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[Research article]

Formulation and Evaluation of Microspheres Containing Aceclofenac

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ABSTRACT

Aceclofenac, a non-steroidal anti-inflammatory drug (NSAID) The chemical name of aceclofenac is Glycolic acid, [o(2,6 dichloroanilino) phenyl] acetate. Adverse effect of aceclofenac is headache, nausea, vomiting, bone marrow problems, dizziness constipation. Elimination half-life is 4 hrs. The main objective of this research work was to prepare hydroxyl propyl methyl cellulose and eudragit microspheres loaded with aceclofenac and *invtro* relese study.In the present study, solvent evaporation method is used for preparation microspheres. The polymers hydroxylpropyl methylcellulose and eudragit was dissolved and added to the 0.2% PVA solution and stirred it for 2 hrs. Microspheres were spherical shape and smooth surface. Infrared spectra showed identical peaks of drug and polymers. Drug entrapment efficiency was found to be (72.32%). In vitro release studies were performed by using shaking flask method about (89.59 %) drug was released in 12 hrs.

Keywords: Aceclofenac, Microspheres, HPMC, Eudragit, Solvent evaporation.

INTRODUCTION

Novel drug delivery systems (NDDS) offer many advantages[1], which include improved therapy by increasing the efficacy and duration of drug activity, increased patient compliance through decreased dosing frequency and convenient routes of administration, and improved targeting for a specific site to reduce unwanted side effects. The challenge for both drug and drug delivery companies is to deliver both existing and emerging drug technologies in a manner that improves the current benefits enjoyed by the patients.

The range of techniques for the preparation of microspheres offers a variety of opportunities to control aspects of drug administration. There are various approaches in delivering a therapeutic substance to the target site in a sustained controlled release fashion. This approach facilitates the accurate delivery of small quantity of the potent drugs, reduced drug concentration at the site other than the target site and the protection of the labile compound before and after the administration and prior to appearance at the site of action. One such approach is using microspheres as carriers for drugs[2].

Microspheres are defined as "Monolithic sphere or therapeutic agent distributed throughout the matrix either as a molecular dispersion of particles" They can also be defined as structure made up of continuous phase of one or more miscible polymers in which drug particles are dispersed at the molecular or macroscopic level. Microspheres are the carrier linked drug delivery system in which particle size is ranges from (1-1000μm) range in diameter having a core of drug and entirely outer layers of polymers as coating material[18-20].

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Microencapsulation is used to modify and retard drug release. Due to small particle size of microspheres, they are widely distributed throughout the gastrointestinal tract which improves drug absorption and reduces side effects due to localized build-up of irritating drugs against the gastrointestinal mucosa[3-4].

Incorporation of solid, liquid or gases into one or more polymeric coatings can be done by micro encapsulation technique. The different methods used for various microspheres preparation depends on particle size, route of administration, duration of drug release and these above characters related to rpm, method of cross linking, drug of cross linking, evaporation time, co-precipitation etc[5-6]. The various methods of preparations are Phase separation coacervation, Spray drying, Solvent evaporation, Spray coating and pan coating, Freeze drying, Polymerization, Thermal cross linking.

MATERIALS AND METHODS

Aceclofenac (Yorrow Chem, Products Ltd, Mumbai), Hydroxy Propyl Methyl Cellulose K4M (SD Fine Chem Ltd, Mumbai), Eudragit (SD Fine Chem Ltd, Mumbai), Poly Vinyl Alcohol (SD Fine Chem Ltd, Mumbai). All the ingredients and reagents were used Analytical grade.

Table no: 1. Formulation design for Aceclofenac Microspheres

S.No	Ingredients	ACE 1	ACE 2
1	Aceclofenac	100mg	100mg
2	HPMC K4M	100mg	200mg
3	Eudragit	100mg	200mg
4	Poly Vinyl Alcohol	0.4%(W/V)	0.4%(W/V)

Solvent evaporation method[7]

Aceclofenac microspheres were prepared by dissolving the drug in polymer, which was previously dissolved in the chloroform. The resulting solution was added to the aqueous phase containing 0.2% sodium of PVA as an emulsifying agent and the mixture was then agitated using a propeller with the rotation speed 500 rpm. The dispersed drug, Eudragit, HPMC were immediately transformed into fine droplets, which subsequently solidified into rigid microspheres due to solvent evaporation. The particles were collected by filtration, washed with dematerialized water, and desiccated at room temperature for 24 hrs.

RESULTS AND DISCUSSION

Results

FTIR[8]:

FT-IR studies shown that there were no chemical interaction between drug and polymers.

