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FLOATING MICROSPHERES OF CURCUMIN: FORMULATION, CHARACTERIZATION AND *IN VITRO* EVALUATION

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ABSTRACT

The objective of the present study was to develop floating microspheres of curcumin in order to achieve an extended retention in the upper GIT, which may result in enhanced absorption and there by improved bioavailability. The microspheres were prepared by solvent evaporation method using polymers such as hydroxyl propyl methyl cellulose (HPMC K 15 M), ethyl cellulose in different ratios and curcumin in each formulation. *In vitro* drug release were performed by USP apparatus type I and the microspheres were characterized by polymer compatibility by using FT-IR. The yield, particle size, Buoyancy percentage, drug entrapment efficiency, and *in vitro* drug release were studied. The result showed that microspheres yielded 63.81-64.36%. The particle size was distributed between14.60-20.76 µm, drug entrapment efficiency was 57.4-63.8%, and Buoyancy percentage was 48.3-68.3%. The best drug release profiles were seen with formulation 5 at the ratio of drug to polymer of 1:6.

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 intersubject 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).

Curcumin was used as model drug. Curcumin a bioactive natural product. It is used in treating in gastric and duodenal ulceration and also used as antibacterial, antiprotozoal, antiviral, hypolipemic, hypoglycemic, anticoagulant, antioxidant. It is poorly absorbed from the gastro intestinal tract and has a short elimination half life (8,9). The objective of the present study was to develop floating microspheres of curcumin in order to achieve an extended retention in the upper GIT, which may result in enhanced absorption and thereby improved bioavailability. The prepared microspheres were evaluated for size, *in vitro* curcumin release, buoyancy and incorporation efficiency. The effect of various formulation variables on the size and drug release was investigated.

EXPERIMENTAL

Material and apparatus

Curcumin was obtained as gift sample from konark herbal. Hydroxy propyl methyl cellulose (HPMC), Ethyl cellulose (EC), Dichloromethane (DCM), Ethanol, Conc. Hydrochloric acid (HCl), and Tween 80 were obtained from merck company.

U.V\ VS spectrophotometer (Systronic), was used for drug analysis.

Preparation of microspheres

Microspheres were prepared by the solvent evaporation technique as employed by Struebel *et al.* (16). Curcumin, HPMC and EC were dissolved in a mixture of ethanol and dichloromethane at room temperature (Table I). This was poured into 250 ml water containing 0.01% Tween 80 maintained at a temperature of 30–40 °C and subsequently stirred at 300 rpm for 20 min to allow the volatile solvent to evaporate. The microspheres formed were filtered, washed with water and dried in vacuum

Characterization of microspheres

Size and shape of microspheres – The size of microspheres was determined using a microscope fitted with an ocular micrometer and stage micrometer. Scanning electron microscopy (SEM) (IIT KARAGPUR) was performed to characterize the surface of formed microspheres.

Buoyancy percentage – Microspheres (0.3 g) were spread over the surface of a USP XXIV dissolution apparatus (type II) filled with 900 ml 0.1 mol L–1 HCl containing 0.02% Tween 80 (17). The medium was agitated with a paddle rotating at 100 rpm for 8 h. The floating and the settled portions of microspheres were recovered separately. The microspheres were dried and weighed. Buoyancy percentage was calculated as the ratio of the mass of the microspheres that remained floating and the total mass of the microspheres.

Incorporation efficiency (IE) – To determine the incorporation efficiency, microspheres were taken, thoroughly triturated and suspended in a minimal amount of alcohol. The suspension was suitably diluted with water and filtered to separate shell fragments. Drug content was analyzed spectrophotometrically at 488 nm.

In vitro release – A USP basket apparatus has been used to study *in vitro* drug release from microspheres (18–20). In the present study, drug release was studied using a modified USP XXIV (17) dissolution apparatus type I (basket mesh # 120, equals 125 _m) at 100 rpm in distilled water and 0.1 mol L–1 HCl (pH 1.2) as dissolution fluids (900 ml) maintained at 37 ± 0.5 °C. Withdrawn samples (10 ml) were analyzed spectrophotometrically at 488nm. The volume was replenished with the same amount of fresh dissolution fluid each time to maintain the sink condition. All experiments were performed in triplicate.

Linear regression was used to analyze the *in vitro* release mechanism.

