for 3 hours with maintaining a temperature of 60^0C. The content was taken out to a watch glass, washed with doubled distilled water & dried.

Results & Discussions

SEM Analysis:

In figure 1 the micrographs show irregular in size & shape of formulation of HPMC-*g*-Acrylic acid. These were ranges from 10-150 micron in size. The irregular graft polymer smoothed in surface.

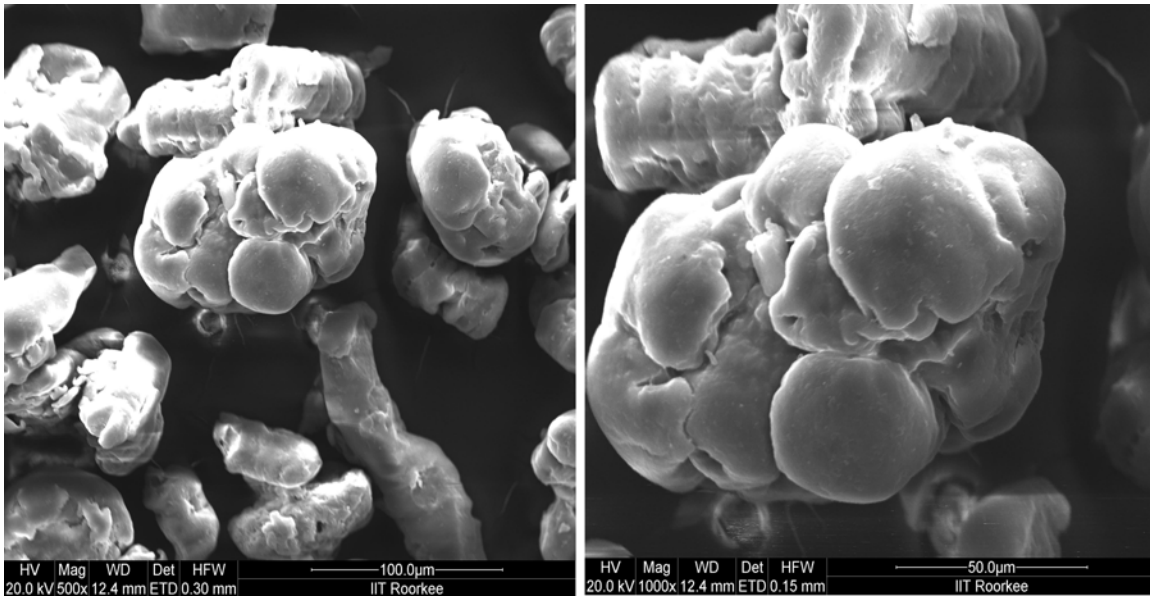

Fig1. SEM image for HPMC-*g*- Acrylic acid

FTIR Analysis

The specific absorption bands at 3419 cm^{-1} corresponding to OH group stretching (secondary hydro group/secondary aliphatic alcohol) and at 1617 cm^{-1} corresponding to CH=CH stretching. Peak around 1637cm^{-1} may be due to the C=O stretching of COOH. The peak found at 1384 cm^{-1} corresponding to C-H deformation of alkane. The peak at 1116 cm^{-1} may be due to C-O stretching in C-O-C group.

