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Research Article

Formulation and characterization of floating microspheres of ibuprofen

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ABSTRACT

Floating drug delivery system (FDDS) is one of the novel drug delivery system (NDDS). Floating drug delivery system have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting gastric emptying rate for a prolong period of time. Ibuprofen is nonsteroidal anti-inflammatory drugs (NSAIDS) with short elimination halflife. Floating microspheres of ibuprofen were prepared by solvent evaporation method using Ethylcellulose as polymer, cyclohexane, tween80 and dichloromethane. In this formulation tween80 was used in different concentration. The floating microspheres was evaluated such as micromeritic properties, particle size distribution, percentage yield, incorporation efficiency, IR spectroscopy, scanning electron microscopy and drug release of microspheres. Result showed that as the concentration of tween80 increased it affected the particle size, percentage yield, incorporation efficiency and drug release of microspheres. The micromeritic properties were found to be good and scanning electron microscopy confirmed their hollow structure with smooth surface. Formulation F4 which exhibited excellent micromeritic properties, percentage yield, incorporation efficiency, and percentage drug release was 61.84% for period of 12 hours. Result of our present study suggests that floating microspheres of ibuprofen can be successfully designed to develop sustained drug delivery which can reduce dosing frequency.

Key words: FDDS, NDDS, NSAIDs, Ibuprofen, Floating microspheres

INTRODUCTION

Floating Drug Delivery Systems (FDDS) or Hydrodynamically Balanced Systems (HBS) are among the several approaches that have been developed in order to increase the gastric residence time (GRT) of dosage forms[1–3]. Both single and multiple unit systems have been developed. The single-unit floating systems are more popular but have a disadvantage owing to their 'all-or-nothing' emptying process leading to high variability of the gastrointestinal transit time[4,5]. Still, the multiple-unit dosage forms may be better suited because they are claimed to reduce the inter subject variability in absorption and lower the probability of dose dumping[6]. Such a dosage form can be distributed widely throughout the gastrointestinal tract (GIT), affording the possibility of a longer lasting and more reliable release of the drug from the dosage form[7]. Both natural and synthetic polymers have been used to prepare floating microspheres. Kawashima *et al.* prepared hollow microspheres or micro balloons of ibuprofen by the emulsion-solvent diffusion method using acrylic polymers[8]. The microspheres exhibited good *in vitro* floatability and drug release decreased drastically with increasing polymer concentration. Floating microspheres of cellulose acetate loaded with four different drugs were prepared using the solvent diffusion-evaporation method[9]. The microspheres remained buoyant for more than 12 hours. Methylcellulose and chitosan micropellets loaded with lansoprazole had a lower density than gastric contents and exhibited better encapsulation efficiencies[10]. Other polymer solution systems that have been used to prepare floating microspheres are polycarbonate/dichloromethane[11, 12], cellulose acetate butyrate/Eudragit RL100 mixture in acetone[13] and Eudragit S100/*i*-propanol[14].Ibuprofen is a non-steroidal anti-inflammatory drug, which possesses analgesic and mild antipyretic action, because of its short half-life (1-3 hours) it was selected as model in this study[15]. Its activity is more than indomethacin, naproxen and other NSAIDS. Ibuprofen mediating the inflammation by acting on cyclooxygenase and it inhibit the lipoxygenase pathway, these decreases the production of leukotrienes by the leukocytes and the synovial cells. It also masks T cell suppressing the production of rheumatoid factors. Most frequent adverse effects occurring with

ibuprofen are gastro intestinal disturbance; peptic ulceration and gastrointestinal bleeding have been reported. Hypersensitivity reaction, abnormalities of liver function including intestinal nephritis or the nephritic syndrome. Sustained drug delivery of ibuprofen will reduce these toxicities considerably by maintaining a low and constant level of drug in the blood[16, 17].

MATERIALS AND METHODS

Material

Ibuprofen (Sun Pharma Baroda), Ethylcellulose (SD fine chemicals Ltd. Mumbai, India), Dichloromethane (Rankem), Cyclohexane (Rankem), Tween 80 (Thomas baker Pvt. Limited), HPLC water (Rankem), HPLC grade methanol (Qualigens), Whatman filter paper , Mechanical stirr (Remi motor), double beam spectrophotometer (Systronic), Electronic balance (Vibra & Essae). All other chemical and reagent used in this study were of analytical grade.

