Research Article

Fabrication of tulsi extract loaded microballoons: *In vitro* characterization and antimicrobial potential

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ABSTRACT

The floating microballoons are being commonly utilized to obtain prolonged gastric residence time. The objective of this study involves development and characterization of tulsi extract loaded floating microballoons. Tulsi extract loaded microballoons were prepared by the solvent evaporation technique at different concentrations of polymers (hydroxypropyl methyl cellulose [HPMC] K4M) and ethyl cellulose (EC) in organic solvent system. Microballoons were characterized for their particle size, surface morphology, production yield, loading efficiency, buoyancy percentage, and *in vitro* drug release studies. Characterization observations drawn shows increase in polymer concentration increases particle size, loading efficiency, and buoyancy percentage, and drug release. Formulation (F3) was observed to show optimized results for particle size, particle yield, loading efficiency, buoyancy percentage, and *in vitro* drug release. The *in vitro* release studies result showed that formulation comprising higher proportion of EC exhibited much retarded drug release as compared to formulation comprising higher proportion of concentrations of HPMC K4M.

Keywords: Antibacterial potential, ethyl cellulose, microballoons, percentage buoyancy

Introduction

The most preferred route for the administration of drugs is oral route. Drugs administered orally have several physiological limitations, such as gastrointestinal (GI) transit time, incomplete drug release, and short residence time of the pharmaceutical dosage forms in the absorption region of GI tract.[1] Bioavailability of sustained-release dosage forms lowers due to these factors and even if slow release of drug is attained, the drug released after passing the absorption site is not utilized, thus lowering the efficacy of the drug. Floating drug delivery systems or hydrodynamically balanced systems are among the several approaches that have been developed to increase the gastric residence time of dosage forms. Both single and multiple unit systems have been developed.[2] The single unit floating systems have a disadvantage of owing to their "all-or-nothing" emptying process leading to high variability of the GI transit time. Still, the multiple unit dosage forms are better suited because they reduce the inter variability in absorption and lower the probability of dose dumping.[3] For preparation of floating microspheres, both natural and synthetic polymers are used. Polycarbonate/dichloromethane, Eudragit S100/i-propanol, and CAB/Eudragit RL mixture in acetone are the most popular polymeric systems used for preparation of microballoons.

Microballoons are spherical empty particles having internal hollow structure with air inside. Microballoons incorporating a drug dispersed or dissolved throughout particle matrix have the potential for controlled release of drugs. Certain types of drugs can benefit from using gastroretentive devices.[4]These includes the drugs acting locally in the stomach; drugs that are primarily absorbed in the stomach; drugs which are poorly soluble at an alkaline pH; drugs with a narrow window of absorption; drugs absorbed rapidly from the GI tract and drugs that degrade in the colon.

Tulsi is described as sacred and medicinal plant in ancient literature. The name tulsi is derived from "Sanskrit," which means "matchless one." It belongs to the family *Labiatae*, having botanical name *Ocimum sanctum* (Linn). Tulsi is available in two types - Vanya (wild) and gramya (grown in homes). They both have identical uses, but the former has darker leaves.[5] Tulsi is a popular home remedy for various ailments such as wound, bronchitis, liver diseases, catarrhal fever, otalgia, lumbago, hiccough, ophthalmic, gastric disorders, genitourinary disorders, skin diseases, various forms of poisoning, and psychosomatic stress disorder. It is also hasaromatic, stomachic, carminative, demulcent, diaphoretic, diuretic, expectorant, alexiteric, vermifuge, and febrifuge properties.[6] In view of these facts, an attempt has been made to use the various

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pharmacological activities of the herb into novel drug delivery system. Therefore, tulsi extract was chosen as drug of choice in treatment of gastric ulcers as sustained release oral dosage form. Thus, the aim of this research work was to design, develop, and characterize tulsi extract loaded floating microballoons.

Materials and Methods

Materials

Tulsi extract (Manufactured by Vivaan Herbals and Healthcare, Ahmedabad) was purchased from the local pharmacy, Noida. Ethyl cellulose (EC), hydroxypropyl methylcellulose (HPMC K4M), and Tween 80 were purchased from the Central Drug House, New Delhi, India. All other solvents and chemicals were of analytical grade.

Methods

Preparation of microballoons

Microballoons were prepared by the solvent evaporation technique. Tulsi extract, HPMC K4M, and EC were dissolved in a mixture of ethanol and dichloromethane at room temperature as discussed in Table 1. These were poured into 250 ml water containing 0.01% Tween 80 maintained at a temperature 30-40°C and were subsequently stirred so as to allow the evaporation of volatile solvent.[7] The prepared microballoons were filtered, washed with water, and dried at 40°C.

