INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACY AND CHEMISTRY

Available online at www.ijrpc.com

Research Article

FORMULATION AND IN VITRO CHARACTERIZATION OF FLURBIPROFEN NANOSPONGES

A. Pavani* and B. Rama

Department of Pharmaceutics, Mallareddy Institute of Pharmaceutical sciences, JNTU Hyderabad, Telangana, India.

ABSTRACT

The Aim of this work is to the development and evaluation of Nanosponges drug delivery system of Flubriprofen by using solvent evaporation method, and solvent diffusion method. Flubriprofen is a BCS classII drug, having an half life of <4.7 hours,which wasn't suitable for maintaining constant plasma concentrations. So flubriprofen was formulated as a nonosponge formulation for effective drug release, by using β cyclodextrin and HP-β cyclodextrin, by using two different techniques like Emulsion solvent evaporation and solvent Diffusion method. SEM photographs revealed the spherical nature of the nanosponge in all variations. With the revealed results by different evaluation parameters, it is concluded that nanosponge drug delivery system has become highly competitive and rapidly evolving technology and more and more research are carrying out to optimize cost-effectiveness and efficacy of the therapy. The formulation F6 has better results than other eight formulations. F6 have its particle size 350nm, entrapment efficiency 96.24%, drug release release 96% % in 12 hour, The optimized formulation F6 has coefficient of determination (R^2) values of 0.962, 0.933, 0.910 and 0.648 for Zero order, First order, Higuchi and Korsmeyer Peppas respectively. A good linearity was observed with the Zero order, the slope of the regression line from the Higuchi plot indicates the rate of drug release through the mode of diffusion and to further confirm the diffusion mechanism, data was fitted into the Korsmeyer Peppas equation which showed linearity with n value of 1.13 for optimized formulation(F6). Thus n value indicates the super case II transport mechanism.

Keywords: Flurbiprofen, β-cyclodextrin, HP-β cyclodextrin, Emulsion solvent evaporation.

1. INTRODUCTION

Nanosponges are porous polymeric delivery systems that are small spherical particles with large porous surface. These are used for the passive targeting of cosmetic agents to skin, there by achieving major benefits such as reduction of total dose, retention of dosage form on the skin and avoidance of systemic absorption[1]. These nanosponges can be effectively incorporated onto topical systems for prolonged release and skin retention thus reducing the variability in drug absorption, toxicity and improving patient compliance by prolonging dosing intervals. Nanosponges can significantly reduce the irritation of drugs without reducing their efficacy.The size of the nanospongs ranges from 250nm-1µm in diameter[2].

Nanosponges are a new class of tiny sponges that are about the size of a virus, filling them with a drug and attaching- special chemical "linkers" that bond preferentially to a feature found only on the surface of tumour cells and then injecting them into the body. These tiny sponges circulate around the body until they encounter the surface of a tumour cell where they stick on the surface (or are sucked into the cell) and begin releasing their potent drug and begin releasing their potent drug in a controllable and predictable fashion[3].

Nanosponges are made up of microscopic particles with few nanometers wide cavities, in which a large variety of substances can be encapsulated. These particles are capable of carrying both lipophilic and hydrophilic substances and of improving the solubility of

poorly water soluble molecules [4]. Nanosponges are encapsulating type of nanoparticles which encapsulates the drug molecules within its core [5]. As compared to other nanoparticles, nanosponges are insoluble in water and organic solvents, porous, non toxic and stable at high temperatures up to 300^0c .

Nanosponges offers enhanced product performance; extended release; reduced irritation and hence improved patient compliance; improved product elegancy; oil control: It can absorb oil up to 6 times its weight without drying; improved formulation flexibility; improved thermal, physical, and chemical stability; flexibility to develop novel product forms; These are also non-irritating, non-mutagenic, non-allergenic and non-toxic.

