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FORMULATION OF INVITRO EVALUATION OF GASTRO RETENTIVE DRUG DELIVERY OF GLYCERRHIZA EXTRACT

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ABSTRACT

Gastro retentive systems can remain in the stomach region for several hours and can significantly prolong the gastric residence time of drugs thereby improving the drug bio-availability. Floating Drug Delivery Systems promises to be a potential approach for gastric retention. Floating tablets of Glycerrhiza extract were prepared by direct compression method using HPMC of various grades and sodium bicarbonate as gas forming agent. Floating tablets were evaluated for floating lag time, drug content and invitro dissolution profile. The lag time ranged between 29-4140 sec and buoyancy time for the formulations remained 24 hrs. The drug content was found to be under limits, Drug release percentage was between 31.56-50.54 in 8 hrs and kinetic studies showed the formulations fitting all the models similarly. From the study it is evident that a promising controlled release by floating tablets of Glycerrhiza extract can be developed and different excipient ratios affected the drug release and floating time. Further detailed investigations are required to establish the invivo efficacy of the formulations.

KEY WORDS: Floating tablets, Gastroretentive drug delivery, Hydroxy Propyl Methyl Cellulose, Glycerrhiza extract.

INTRODUCTION

Gastric emptying of dosage forms is an extremely complex process and ability to prolong and control the emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms. Several difficulties are faced in designing controlled release systems for better absorption and enhanced bioavailability. One of such difficulties is the inability to confine the dosage form in the desired area of the gastrointestinal tract. Prolonging gastric retention of the dosage form extends the time for drug absorption therefore improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. Gastro retentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. The controlled gastric retention of solid dosage forms may be achieved by the mechanisms of mucoadhesion[1,2], flotation[3], sedimentation , expansion[7], modified shape systems, or by the simultaneous administration of pharmacological agents that delay gastric emptying[4,5].

FDDS promises to be a potential approach for gastric retention. Although there are number of difficulties to be worked out to achieve prolonged gastric retention, a large number of companies are focusing toward commercializing this technique. The following approaches have been used for the design of floating dosage forms of single and multiple-unit systems[12]. Floating drug delivery systems are classified depending on the use of formulation variables as effervescent and non-effervescent systems[6,7].

Recently sustained release floating capsules of Nicardipine hydrochloride were developed and were evaluated in vivo. The formulation compared with commercially available MICARD capsules using rabbits. Plasma concentration time curves showed a longer duration for administration (16 hours) in the sustained release floating capsules as compared with conventional MICARD capsules (8 hours)[8,9].

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These systems are particularly advantageous for drugs that are specifically absorbed from stomach or the proximal part of the small intestine, eg. Riboflavin and Furosemide. Furosemide is primarily absorbed from the stomach followed by the duodenum. It has been reported that a monolithic floating dosage form with prolonged gastric residence time was developed and the bioavailability was increased. AUC obtained with the floating tablets was approximately 1.8 times those of conventional furosemide tablet[10,11].

In present investigation, Glycerrhiza extract is formulated as the gastroretentive drug delivery system in the form of floating tablets by using polymers, HPMC K4M, HPMC K15M, and HPMC K100M.

MATERIALS AND METHODS

Materials

Glycerrhiza extract from Tulsi amrit, HPMC (Hydroxy Propyl Methyl Cellulose) HPMC k 4 M, HPMC k 15 M, HPMC k 100 M were gift samples from Matrix laboratories and all the other excipients were bought from SD Fine Chem LTD., Mumbai[12].

Preparation of floating tablets of Glycerrhiza extract

Floating tablets containing Glycerrhiza extract as an active material were prepared by direct compression method by effervescent approach. Briefly drug and HPMC K4M, HPMC K15M, HPMC K100M, Sodium bicarbonate, Lactose and Magnesium stearate were mixed geometrically with each of the polymer. Various formulations were prepared by using different ratios of polymers and floating agent. Sodium bicarbonate acts as a gas-generating agent helpful for floating. These powders were grinded and blended together and punched into tablets in direct compression method by using ELITE multistation punching machine in a die (13 mm diameter) at 50 kg/cm^2 pressure for 1 min to produce floating tablets[13].