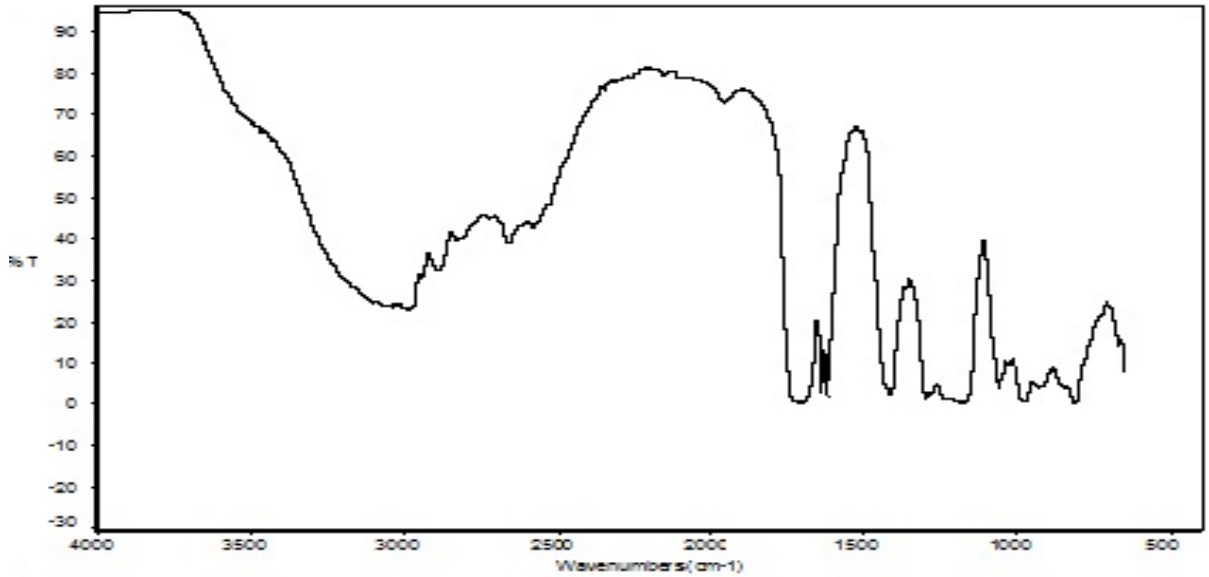

Fig 2. FTIR of HPMC-*g*- Acrylic acid

XRD Analysis

The subsequent peak reading shows that the diffraction decreases at low intensities. As the angles increase the peaks are broaden which shows the formed product is also a partial crystalline structure. XRD results evidence that grafted AA chains were formed after graft copolymerization, which enlarges the proportion of amorphous regions and makes the percentage crystalline in low value.

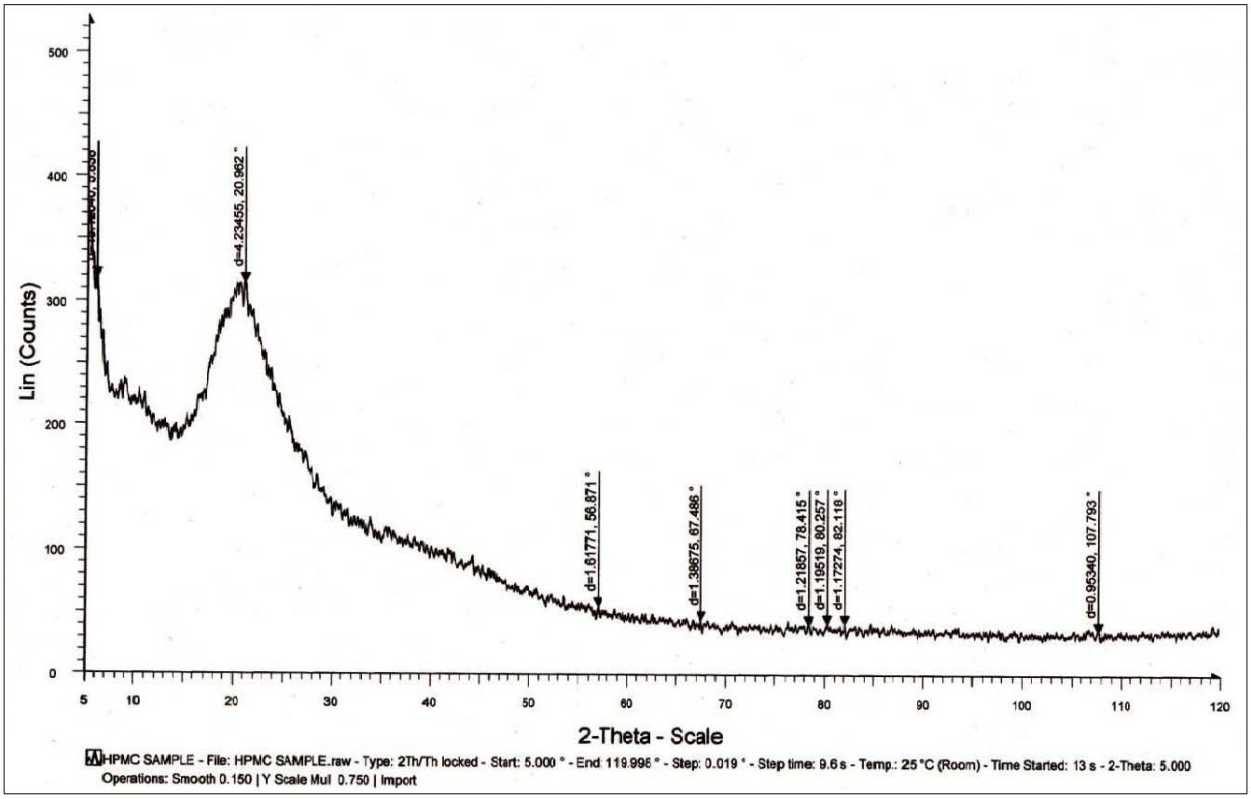

Fig 3. XRD of HPMC-*g*- Acrylic acid

Swelling Property

Three dried samples of 1gm each accurately measured were taken in 3 separate beakers of 50 ml and to these beakers added distilled water, NaCl solution and buffer respectively and leveled. These test samples were allowed to swell in these medium for 12 days and the swelling weight were measured at regular interval of 3hours, 24 hours, 72hours, 140hours, 216hours and 288hours.