1.1 Advantages[6-9]

1) This technology provide entrapment of active contents and side effects are less.
2) It provides improved stability, elegance and formulation flexibility.
3) It is non-mutagenic.
4) Non-irritating, non-toxic.
5) It provide extended release condition which is continuous action up to 12hr.
6) Drug is protected from degradation.
7) Therapeutic provide onset of action. Formulations are cost effective.
8) It can be used to mask unpleasant flavours and to convert liquid substances to solids2. Less harmful side effects (since smaller quantities of the drug have contact with healthy tissue).
9) Nanosponge particles are soluble in water, so encapsulation can be done within the nanosponge, by the addition of chemical called an adjuvant reagent.
10) Predictable release.
11) Biodegradable.

2 MATERIALS AND METHODS

2.1 MATERIALS

Flubriporfen procured by Glochem Industries Limited, Hyderabad. β-Cyclodextrin , Polyvinyl alcohol (PVA), HP β cyclodextrin , Dichloromethane and Distilled Water purchased from BMR Chemicals, Hyderabad respectively.

2.2 Method of Preparation of Nanosponges by solvent Evaporation method

Nanosponges using different proportions of β-cyclodextrin ,HP β-cyclodextrin, as rate retarding polymer and co-polymers like polyvinyl alcohol were prepared by solvent evaporation method. Disperse phase consisting of Flurbiprofen (1gm) and requisite quantity of PVA dissolved in 10 ml solvent (dichloromethane) was slowly added to a definite amount of PVA in 100ml of aqueous continuous phase, prepared by using magnetic stirrer. The reaction mixture was stirred at 1000 rpm on a magnetic stirrer for 2hours and kept on hot plate upto complete removal of organic solvent from the formulation. The nanosponges formed were collected by filtration through whatman filter paper and dried in oven at 50^0C for 2 hours. The dried nanosponges were stored in vaccum desicator to ensure the removal of residual solvent.

2.3 Method of preparation of Nanosponges by Solvent Diffusion Method

Nanosponges prepared by using different proportion of β-cyclodextrin ,HP β-cyclodextrin and polyvinyl alcohol. The dispersed phase containing β-cyclodextrin ,HP β-cyclodextrin and drug was dissolved in 20ml dichloromethane and slowly added to a definite amount of polyvinyl alcohol in 100ml of aqueous continuous phase. The reaction mixture was stirred at 1000rpm for 2 hrs. The nanosponges formed were collected by filtration and dried in oven at 40^0 c for 24 hrs.The dried nanosponges were stored in vacuum desiccators to ensure the removal of residual solvent.

2.4 Evaluation parameters of Nanosponges

The Nanosponges was evaluated for various parameters

A. Entrapment efficiency

The 100mg of the Flurbiprofen weight equivalent nanosponge suspension was analyzed by dissolving the sample in 10ml of distilled water. After the drug was dissolved 10ml of clear layer of dissolved drug is taken. Thereafter the amount of drug in the water phase was detected by a UV-spectrophotometric method at 246nm (U.V Spectrophotometer, systronics). The test was repeated with another nanoparticulate sample. The amount of the drug in the suspension was analyzed by centrifugation at 500rpm for 5 mins and by measuring the concentration of the drug in the clear supernatant layer by the UV-spectrophotometric method. The concentration of the drug is determined with the help of calibration curve. The amount of drug inside the particles was calculated by subtracting the amount of drug in the aqueous phase of the suspension from the total amount of the drug in the nanoparticle suspension.

The entrapment efficiency (%) of drug was calculated by the following equation.

B. Scanning electron microscopy

The morphological features of prepared nanospongess are observed by scanning electron microscopy at different magnifications.