Determination of drug entrapments efficiency [9]

Microspheres (100 mg) were suspended in 25 ml of methanol. After 24 hrs, the solution was filtered and the filtrate was analyzed for UV-Spectrophotometer at 275 nm.

SEM

The microparticles were coated uniformly with gold-palladium by using Sputter coater (POLARON SC-76430), after fixing the sample in individual stabs. All samples were randomly examined for surface morphology of microspheres by using scanning electron microscope (SEM; LIO-430).

STANDARD CALBARATION CURVE

100mg of Aceclofenac was dissolved in small amount of phosphate buffer saline p^H7.4 and volume was made up to 100ml using phosphate buffer saline 7.4 from this stock solutions serial dilutions were done to obtain solutions in the concentration ranging from 100-1.0-10amg/ml. The absorbance of solutions were measured at 275nm Using UV-Visible Spectrophotometer. A graph of concentration vs absorbance was plotted.

In vitro dissolution studies

Shaking flask method [10]

Drug loaded microspheres equivalent to 100mg of drug were weighted and transferred into 250ml conical flask. To the 100ml of 7.4PH phosphate buffer saline was added, then the flask were kept in a metabolic shaker and shaker was adjusted to 50 horizontal shaker per minute at 37±0.5C. 1ml of the

drug releasing media was withdrawn at various time interval of 30min,1,2,3,4,5,6,7,8,9 , 10 and 12 hours and replaced by the same volume of phosphate buffer saline. These samples were filtered through 0.45 m membrane filter. The filtrate was diluted suitably. The drug was estimate in each batch by UV-Visible Spectrophotometer at 275 nm.

Discussion

Percentage of entrapment

The percentage of entrapment was determined for all the batches, the results were shown according to formulation.

The encapsulation efficiency was found in the range of 57.35%, 70.35% for AFC-1 and AFC-2 respectively.

SEM Studies

The microspheres were found to be discrete, spherical and free flowing. The nature of the microspheres indicates that the microspheres were multinucleated, monolithic type.

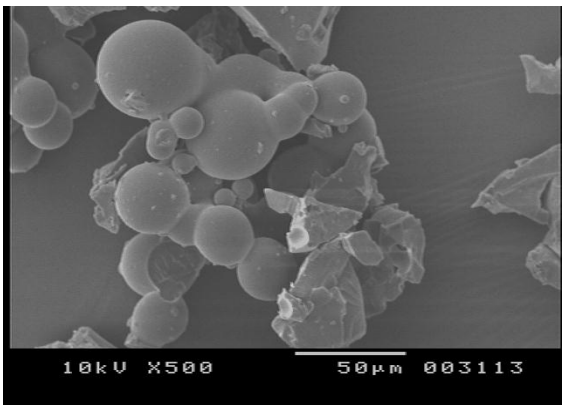


Fig no: 1(a)SEM of Ace 1:2 ratio 500x

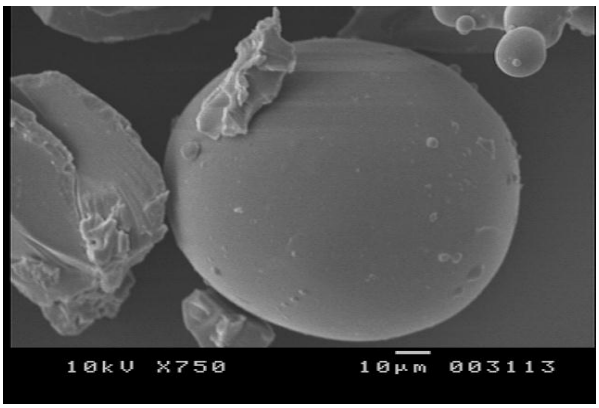


Fig no: 1(b) SEM of Ace 1:2 ratio 750x

Table no: 2. Absorbance of ACE

Sl. No	Concentration	Absorbance (µg/ml)
0	0	0
1	1	0.0581
2	2	0.105
3	3	0.165
4	4	0.201
5	5	0.264
6	6	0.32
7	7	0.362
8	8	0.415