Characterization of tulsi extract loaded microballoons

Particle size

The size of microballoons of every formulation was observed using a microscope fitted with an ocular micrometer, and stage micrometer and average particle size was measured.[8]

Shape and surface morphology

Scanning electron microscopy (SEM) technique was used for determining the surface morphology of the microballoons. The SEM sample was prepared by sprinkling the powder on the tape stuck attached to aluminum stub. The stubs were coated using the mixture of gold and palladium at a thickness of 250-450 Å under an argon atmosphere in high vacuum evaporator at a voltage of 20 KV, current 10 mA, and low pressure.[9] Photomicrographs were taken on random screening of coated samples using SEM.

Percent loading efficiency and percentage yield

About 20 mg of hollow microspheres were weighed and triturated thoroughly ant were dissolved with 10 ml of ethanol in volumetric flask. The volume was made up using 0.1 N HCl. The resulting mixture was filtered using Whatman Filter Paper No. 44 and further diluted to measure absorbance at 470 nm and 0.1 N HCl was taken as blank.[10] The percentage drug entrapment was calculated as follows:

$$\text{Percent loading efficiency} = \frac{\text{Amount of drug actually present}}{\text{Theoretical drugload expected}} \times 100$$

$$\text{Percentage yield} = \frac{\text{Total weight of hollow microspheres}}{\text{Total weight of all nonvolatile component}} \times 100$$

In vitro buoyancy

The buoyancy test of the microballoons was carried out using USP II (paddle type) dissolution apparatus. Dissolution test solution of simulated gastric fluid (SGF) containing Tween 80 (0.02% v/v) was used as a dispersion medium to simulate gastric fluid. The microballoons were spread over the surface of the SGF, pH 1.2 (900 ml, 37 ± 0.5°C), which was agitated by a paddle rotated at 100 rpm for 12 h. After agitation for a previously determined interval, the microballoons that were floating and the ones that settled to the bottom of the flask were recovered separately. After drying, the fraction of the microballoons was weighed.[11] The % buoyancy of the microballoons was calculated by the following formula:

$$\% \text{ Buoyancy} = \frac{\text{Weight of floating microballoons after drying}}{\text{weight of floating + settled microballoons after drying}} \times 100$$

In vitro drug release studies

The *in vitro* drug release from microballoons was determined using USP II dissolution apparatus. The dissolution test was performed using 0.1 NHCl (pH 1.2) as dissolution fluid (900 ml) maintained at 37 ± 0.5°C at 100 rpm. The samples (5 ml) of the solution were withdrawn from the dissolution apparatus for 12 h, and the samples were replaced with fresh dissolution medium each time to maintain the sink condition. Withdrawn samples were analyzed using ultraviolet visible double beam spectrophotometer at 470 nm against suitably constructed calibration curve.[12] All measurements were carried out in triplicate, and average values were plotted.

Results and Discussion

The formulation of tulsi extract loaded floating microballoons was successfully carried out by utilizing HPMC K4M and EC as sustained release polymers via solvent evaporation technique. Solvent mixture,

Table 1: Formulation table for tulsi extract loaded microballoons

Formulation code	HPMC K4M (mg)	EC (mg)	Solvent ratio (ethanol+dichloromethane)	Tween 80 (%)	Tulsi extract (ml)
F1	250	250	1:1	0.01	2
F2	250	450	1:1	0.01	2
F3	450	650	1:1	0.01	2
F4	450	250	1:1	0.01	2
F5	650	450	1:1	0.01	2
F6	650	650	1:1	0.01	2

HPMC: Hydroxypropyl methyl cellulose, EC: Ethyl cellulose

Table 2: Characterization of tulsi extract loaded microballoons

Parameters	Formulation code					
	F1	F2	F3	F4	F5	F6
Particle size	70.31±1.27	72.89±1.75	81.96±1.93	85.32±2.15	99.22±2.07	108.39±1.32
Production yield	73.65±1.43	76.27±1.05	78.06±2.76	77.79±1.23	80.32±2.41	82.38±1.15
Percentage loading efficiency	73.35±0.619	74.42±0.22	75.23±1.23	76.12±0.987	78.37±1.76	79.29±1.59
Percent buoyancy	71.72±1.45	73.92±2.32	75.39±1.89	74.58±0.13	86.23±0.49	88.14±0.94
In vitro drug release	92.39±1.04	87.73±2.75	84.12±2.08	89.29±1.76	90.38±1.23	88.12±1.07

