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CAPECITABINE LOADED POLYMERIC NANOPARTICLES FOR COLORECTAL CANCER TARGETING

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ABSTRACT

Colorectal cancer is cancer that starts in colon and rectum. As the colon and rectum are the most interior part of gastrointestinal tract, it is a great challenge to target drug to colon and rectum for the local treatment of colorectal cancer. The aim of the current research was to develop Capecitabine loaded Eudragit S 100 nanoparticles for colorectal cancer targeting which would release drug neither in stomach nor in small intestine as Eudragit S 100 is a pH sensitive polymer, would release drug only in colorectal region. Six formulations of Capecitabine loaded Eudragit S100 nanoparticles with varying concentration of drug and polymer were prepared by nanoprecipitation method. The formulations were optimized in order to maximize % drug entrapment efficiency and minimize particles size. The optimized formulation was evaluated for % drug entrapment efficiency, zeta potential, particle size distribution, Fourior transform infrared (FT-IR) spectroscopy analysis, differential scanning calorimetry (DSC) study, transmission electron microscopy (TEM) analysis, in vitro drug release and cytotoxicities study using HT 29 cell lines and pharmacokinetic study by using rabbit model.

KEYWORDS: Colorectal cancer; Eudragit S100; nanoprecipitation; pH sensitive polymer.

INTRODUCTION

Capecitabine is recommended for the treatment of advanced stage of colorectal cancer. Colon targeting may improve local concentration of drug in colon region to a level which is not feasible by unmodified oral drug delivery.In the current research Eudragit S100 nanoparticles were developed by nanoprecipitation method. Eudragit S100 is a pH sensitive polymer which will release drug only in colon.

OBJECTIVE

To localize the drug at colon and rectal area and enhance the bioavailability of the drug at the tumor site.

Experimental Method

Capecitabine loaded nanoparticles were prepared according to modified nanoprecipitation method. The different ratios of drug and polymers as per Table 1 were accurately weighed and dissolved in 10 ml of acetone. The organic phase containing both drug and polymers was slowly added drop wise to the aqueous phase containing 0.5% poloxamer 188 with the help of syringe and stirred magnetically at room temperature until complete evaporation of organic solvent. Then the nanosuspension was filled in vials and freeze dried for 24 h.

RESULT AND DISCUSSION

Nanoprecipitation method was selected as the drug is hydrophobic in nature. Taking into account the values of PDI, Particle size, zeta potential and entrapment efficiency W3 formulation was selected as optimized batch. The PDI, particle size, zeta potential and entrapment efficiency of W3 formulation were found to be 0.438, 110.4 nm,-22.9ev&53.8% respectively. The in vitro drug release study using dialysis membrane was found to be sustained for 24 h. As there was no drug release in 0.1 N HCl for 2h and not in significant release in phosphate buffer pH 6.8 but it released in 7.4 phosphate buffer solution it can be assumed that drug will not release in stomach and intestine but only would release in colorectal area in alkaline environment.

TABLE 1: Characterization of all formulations.

Code	CAP: WS100	Particle size (nm)		PDI		Zeta Potential (mv)		% entrapment efficiency	
		Poloxamer	PVA	Polmer	PVA	Poloxamer	PVA	Poloxamer	PVA
W1	1:1	321.3	317.0	0.630	0.884	-10.9	-6.09	46.4	42.8
W2	1:2	246.6	288.2	0.651	0.790	-12.9	-10.2	45.6	52.8
W3	**1:3**	**110.4**	**295.2**	**0.438**	**0.418**	**-22.9**	**-6.04**	**65.9**	**53.8**
W4	1:4	146.4	315.6	0.286	0.470	-22.5	-6.53	48.5	43.6
W5	1:5	232.3	280.4	0.381	0.360	-15.6	-10.6	53.9	49.8

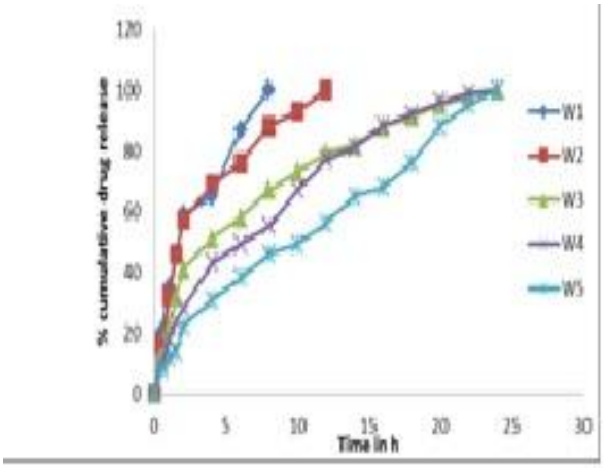

Fig.1 Release profile of all formulations.

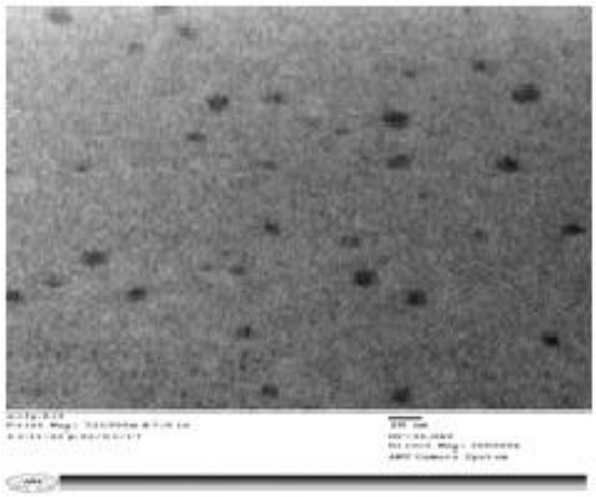

Fig. 2 TEM images of optimized formulation.

CONCLUSION

Capecitabine loaded Eudragit S 100 NPs can be formulated by nanoprecipitation method and can be targeted successfully to the colon for the treatment of colorectal cancer treatment.

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