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Preparation and Optimization of Piroxicam Loaded Eudragit S 100 Microspheres Using O/O Emulsion Solvent Evaporation Method.

Shaheda Sultana*, Kalla Madhavi, Syed Umar Farooq, D Sudheer Kumar.
1.Department of Pharmaceutics, Care College of Pharmacy

ABSTRACT

The objective of the present investigation was to prepare colon targeted piroxicam loaded Eudragit S 100 microspheres and evaluate its properties. The microspheres were prepared by using "O/O solvent evaporation" technique. The formulation was optimized by investigating the influence of various process variables like stirring speed, drug: polymer ratio and percentage of emulsifier on the fabrication and the prepared microspheres were evaluated for *in vitro* properties. Piroxicam loaded Eudragit S 100 microspheres were successfully prepared using "O/O solvent evaporation" method. Microspheres prepared using 1:5 drug: polymer ratio, with a stirring speed of 1000 rpm, and 1.0% w/v concentration of emulsifying agent was selected as an optimized formulation. In vitro drug release were performed in pH 1.2 (0.1N HCl) for 2h and in pH 6.8 phosphate buffer for next 2h followed by 7 pH phosphate buffer up to 24 h. The release pattern of drug was slow at low pH values and increased on rise in pH. The drug release followed Higuchi model.

Keywords: Emulsion solvent evaporation method; Piroxicam loaded Eudragit microspheres.

*Corresponding Author Email: shahedasultana64@gmail.com
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INTRODUCTION

Microspheres are the carrier linked drug delivery system in which particle size ranges from (1-1000 µm) in diameter having either a core of drug and entirely outer layers of the polymers as coating material or the drug dispersed evenly in the homogenous matrix of the polymer. They are generally biocompatible, can provide high bioavailability and are capable of sustained release for long period of time. The drug loaded microspheres are delivered to the target area by passive means (trapping by size) or active means (magnetic targeting).

Piroxicam is a potent acidic NSAID used for the treatment of rheumatoid arthritis but the major side effect after oral administration is irritation of the gastrointestinal tract which can be overcomed by microparticulate drug delivery system. Eudragit S 100, a pH sensitive enteric polymer, was used to selectively deliver the drug to colon.

MATERIALS AND METHOD

Piroxicam was obtained as a gift sample from Trident laboratories. Eudragit S 100 was obtained from MSN laboratories and all other chemicals used were of pharmaceutical grade.

Preparation of Piroxicam microspheres:

The piroxicam microspheres were prepared by O/O emulsion solvent evaporation method. Accurately weighed 100 mg of drug and 200 mg of polymer were taken and dissolved in mixture of 10 ml of acetone and 5 ml of ethanol.1% W/V span 80 was taken in 100 ml of heavy liquid paraffin and kept under propeller stirrer. Solution of drug and. polymer mixture was added drop by drop to liquid paraffin containing span 80 while stirring. Stirring was continued for 3-4 hrs, for complete removal of solvent. After that the microspheres were filtered with Whatman filter paper. Collected microspheres were washed with 50 ml of petroleum ether 4-5 times to remove liquid paraffin and dried.

Optimization of some process parameters:

Effect of drug-polymer ratio:

Eudragit microspheres were prepared using various drug polymer ratios, i.e., 1:2, 1:3, 1:4, and 1:5, 1:6 where stirring speed (1000 rpm) and emulsifier concentration (1.0% w/v) were kept constant.

Effect of emulsifier concentration:

Microspheres were prepared using various emulsifier concentrations, i.e., 0.50, 0.75, 1.0, 1.25, 1.50, where drug: polymer ratio (1:5) and the stirring speed (1000 rpm) were kept constant

Effect of stirring rate:

Microspheres were prepared at various stirring rates, i.e., 500, 1000,

1500 rpm, where drug polymer ratios (1:5) and the emulsifier concentration (1.0% w/v) were kept constant.

In vitro characterization of Piroxicam microspheres:

Percentage yield:

Weight of the prepared microspheres were weighed. The practical yield is the weight of completely dried microspheres and the theoretical yield is the total weight of drug, polymer and all other additives. The percentage yield was calculated by using the following formula.