Fig no: 2 Standard curve of ACE

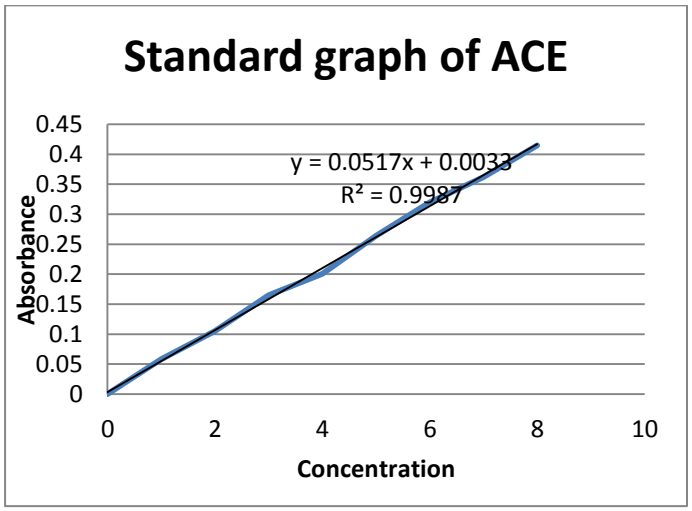


Table no: 3. Invitro release profile of microspheres of Ace-1

TIME (hours)	Absorbance	Concentration (mcg/ml)	% Drug release	Cumulative % drug release
0.5	0.453	8.7251	8.7251	8.7251
1	0.721	13.9493	13.9493	14.0366
2	1.086	21.0643	21.0643	21.291
3	1.493	28.9981	28.9981	29.4355
4	1.925	37.4191	37.4191	38.1465
5	2.263	44.0078	44.0078	45.1094
6	2.582	50.2261	50.2261	51.7677
7	2.965	57.692	57.692	59.7359
8	3.22	62.6628	62.6628	65.2836
9	3.642	70.8889	70.8889	74.1363
10	3.973	77.3411	77.3411	81.2974
11	4.265	83.0331	83.0331	87.7628
12	4.567	88.9201	88.9201	94.4802

Table no: 4. Invitro release profile of microspheres of ACE-2

Time (hours)	Absorbance	Concentration (mcg/ml)	% drug release	Cumulative % drug release
0.5	0.291	5.5673	5.5673	5.5673
1	0.634	12.2534	12.2534	12.3091
2	1.032	20.0117	20.0117	20.1899
3	1.395	27.0877	27.0877	27.466
4	1.821	35.3918	35.3918	36.041
5	2.169	42.1754	42.1754	43.1785
6	2.456	47.77	47.77	49.1949
7	2.835	55.1579	55.1579	57.0605
8	3.113	60.577	60.577	63.0312
9	3.571	69.5049	69.5049	72.5648
10	3.887	75.6647	75.6647	79.4197
11	4.201	81.7856	81.7856	86.2972
12	4.328	84.2612	84.2612	89.5907