C. Dissolution study

For the oral dosage forms the in vitro dissolution study must be conducted in the dissolution medium which simulate the in-vivo conditions (actual physiological conditions). The in vitro drug release studies for the prepared formulation were conducted for a period of 12 hrs using an Electro lab model dissolution tester USP Type-1 apparatus (rotating basket) set at 50 rpm and a temperature of 37± 0.5°C weight equivalent to 100mg of Flurbiprofen nanosponge was filled in capsule and kept in basket apparatus and placed in the 900ml of the medium. At specified intervals 5ml samples were withdrawn from the dissolution medium and replaced with fresh medium to keep the volume constant. The absorbance of the sample solution was analyzed at 246nm for the presence of model drug, using a UV-visible spectrophotometer.

3 RESULTS AND DISCUSSION

3.1 Determination of absorption maximum (λmax)

Determination of Flurbiprofen λ-max was done in 6.8 pH phosphate buffer for accurate quantitative assessment of drug dissolution rate. The Flurbiprofen peak value is 246.

The linearity was found to be in the range of 2-12 µg/ml in 6.8 ph buffer. The regression value was closer to 1 indicating the method obeyed Beer-lamberts' law.

3.2 Compatibility Studies

Compatibility with excipients was confirmed by FTIR studies. The pure drug and polymers were subjected to FTIR studies. In the present study, the potassium bromide disc (pellet) method was employed.

3.3 Evaluation of Flurbiprofen Nanosponge

The Nanosponge was prepared by solvent evaporation method using βcyclodextrin and HP- βcyclodextrin, as rate retarding polymers, PVA and dichloromethane as crosslinking agents. The prepared nanosponges were evaluated for its different parameters which revealed many interesting results for efficient preparation of the nanosponge. FTIR spectroscopy analyses indicated the chemically stable, amorphous nature of the drug in these nanosponge. SEM photographs revealed the spherical nature of the nanosponge in all variations. With the revealed results by different evaluation parameters, it is concluded that nanosponge drug delivery system has become highly competitive and rapidly evolving technology and more and more research are carrying out to optimize cost-effectiveness and efficacy of the therapy. The formulation F6 has better results than other eight formulations. F6 have its particle size 350nm, entrapment efficiency 96.24%, drug release release 96% in 12 hour. By comparing the two different methods i.e, solvent evaporation and solvent diffusion method it was clearly observed that solvent evaporation was found to be better than the solvent diffusion method, as the formulations shows better drug release with solvent evaporation than the solven diffusion method.The optimized formulation F6 has coefficient of determination (R2) values of 0.962, 0.933, 0.910 and 0.648 for Zero order, First order, Higuchi and Korsmeyer Peppas respectively. A good linearity was observed with the Zero order, the slope of the regression line from the Higuchi plot indicates the rate of drug release through the mode of diffusion and to further confirm the diffusion mechanism, data was fitted into the Korsmeyer Peppas equation which showed linearity with n value of 1.13 for optimized formulation (F6). Thus n value indicates the super case II transport mechanism.

4 CONCLUSION

From the evaluation studies it can be concluded that flurbiprofen loaded nanosponges using solvent evaporation method is better than emulsion solvent diffusion method. Among them HPβ Cyclodextrin with higher concentration showed sustained release than β-Cyclodextrin.

Table 1: Formulation table of Flurbiprofen loaded nanosponges using solvent evaporation method

S.NO	Excipients	F1	F2	F3	F4	F5	F6
1	Flurbiprofen (gm)	1.0	1.0	1.0	1.0	1.0	1.0
2	β-cyclodextrin (gm)	1	2	3	--	--	--
3	HPβ Cyclodextrin	--	--	--	1	2	3
4	PVA (gm)	2	2	2	2	2	2
5	Dichloromethane (ml)	20	20	20	20	20	20
6	Water	150	150	150	150	150	150

Table 2: Formulation table of Flurbiprofen loaded nanosponges using Emulsion Solvent diffusion method

S.NO	Excipients	F7	F8	F9	F10	F11	F12
1	Flurbiprofen (gm)	1.0	1.0	1.0	1.0	1.0	1.0
2	PVA (gm)	0.5	0.5	0.5	0.5	0.5	0.5
3	β-cyclodextrin (gm)	0.5	1.0	1.5	--	--	--
4	HPβ Cyclodextrin	--	--	--	0.5	1.0	1.5
5	Ethanol (ml)	10	10	10	10	10	10
6	Water	150	150	150	150	150	150