All the readings are in triplicate (mean±standard deviation)

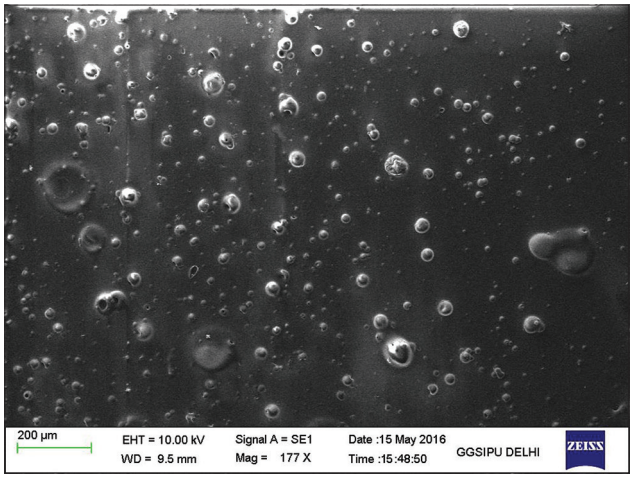

Figure 1: Scanning electron microscopy photomicrograph of tulsi extract loaded microballoons

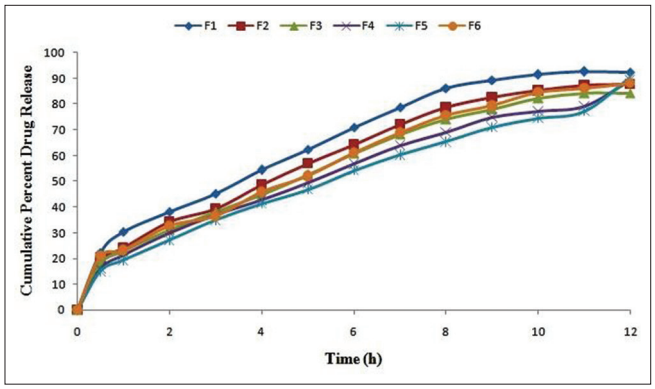

Figure 2: *In vitro* drug release profiles of tulsi extract loaded microballoons

i.e., ethanol and dichloromethane were employed to make polymeric solution. Several formulations were made by varying the concentration of EC and HPMC K4M. From the results of particle size, the particle size of all microballoons preparations were found to be in the range of 70.31 nm ± 1.27 to 108.39 nm ± 1.32 as shown in Table 2. The reason for an increase in particle size may be attributed to increase in polymeric concentration which in turn makes the solution viscous.[13] Stirring efficiency in viscous solution decreases which causes large microparticles to be formed. The SEM photomicrographs showed that the fabricated microballoons were spherical and exhibited a porous surface to ease diffusion of fluid inside the microballoon.[14,15] The SEM photomicrograph of tulsi extract loaded microballoon is shown in Figure 1. Production yields were found to be in the range of 73.65 ± 1.43, 76.27 ± 1.05, 78.06 ± 2.76, 77.79 ± 1.23, 80.32 ± 2.41, and 82.38 ± 1.15 for all microballoons formulations as shown in Table 2. The percent loading efficiency of prepared microballoons was in the limit of 73.35 ± 1.27 to 79.29 ± 2.12. The buoyancy percentage for all batches was almost above 70%, which was studied for 12 h. The highest percentage was obtained with formulation F6. Average buoyancies in percentage were found to be in the range of 71.72 ± 0.45% to 88.14 ± 0.34% for F1 to F6 formulations. In general, as quantity of polymer increases, buoyancy percentage also increases.[16] During formation of microballoons, volatile solvent evaporates from the polymeric mixture leaving behind the hollow microballoon. The *in vitro* release studies of tulsi extract loaded microballoons demonstrated release in the range of 84.12-92.39% up to 12 h. Results displayed that the concentration of polymer in formulation is the main aspect governing the drug release from microballoon formulation. An increase in diffusional path length may be the reason with increase in polymer concentration. This may retard the overall release of drug from polymer matrix. The release profile of tulsi extract from microballoons for all formulations was shown in Figure 2.

Conclusion

The optimized formulation for tulsi extract loaded microballoons was obtained with high range of EC and a medium range of HPMC K4M. The drug release from all the formulations displayed a sustained release pattern which could offer both local and systemic actions.

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