Percentage yield = Practical yield/Theoretical yield X 100

Particle size analysis

Particle size analysis of the microspheres was performed under compound microscope with 45x magnification lens and average particle size was determined by measuring 100 particles using pre calibrated eye piece micrometer.

Entrapment efficiency:

Entrapment efficiency is the percentage of drug entrapped in the microspheres.50 mg microspheres were accurately weighed and triturated with 10 ml of methanol and kept for 12 h. After filtration appropriate dilutions were made with methanol and the absorbance was measured with UV-VIS spectrophotometer at 240 nm. The entrapment efficiency was calculated using the following formula.

Entrapment efficiency= Amount of drug actually present/Theoretical drug loaded expected × 100

Scanning Electron Microscopy:

The particles are vacuum dried and coated with a thin gold palladium layer with a sputter coater unit and observed microscopically at an accelerating voltage of 10 K V.

Fourier Transform Infrared study:

The analytical technique used for drug excipient compatibility study was FTIR with Attenuated Total Reflectance (ATR) technique. A small portion of a sample was placed on the zinc selenide crystal and spectrum was taken. The IR spectra of formulation was compared with the IR spectra of pure drug and observed for any spectral changes**.**

Micrometric properties:

The flow property of prepared microspheres was determined using fixed base cone method. Bulk density was calculated using bulk density apparatus, tapped density was calculated by a 10 ml graduated cylinder and by using bulk density and tapped density data compressibility index and hausner's ratio were calculated.

***In vitro* drug release study:**

Microspheres equivalent to 100 mg of drug content were accurately weighed and filled into the dialysis bag and the bag was dipped in 900 ml dissolution medium at 37^0C± 0.5^0C in USP -II (paddle) apparatus at a speed of 50 rpm. The study was carried out in 0.1 N HCL (2h), pH 6.8 (2h) and in pH 7 phosphate buffer up to 24h. 5ml aliquots of dissolution media were withdrawn at suitable time intervals and replaced with fresh medium. The samples were filtered and analyzed after appropriate dilution by UV-spectrophotometer.

Drug release kinetics:

Drug release data was plotted in kinetics models to determine drug release kinetics.

Stability Studies:

Accelerated stability studies was conducted for the optimized formulation about 3 months in stability chamber, as per ICH guidelines.

Ex vivo studies:

Ex vivo targeting efficiency study was carried out to check the efficiency of the formulation to target to colon. Roentgenography study a comparatively safer technique was carried out in healthy rats to access the *in vivo* performance. The behaviour of piroxicam microspheres in rat was observed using a radiographic imaging technique. It involves the use of radio-opaque markers such as barium sulphate, incorporated in the formulation to determine the position of the microspheres. Healthy rat of 250g was fasted overnight and on the next day morning microspheres was administered followed by giving 25 ml of water. X-ray images were taken under the supervision of a radiologist, to follow the nature, movement, location and the integrity of the microspheres indifferent parts of gastrointestinal tract (G.I.T).

RESULTS AND DISCUSSION:

Piroxicam microspheres was successfully prepared using O/O emulsion solvent evaporation method.

Effect of drug-polymer ratio:

As the polymer concentration was increased, the mean diameter of the Eudragit S100 microspheres was also increased, may be due to the fact that viscosity increases with increased polymer concentrations, which resulted in larger emulsion droplets and finally results in greater particle size. Entrapment efficiency was increased from 79% to 95% with increase in polymer concentration because more polymer is present in media to produce microspheres for entire drug. As the polymer concentration was increased % yield was also increased from 80% to 96%.

Effect of stirring speed:

Among various stirring speed, stirring at 1000 rpm resulted in formation of uniform microspheres. Higher stirring rate 1500 rpm thus resulted in decrease in particle size of microspheres because of the shearing force needed to reduce the size of emulsion droplet and resulted in irregularly shaped microspheres. Stirring speed had no significant effect on the percentage yield.