Table 1. **Swelling property in different solvents**

Time	Distilled Water (pH 7)	NaCl Solution1% (pH 6.01)	Buffer (pH 6.8)
0 hrs	1.000g	1.000g	1.000g
3 hrs	1.880g	1.400g	1.827g
24 hrs	4.119g	1.933g	6.655g
72 hrs	4.952g	2.666g	14.034g
140 hrs	5.142g	2.800g	24.241g
216 hrs	7.142g	1.733g	31.275g
288 hrs	8.095g	1.200g	31.068g

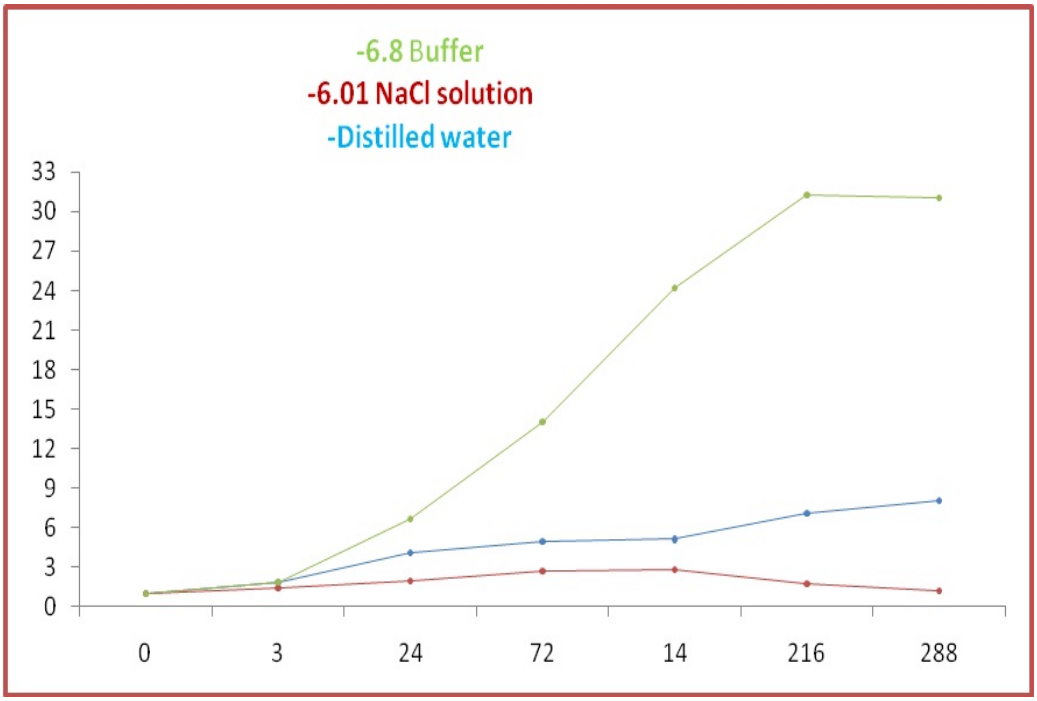

Fig 4. Swelling properties in different buffers

Drug Release

Ciprofloxacin loaded polymeric hydrogel of HPMC-g-AA of which prolonged release study to be undertaken through Dissolution apparatus of USP type 2 & UV visible spectrophotometer of Shimadzu, model no UV3600.

Five mg of ciprofloxacin was accurately weighed in to a 50 ml volumetric flask and dissolved in distilled water. The volume made up to 50 ml with distilled water (100 mcg/ml). Working standard solution 1ml of the above solution was pipette out into a 50 ml volumetric flask and volume made up to 50 ml with distilled water to give a concentration of 2mcg/ml.

Concentrations of 2-20 mcg/ml were prepared by suitably diluting working standard solution with distilled water. The optical densities of these solutions were measured at λ max 266.5 nm using UV visible spectrophotometer. Then the standard plot of absorbance versus concentration was drawn from the data.