Method

Floating microspheres were prepared by solvent evaporation method using distilled water containing tween 80 as continuous phase. The drug and polymer are weighed (as shown in table 1) the polymer was dissolve into dichloromethane and Drug was dissolve into cyclohexane. Polymer solution was codissolve into drug solution at room temperature. The mixture was stirr vigrously to form uniform drug polymer dispersion. The above organic phase was slowly added to 70 ml distilled water containing 0.001% ,0.002% 0.003%.and 0.004% tween 80 by maintain the temperature at 15 – 20°C and emulsified by stirring at 2000 rpm for 15 min. microspheres formed were filtered, washed with water and dried overnight for 40°C.[18]

Characterization

Yield of Floating microsphere

The prepared floating microspheres were collected and weighed. The measured weight was divided by total amount of all non-volatile components which were used for the preparation of microspheres.[19]

% yield = (Actual weight of product / Total weight of excipients and drug) x 100

Incorporation efficiency

Floating microspheres were dissolved in a minimum amount of methanol and drug was extracted into suitable aqueous media (0.1N hydrochloric acid) by evaporating methanol. The solution was filtered through 0.45 µ membrane filter paper, diluted suitably and analyzed for drug content spectrophotometrically at 220 nm using 0.1N hydrochloric acid as blank**.**[20]

Micromeritic properties

The floating microspheres are characterized by their micromeritic properties such as particle size distribution, tapped density, carr's index and angle of repose, and Hausner's ratio.

Infrared spectroscopy

Infrared spectra of ibuprofen, ethylcellulose, and formulations F2 and F4 were carried out by using KBr pellete technique and were recorded on a Perkin Elmer spectrum II FT-IR spectrometer (SAIF, Lucknow, India**).**[21]

Scanning electron microscopy

Dry microspheres were placed on an electron microscope brass stub an coated with gold in an ion sputter. Then picture of microsphere were taken by random scanning of the stub. The SEM analysis of the microspheres was carried out by using LEO – 430 Sturning electron microscope limited Cambridge (Birbal Sahni institute of Palaeobotony 53, university road, Lucknow, India). The microspheres were viewed at an accelerating voltage of 15KV[21].Magnification 1.26KX, 3.00X and 4.00KX detector SE1.

In-vitro Drug release

Drug release from floating microsphere equivalent to 100 mg of drug was carried out using Dissolution appratus XXIV for the first 2 hrs in pH 1.2 with 0.01% tween 80 and 10 hrs in 0.1N HCL buffer (pH 1.2) with 0.01% tween 80. 5 ml of samples were withdrawn at different time intervals and replaced with fresh phosphate buffer; the amount of drug release was analyzed at 220 nm using double beam spectrophotometer (Systronic).[22]

RESULTS AND DISCUSSION

Yield of microspheres

The percentage yield of microspheres was in range 66.91 ± 0.28 to 70.10 ± 0.28 (as shown in table 2). To observe the effect of surfactant concentration on the percentage yield of the resulting microspheres formulation. The percentage yield of microspheres was found to be increased with increasing tween 80 concentrations.

Incorporation efficiency

The incorporation efficiency of formulation F1 to F4 was carried out and found to be in range 72.63 to 89.13 (as shown in table 2).

Micromeritic properties

The particle size distribution of floating microspheres formulation F1 to F4 was found to be 0.06026 to 0.06409 (as shown in table 3). The effect surfactant concentration on the particle size distribution of floating microspheres was found to be increased with increasing concentration of tween 80 (as shown in table 1). The bulk density and tapped density values of formulation F1 to F4 ranges from 0.0561 to 0.0395 gm/cm³ and 0.0842 to 0.0469 gm/cm³ respectively. The Carr's index ranges between 33.33 to 15.38. The values of Carr's index indicate good flow property.

Infrared spectroscopy

The FT-IR spectra study showed no change in the finger print of pure drug spectra, thus confirming absence of drug and polymer interaction.