Effect of emulsifier concentration:

At 0.50% span 80, concentration, the particles showed in irregular in shape as the concentration is not sufficient to stabilize the emulsion droplets. As the concentration was increased from 0.75% to 1.50% the particle size was found to be decreased. As emulsifier is a surface active agent, an increase in its concentration will allow to stabilize a greater surface area, thus leads to smaller particle size. The entrapment efficiency was decreased with increase in the emulsifier concentration in some extent due to the fact that increase leads to stabilization of droplets and hence smaller microspheres are obtained and loss of drug from the surface of smaller microspheres is more than larger one. Increase in emulsifier concentration resulted in increased % yield from 80% to 98.

Micrometric properties:

Micrometric properties was calculated. (Table.1)

Surface morphology:

Surface morphology was studied using Scanning electron microscopy technique. The prepared microspheres was spherical in shape. (Figure 1)

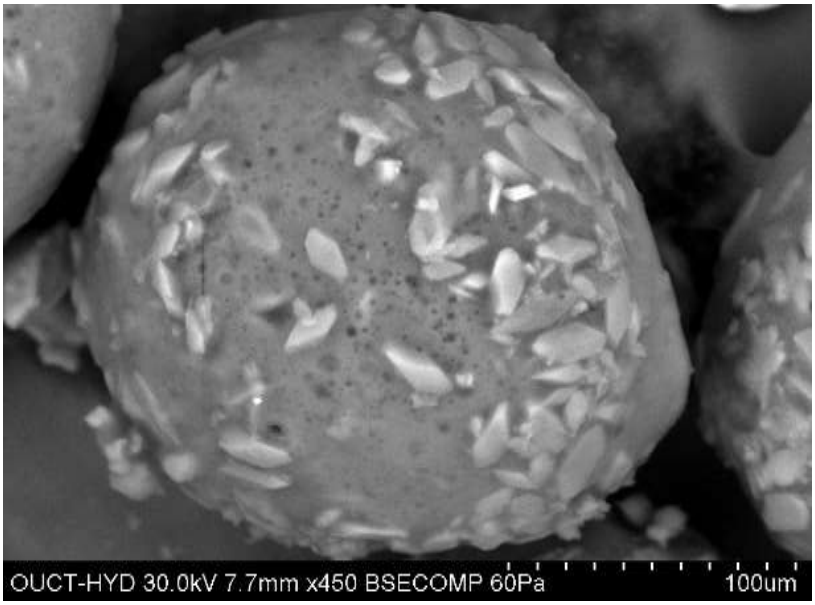

Figure 1: SEM of Piroxicam microsphere

Table 1: Results of Micrometric Properties

Formulation code	Angle of repose (Ɵ)	Bulk density	Tapped density	Carr's index	Hausner's ratio
F_1	31	0.654	0.645	14.46	1.15
F_2	33.01	0.665	0.620	12.53	1.18
F_3	33.33	0.667	0.657	14.04	1.16
F_4	34.65	0.664	0.624	11.04	1.14
F_5	35.10	0.662	0.626	15.89	1.17

Fourier Transform Infrared analysis:

FTIR analysis revealed that there was no interaction between the drug and the polymer.

In-vitro drug release study:

In-vitro drug release study was carried out by using dissolution test. The drug release data was tabulated and profiles were constructed taking time points on x- axis and cumulative amount of drug release on y-axis. The percentage drug release curve showed that drug release was less than 10% upto 2hr i.e, at pH 1.2 and the drug release rate was increased as pH of medium is increased and drug release was maximum in pH 7 buffer. The release rate of piroxicam from microspheres decreased as the polymer concentration increased. This may be due to the fact that the higher polymer concentration resulted in large particle size that resulted in reduce surface area available for drug release.(Figure 2)