Table I. Batch specifications of the prepared microsphere

Batch code	Polymer ratio (HPMC\EC)	Temperature C˚	Solvent ratio (alcohol\DCM)
F1	1:2	30-40	1:1
F2	1:3	30-40	1:1
F3	1:4	30-40	1:1
F4	1:5	30-40	1:1
F5	1:6	30-40	1:1

RESULTS AND DISCUSSION

Floating microspheres were prepared by the solvent evaporation method using HPMC and EC (Table I). The SEM photographs showed that the fabricated microspheres were spherical with a smooth surface and exhibited a range of sizes within each batch (Fig. 1). The microspheres floated for prolonged time over the surface of the dissolution medium without any apparent gelation. Buoyancy percentage of the microspheres was in the

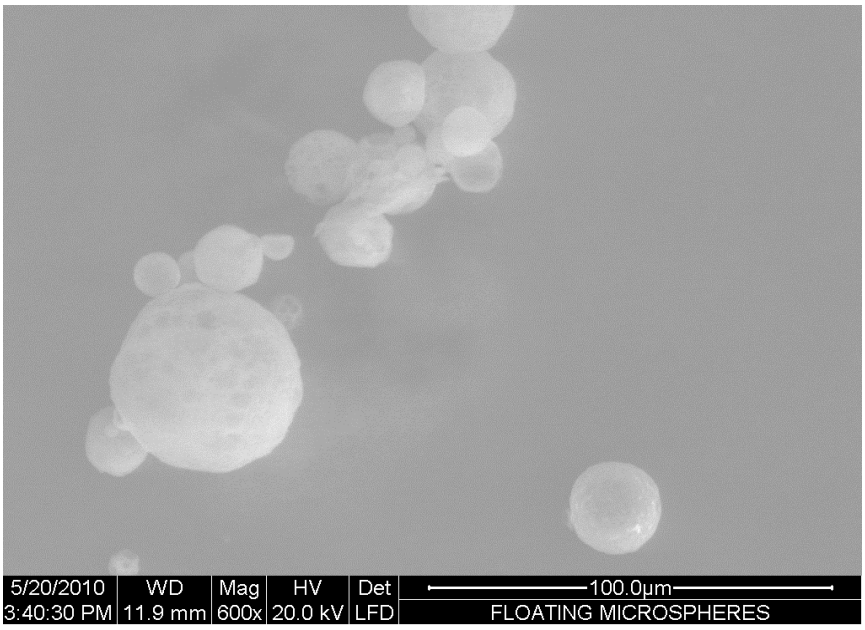
range 48.3(batch F1) to 68.3(batch F5) (Table II).

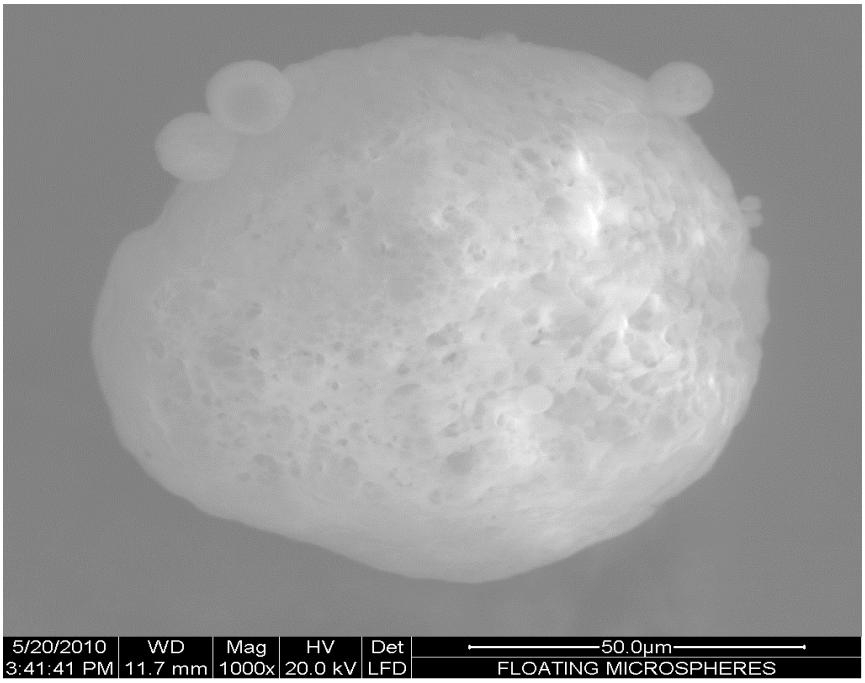
Microspheres were prepared using a gradually increasing EC concentration in combination with a fixed concentration of HPMC to assess the effect of polymer concentration on the size of microspheres. The mean particle size of the microspheres significantly increased with increasing ethyl cellulose concentration and was in the range

14.60 µm to 20.76 µm (Table II). The viscosity of the medium increases at a higher polymer concentration resulting in enhanced interfacial tension. Shearing efficiency is also diminished at higher viscosities (21, 22). This results in the formation of larger particles.