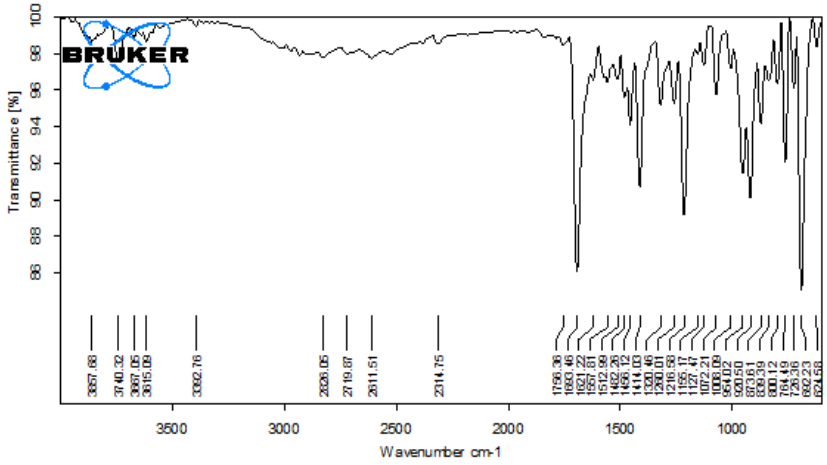

Fig. 1: FTIR Spectra of Flurbiprofen (Pure Drug)