Calibration curve of Glycerrhiza extract

In the preformulation studies, the UV-VIS λ-max of Glycerrhiza extract was determined using UV-VIS Spectrophotometre (Shimadzu, Mumbai) and the calibration curve of Glycerrhiza extract was designed by measuring absorbance at 266 nm in 0.1 N HCl making proper dilutions to yield concentration of 1,2,3,4,5 mcg/ml. FTIR Spectral (Fourier Transform Infrared Spectroscopy) studies for the compalibility study of drug to polymers were performed for Pure Drug, polymers and formulation using FTIR spectrophotometer (Thermo Nicolet)[14].

Physical evaluation of tablets

Drug content

Five tablets from each batch were weighed accurately and average weight was calculated. They were ground and accurate amount of powder equivalent to 10 mg of drug was dissolved in 0.1 N HCl and volume was made upto 100 ml. the solution was filtered through Whatmann filter paper No. 41 and aliquots of 1 ml was taken and volume was made upto 10 ml with same dissolution medium. The absorbance was measured at 266 nm using an UV-VIS Spectrophotometre and the concentration of drug was using calibration curve of Glycerrhiza extract[15].

Floating lag time

The floating lag time and invitro buoyancy time of all formulations were determined. The tablet was placed into a beaker containing 100 ml of 0.1 N HCl. The time required for the tablet to float to the surface and float was determined as floating lag time (FLT) and buoyancy time (BT).

Invitro dissolution studies

The release rate of Glycerrhiza extract from floating tablets was performed using apparatus No.2 of the USP, Thermostatically controlled at 37°C ± 0.5°C. The dissolution test was performed using 900 ml of 0.1 N HCl, stirred at 50 rpm. The amount of drug dissolved from floating tablets was determined spectrophotometrically. Cumulative %drug release was calculated using an equation obtained from a standard curve[16].

RESULTS AND DISCUSSION

Absorption spectrum and Calibration curve

UV-VIS Absorption spectrum of Glycerrhiza extract gave a maximum absorption at 266 nm (λmax) as shown in (Figure 2). The calibration of Glycerrhiza extract yielded a curve with slope 0.047 x and R^2 value 0.997.

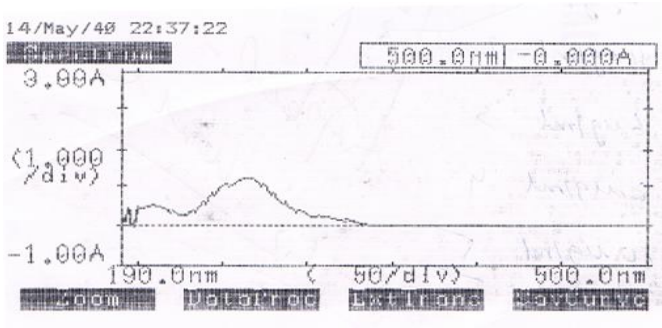

Figure 1. UV-VIS spectrum of Glycerrhiza extract

Drug content

All the formulations were tested for Percentage drug content and the results showed that the drug content in each of the formulation is under limit and uniform. The values accordingly were given in (Table 1).

Floating lag time

The floating tablets of Glycerrhiza extract were prepared by using HPMC K4M, K15M, and K100M. Sixteen different formulations were prepared using different

ratios of polymers. The prepared formulations were evaluated for floating lag time and buoyancy time. Sodium bicarbonate induced carbon dioxide generation in presence of dissolution medium (0.1 N HCl). It was observed that the gas generated is trapped and protected within the matrix, formed by polymers, thus density of the tablet decreased and it becomes buoyant.

Sodium bicarbonate and HPMC K100M had significant effect on lag time of floating tablet. The floating lag time of the formulation f2 was 29 sec (minimum), may be because the ratio of sodium bicarbonate is high and HPMC K100 is low. Lag time of formulation f10 was 4140 sec (maximum), because it contained fewer amounts of Sodium bicarbonate and high amount of HPMC K100.