Scanning electron microscopy (SEM)

Morphology of floating microspheres was examined by scanning electron microscopy. The view of the microspheres showed hollow structure with a smooth surface morphology exhibited range of sizes within each batch. The outer surface of microspheres was smooth and dense, while the internal surface was porous. The shell of microspheres also showed some porous structure it may be caused by evaporation of solvent entrapped within the shell of microsphere after forming smooth and dense layer.

In-vitro Drug release

The drug release from formulation F1 to F4 was as follows. F3 and F4 showed percentage drug release 60.26 to 61.84 at end of 12 hour and formulation F2 and F1 showed percentage drug release 54.38 to 58.70 at end of 12 hr. Among all formulation, F4 was found to be the best formulation as it release ibuprofen in a sustained manner with constant fashion over extended period of time (after 12 hr).

Table 1 - Formulation table of floating microspheres of Ibuprofen

Ingredients	Formulation code			
	F1	F2	F3	F4
Ethylcellulose (mg)	100	100	100	100
Ibuprofen (mg)	50	50	50	50
Dichloromethane (ml)	20	20	20	20
Cyclohexane (ml)	10	10	10	10
Tween 80 (ml)	70 (0.001%)	70 (0.002%)	70 (0.003%)	70 (0.004%)

Table 2 -- Percentage yield and incorporation efficiency of ibuprofen

Formulation code	Percentage yield	Incorporation efficiency
F1	66.91 ± 0.28	72.63
F2	67.86 ± 0.20	80.37
F3	68.69 ± 0.34	86.24
F4	70.10 ± 0.28	89.13

Table 3 - Micromeritic properties of floating microspheres of ibuprofen

Formulation code	Particle size distribution (µm)	Bulk density (gm/cm³)	Tapped density (gm/cm³)	Carr's index	Hausner's ratio
F1	0.06026	0.0561	0.0842	33.33	1.5
F2	0.06371	0.0478	0.0675	28.57	1.4
F3	0.06387	0.0448	0.0575	21.73	1.3

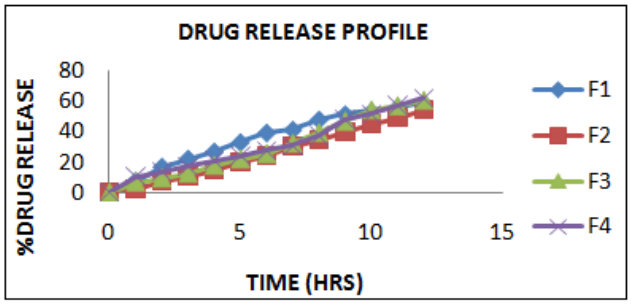

Figure 1 - In-vitro drug release profile of floating microspheres of ibuprofen formulation F1 to F4