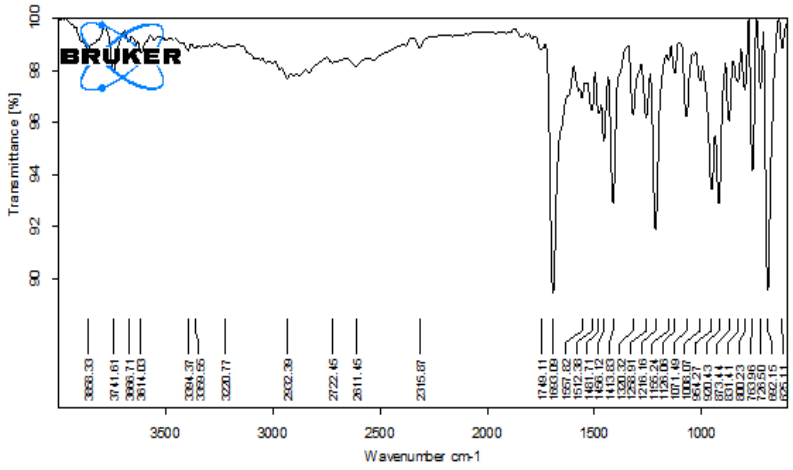

Fig. 2: FTIR Spectra of optimized formulation

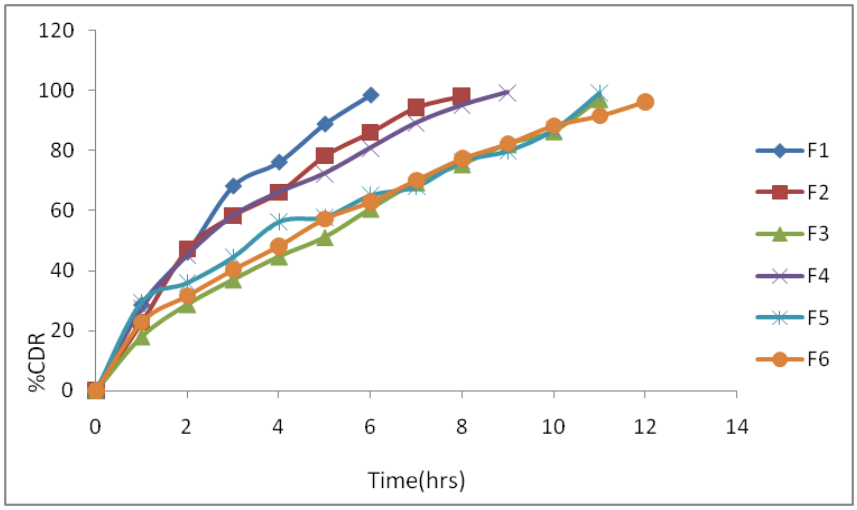

Fig. 3: Percentage Drug Release of F1-F6

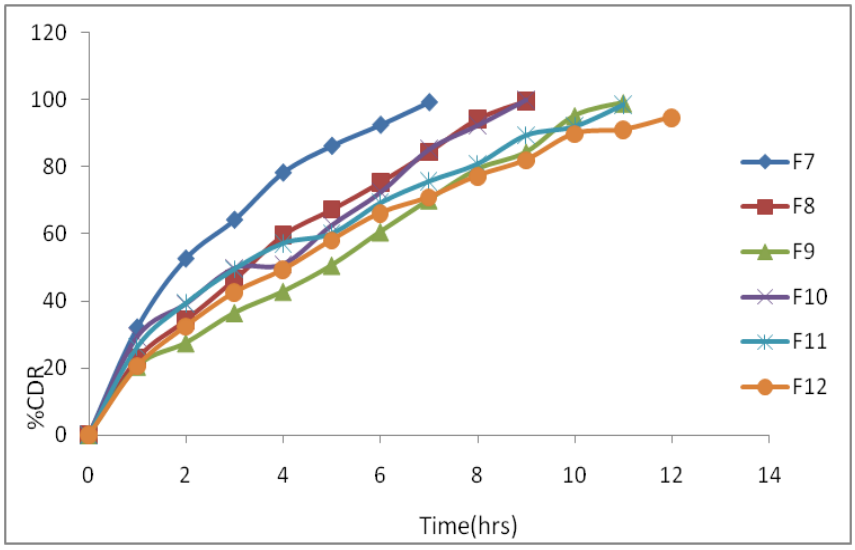

Fig. 4: Percentage Drug Release of F7-F12

6 REFERENCES

1. Carvalho FC, Bruschi ML, Evangelista RC and Gremio MPD. Mucoadhesive drug delivery system. Brazilian Journal of Pharmaceutical Sciences. 2010;46(1):1-17.
2. Meena KP, Dang JS, Samal PK and Namedo KP. Recent advances in microsphere manufacturing technology. International Journal of Pharmacy and Technology. 2011;3(1):854-855.
3. Krishnamoorthy K and Rajappan M. Nanosponges: A novel class of drug delivery system. review. J Pharm Pharm Sci. 2012;15(1):103-11.
4. Trotta F, Cavalli R, Tumiatti W, Zerbinati O, Rogero C and Vallero R. Ultrasound-assisted Synthesis of Cyclodextrin-based Nanosponges. EP. 2013;1786:841 B1.
5. Selvamuthukumar S, Anandam S, Kannan K and Manavalan R. Nanosponges: A Novel Class of Drug Delivery System Review. J Pharm Pharmaceut Sci. 2012;15(1):103-111.
6. Nilesh J, Ruchi J, Navneet T, Brham Prakash G and Deepak Kumar J. Nanotechnology. A Safe and Effective Drug DeliverySystems, Asian Journal of Pharmaceutical and Clinical Research. 2010;3(3):159-165.
7. Nacht S and Kantz M. The microsponge. A novel topical programmable delivery system, In: Topical Drug Delivery Systems. David WO and Anfon HA (ED). 1992;42.
8. Delattre L and Delneuville I. Biopharmaceutical aspects of the formulation of dermatological vehicles. J Eur Acad Derm Vener. 1995;5:S70.
9. http://Sciencematters, Unimelb.edu.au/ 2011/05/nanosponges for targeted-cancer-treatment/visited on 12/10/2011.