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Figure 2. *Invitro* buoyancy of formulation f2

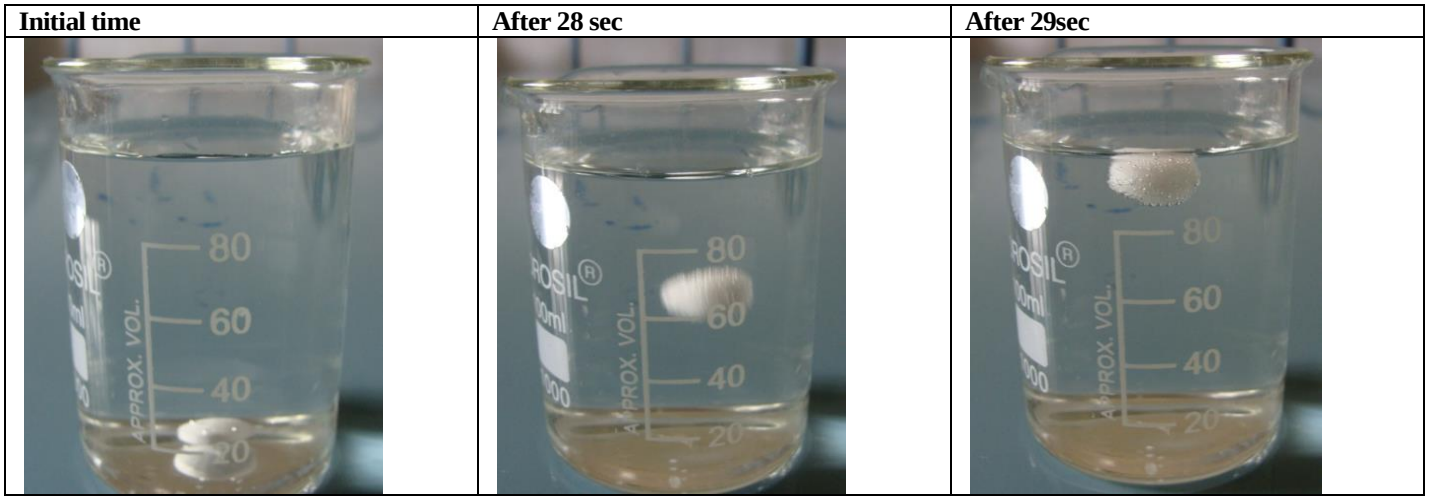

Table 1. Formulation design of Glycerrhiza extract floating tablets

Formulation no.	Ingredients*				Percentage Drug content[a]	floating time (sec)[a]	% Drug release [a]
	Sodium bi-carbonate (mg)	HPMC MK4M (mg)	HPMC MK100M (mg)	HPMC MK15M (mg)			
Form1	25	60	60	30	99.28±0.05	480±3.9	41.18±1.95
Form2	50	60	30	60	98.42±0.7	31±1.02	32.56±2.14
Form3	25	30	30	30	99.03±0.8	58±3.05	38.40±2.43
Form4	50	60	30	30	99.24±0.13	152±3.1	40.05±2.76
Form5	50	30	30	60	102.56±0.47	2283±2.87	43.04±2.94
Form6	25	60	30	30	99.92±0.26	161±2.65	45.73±3.01
Form7	50	30	60	60	100.85±0.32	210±2.52	36.12±2.41
Form8	50	30	60	30	99.52±0.15	49±2.13	48.94±5.65
Form9	25	30	30	60	101.26±0.34	1922±2.11	43.02±3.84
Form10	25	60	60	60	100.67±0.43	4141±198	51.45±4.12
Form11	50	60	60	30	98.48±0.17	242±1.0	40.11±1.32
Form12	50	60	60	60	99.34±0.23	40±1.12	41.24±2.75
Form13	25	30	60	60	100.72±0.36	1022±2.43	38.62±4.18
f14	25	30	60	30	100.68±0.21	3901±1.72	35.19±3.20
f15	25	60	60	60	101.03±0.49	3656±2.04	46.34±2.53
f16	50	30	30	30	102.44±0.53	631±2.1	37.01±5.76

*Each formulation contained drug that is 10 mg; Magnesium stearate-25 mg; Lactose [a]n=3

CONCLUSION

From the study it is evident that a promising controlled release by floating tablets of Glycerrhiza extract can be developed using HPMC polymer and Sodium bicarbonate. All the formulations showed good buoyancy and drug release. It is clear that drug release from the tablets is dependent on the polymer concentration, swelling properties, and dimensions of the tablet.

Declaration.

The authors declare no conflict of interest.

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