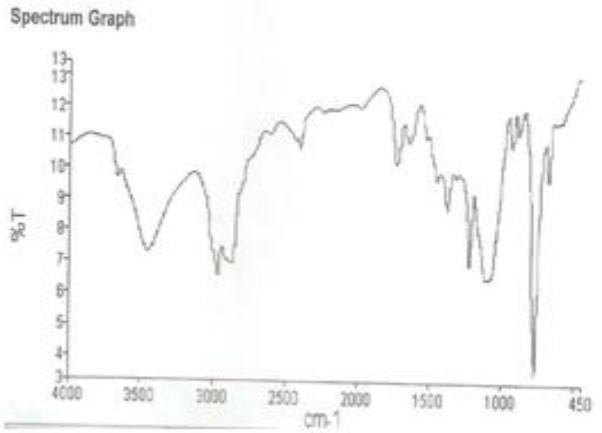

Figure 2 - IR spectra of Ethylcellulose

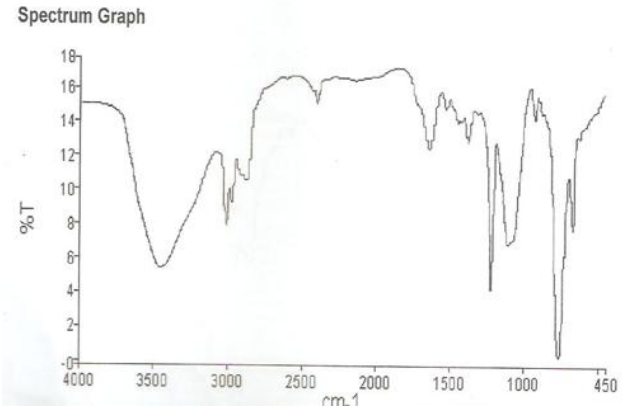

Figure 3 - IR spectra of F2

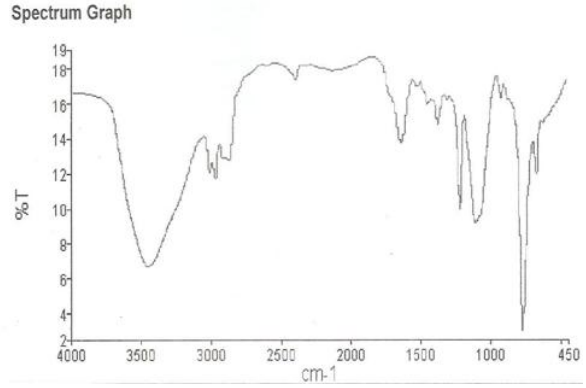

Figure 4 - IR spectra of F4

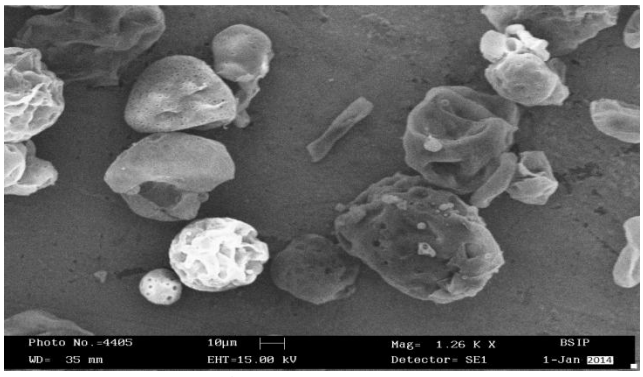

Figure 5 - SEM F1

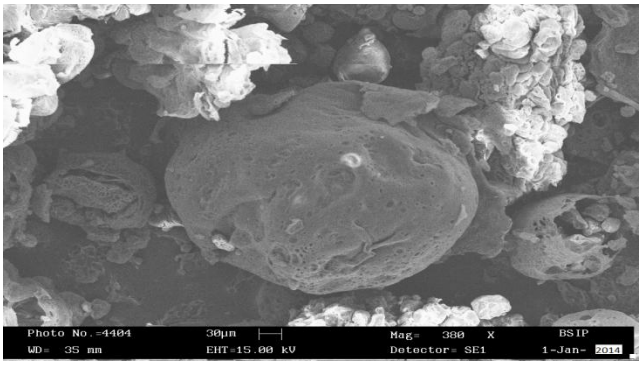

Figure 6 - SEM F2

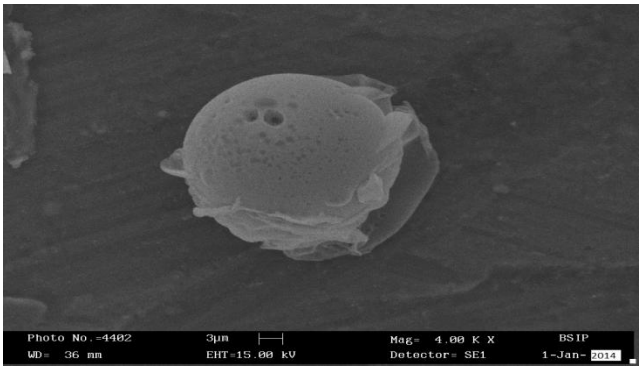

Figure 7 - SEM F4

CONCLUTION

The purpose of present work was to develop floating microspheres of ibuprofen for sustained drug delivery. From the results it seem that formulation F4 was found to be satisfactory in terms of excellent micromeritic properties, yield of microsphere (70.10%), incorporation efficiency (89.13%) and highest in vitro drug release of 61.84% in a sustained manner with constant fashion over extended period of time for 12 hrs. it was observed that concentration of tween80 affected all the evaluation parameter significantly. Hence the prepared floating microspheres of ibuprofen may prove to be potential candidate for safe and effective sustained drug delivery.

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