Fig no: 3. Invitro graphs of Ace-1, Ace-2

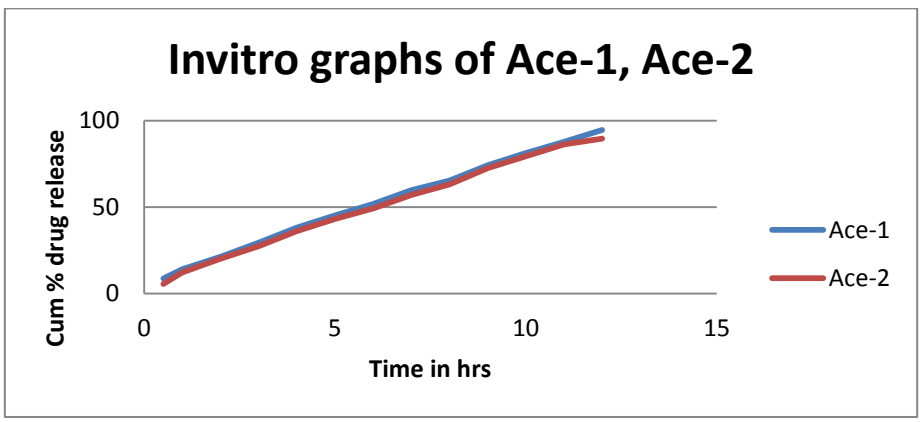


Fig no: 4. FTIR Graph of Aceclofenac Pure Drug

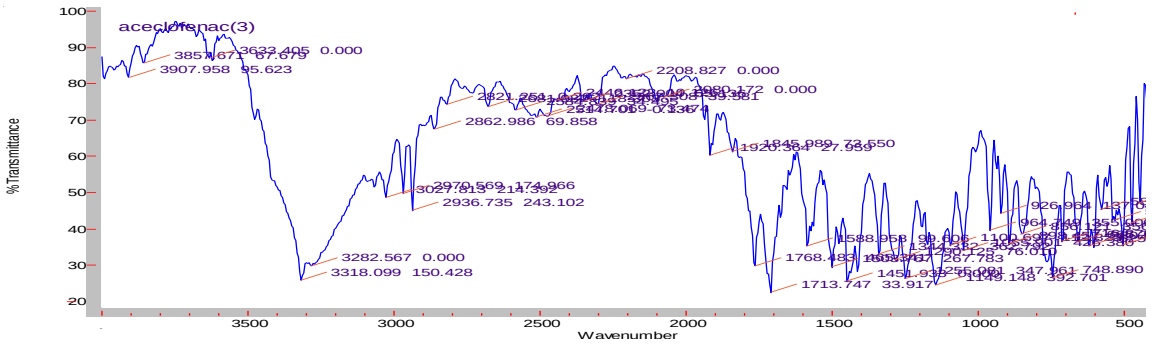


Fig no: 5. FTIR Graph of HPMC

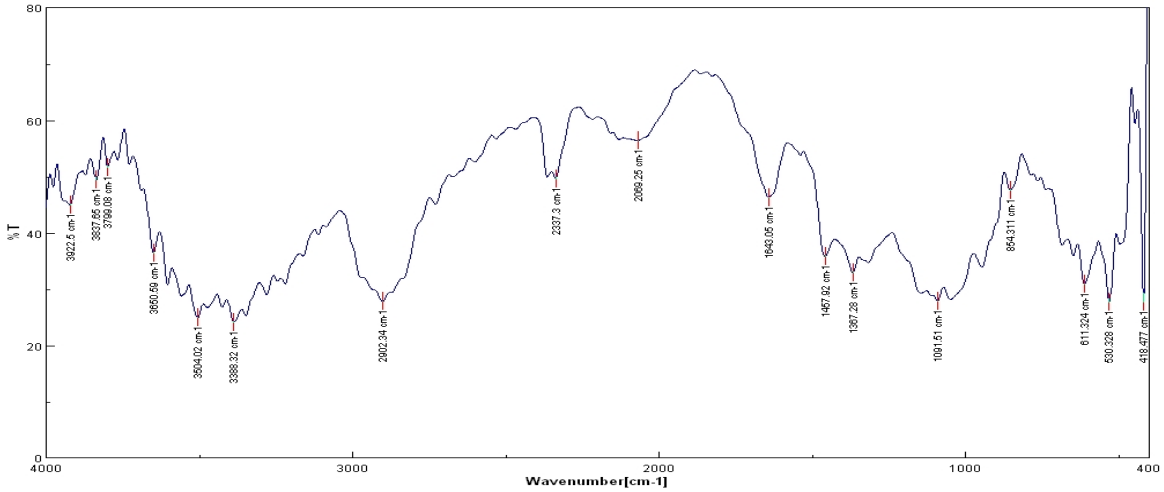
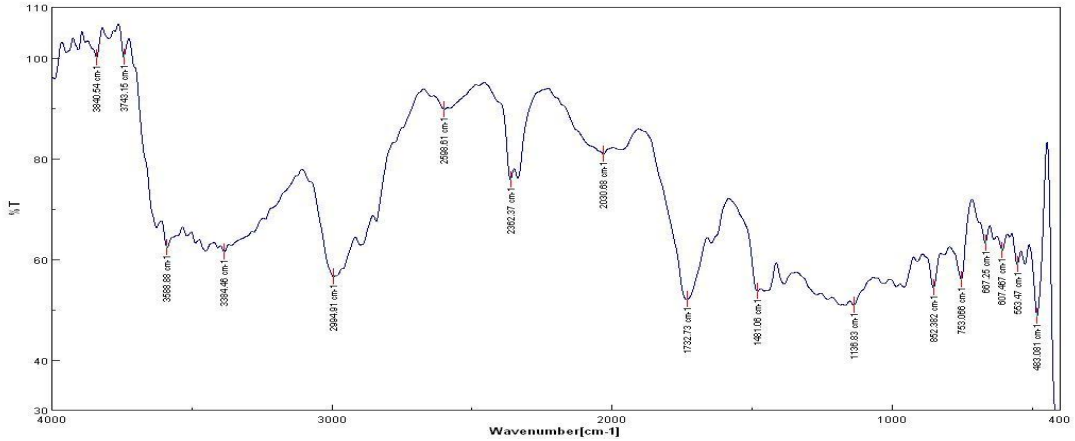


Fig no: 6. FTIR Graph of Eudragit



CONCLUSION

In the present study a satisfactory attempt was made to develop microparticulate drug delivery system of aceclofenac with improved bioavailability. From the experiment results it can be concluded that HPMC, Eudragit polymer is a suitable carrier for the preparation of microspheres of Aceclofenac, Particle size analysis reveals that the microspheres were in the range and all the formulations showed surface characters, *Invitro* studies showed that ACE 1 shows 94.48% ACE2 shows 89.59%. So ACE2 shows sustained release activity, ACE2 formulation may be reduce the adverse effect of Aceclofenac.

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