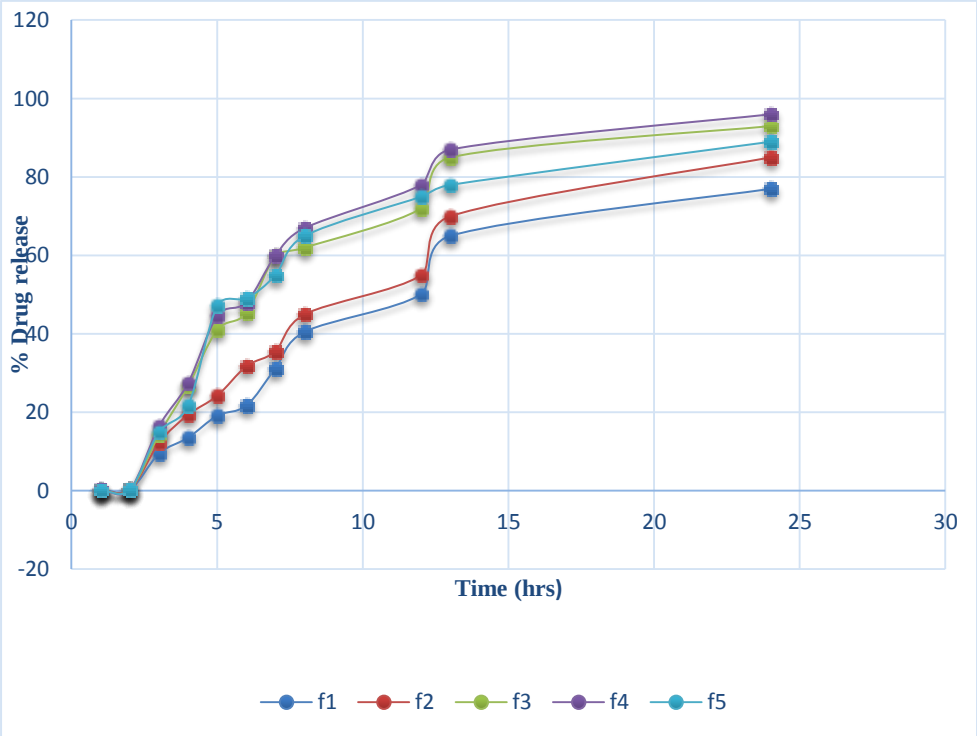

Figure: 2 *In-vitro* drug release

Study of drug release kinetics:

Different kinetic models was applied to the released data of formulations to determine the drug release kinetics based on the regression coefficient obtained and obtained data was tabulated, it is observed that the release from almost all formulations followed Higuchi Kinetics and thus it could be said that the mechanism of release was diffusion rate limited.

Accelerated stability testing:

Stability studies were conducted at 40^0C / 75% RH for 3 months in stability chamber (Thermo lab). Samples were collected at the end of 0 month, 1 month, 2 months, 3 months and assayed for determining drug degradation and the assay value was 98.9% after 3 months.

Ex-vivo studies:

To strengthen the *in vitro* release study finding, *ex vivo* targeting efficiency study was carried out using formulation 1:5. It is shown from the X-ray studies that the microspheres remained in the stomach for the first 2 h and remained intact. Then it has reached large intestine and then reached colon and remained intact for 5 h and disintegrated in the 10 h.

From the obtained results it can be confirmed that Eudragit S100 can be successfully used for colon specific drug delivery.

CONCLUSION:

Piroxicam loaded Eudragit microspheres were ideal for colon targeting.

REFERENCES:

1. Kataria Sahil, Middha Akanksha, Sandhu Premjeet, Ajay Bilandi, Bhawana Kapoor. (2011), Microsphere: A Review. International Journal of Research in Pharmacy and Chemistry; 1(4): 2231-2781.
2. Prasanth v.v, Akash Chakraborthy Moy, Sam T Mathew, Rinku Mathapan. (2011), Microspheres- An Overview. International Journal of Research in Pharmaceutical and Biomedical Sciences; 2(2):2229-3701.
3. Alagusundaram. M, Madhu. Sudan Chetty.C, Uma shankari.K, Attuluri Venkata Badarinath, Lavanya. C, Ram Kanth. S. (2009), Microspheres as a Novel Drug Delivery System- A Review. International Journal of Chem Tech Research; 1(3): 0974-4290.
4. Sam. M.T, Gayathri. D.S, Prasanth. V.V, Vinod. B. (2008), NSAIDs as Microspheres. Internet Journal of Pharmacology; 6(1): 13-28.

5. Giunchedi. P, Conti. B, Magi. L, Conte. U. (1994), Cellulose acetate butyrate and poly caprolactone for Ketoprofen spray dried microspheres preparation. Journal of Microencapsulation; 11(4): 381-393.