Table II. Various formulation parameters for microspheres

Batch code	Mean particle size (um)	Incorporation efficiency (%)	Buoyancy (%)
F1	14.60	57.4	48.3
F2	14.92	58.1	55
F3	18.29	60.9	65
F4	18.80	61.7	66.6
F5	20.76	63.8	68.3

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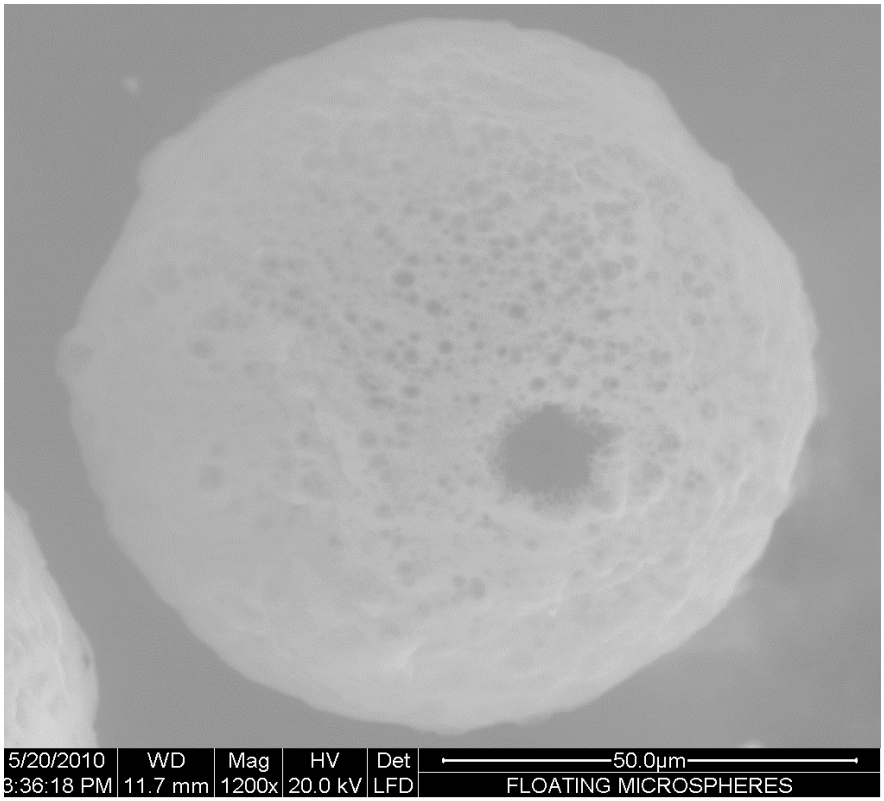
FLOATING MICROSPHERES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FLOATING MICROSPHERES

Fig. 1.Scanning electron microphotografof floating microspheres (batch F5). The size range of microspheres.

In vitro Curcumin release studies were performed in 0.1 mol L–1 HCl for 12 h. The cumulative release of Curcumin significantly increased with increasing ethyl cellulose concentration.

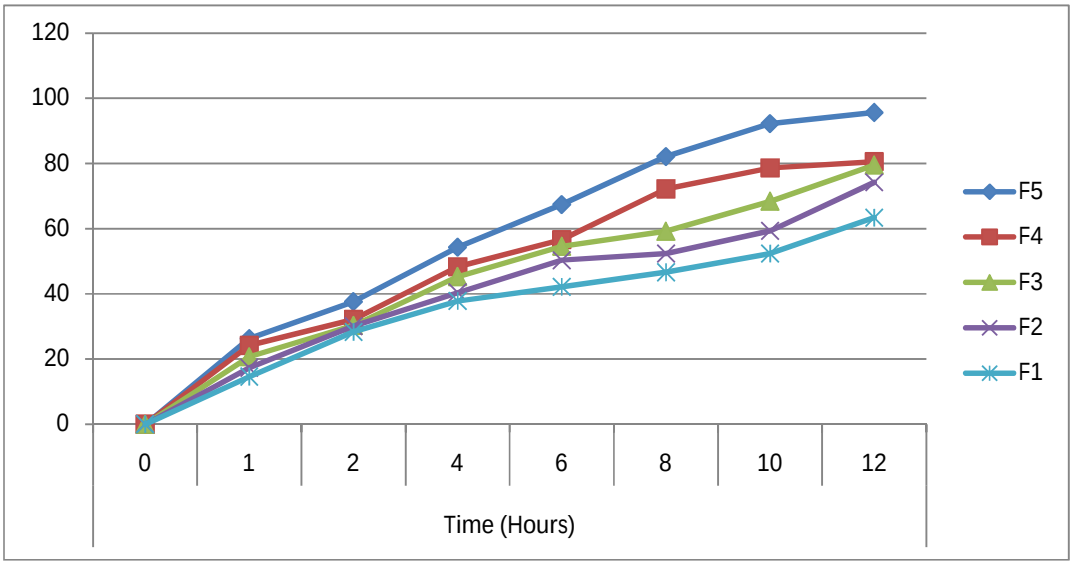

Fig. 2. Cumulative Percent Drug Release

CONCLUSIONS

In vitro data obtained for floating microspheres of curcumin showed excellent floatability, good buoyancy and prolonged drug release. Microspheres of different size and drug content could be obtained by varying the formulation variables. Diffusion was found to be the main release mechanism. Thus, the prepared floating microspheres may prove to be potential candidates for multiple-unit delivery devices adaptable to any intragastric condition.

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