Table 2. Drug release profile from hydrogel

Concentration(mcg/ml)	Absorbance
0	0
2	0.034
4	0.057
6	0.087
8	0.109
10	0.139
12	0.161
14	0.192
16	0.217
18	0.238
20	0.269

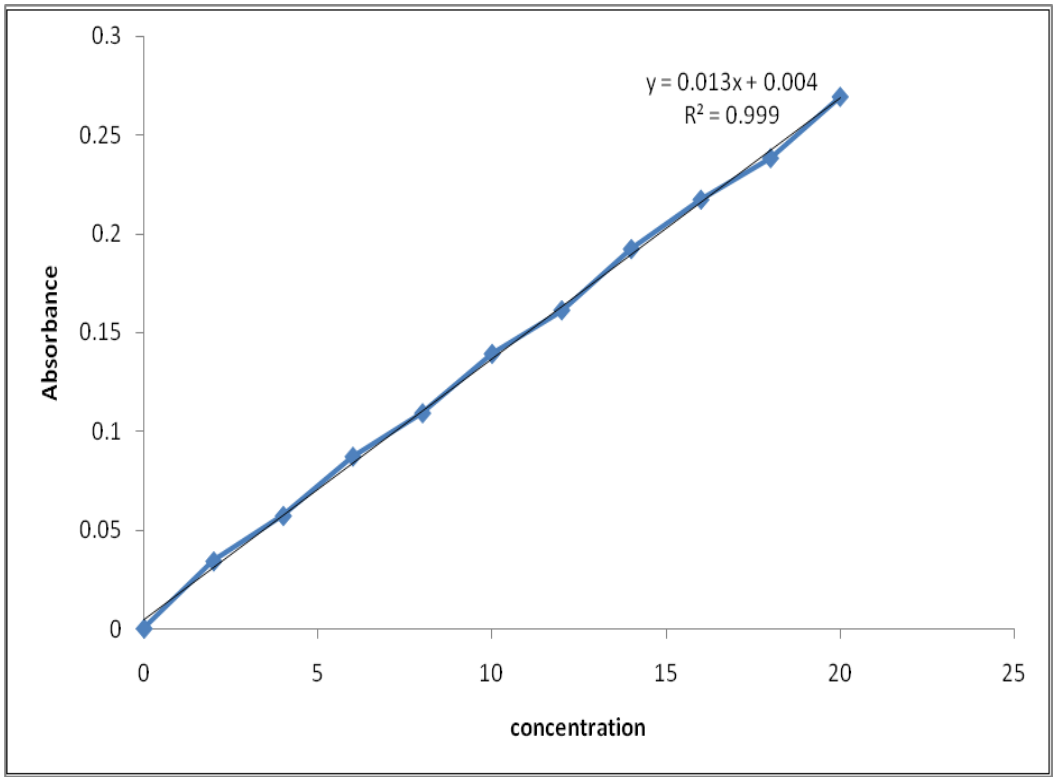

Fig 5.Standard curve of ciprofloxacin at 266.5 nm

Biodegradation

The cultured sample and blank solution were titrated against Na_2CO_3 (N /50) (Y ml) using phenolphthalein indicator until the pink color persists for at least 30 s. The amount of CO_2 released was determined.

Table 3. The value of CO_2 concentration (in ppm)

Days	For S.Aurious	For Lactic Acid Bacillus	For Diastase
7	1188 ppm	501.6 ppm	1126 ppm
14	915.2 ppm	378.4 ppm	924 ppm
21	774.4 ppm	316.8 ppm	756.8 ppm

From the above results the taking days versus carbon dioxide concentration which shows a marked decrease in CO_2.

Conclusions

Hydrogels have played a very important role in biomedical applications. Thus proposed method was found to be simple and selective for characterization of drug loaded graft polymer in the form of hydrogel.

References

1. Laurence L. Brunton, Text book of Goodman & Gilman's, The Pharmacological Basis Of Therapeutics - Sulfonamides, Quinolones, And Agents For Urinary Tract Infections - William A. Petri, Jr., ISBN: 0-07-146892-7, 11th Ed. (2006), Chapter 43.
2. Le Bourlais C. A., Treupel-Acar L., Rhodes C.T., Sado P. T, Leverge R, New ophthalmic drug delivery systems, Drug Dev. Ind. Pharm. 1995, 21, 19– 59.
3. Yoo MK, Release of ciprofloxacin from chondroitin 6-sulfate-graft-poloxamer hydrogel in vitro for ophthalmic drug delivery. Drug Dev Ind Pharm. 2005 May, 31(4-5):455-63.
4. Chien-Chi Lin, Hydrogels in controlled release formulations: Network design and mathematical modeling, C.-C. Lin, A.T. Metters / Advanced Drug Delivery Reviews 58 (2006) 1379–1408.
5. Dietrich W. Beelen, Blood May 15, 1999 vol. 93 no. 10 3267-3275.
6. Sangita D.kute, Formulation approaches in ocular drug delivery system, IJPT, June 2010, Vol. 2, Issue No.2, 118-145.
7. K.S. RATHORE, Insitu gelling ophthalmic drug delivery system: an overview, Int J Pharm Pharm Sci, Vol 2, Suppl 4, 3034