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DIALLYLDISULFIDE CONTAINING POLYMERIC NANOPARTICLES FOR SITE-SPECIFIC DELIVERY IN COLON CANCER

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ABSTRACT

Effective delivery of drugs to colon is a challenge, as the drug needs to be protected from gastrointestinal environment and should be released intact in colon. Present study is aimed to develop a site-specific nanoparticulate formulation containing herbal anti-cancer agent in treatment of colon cancer. The Diallyl disulfide nanoparticles (DADS-NPs) were prepared by nanoprecipetation method and optimized formulation was selected using Box-Behnken design (BBD). The particle size of NPs was found to be 108 nm. The encapsulation efficiency was found to be 77.24%. and *in-vitro* release data has revealed controlled and prolonged drug release up to 72h.

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INTRODUCTION:

Targeted drug delivery systems provides medication intact to targeted site by improving its safety, efficacy and lowering the frequency of dose, due to which there has been increased interest in formulation of site-specific drug delivery system. Colon-specific drug delivery systems can be advantageous to target the drugs directly to the colon in malignancies like cancer of colon and rectum. This site-specific drug delivery system can achieve high concentration of drugs in colon to improve its bioavailability and to lower its systemic toxicity. The potential of DADS as an anticancer agent in colon cancer has extensively been investigated. The present study is aimed to develop a nano-particulate drug delivery system containing a herbal anti-cancer agent, Diallyldisulfide, for colorectal cancer cells as they show enhanced permeation, accumulation and retention in the tumor tissue[1].

MATERIAL AND METHODS:

Material

PLGA (75:25) was obtained as gift sample from Corbion Purac (Netherlands). DADS were procured from Sigma Aldrich. All other chemicals and reagents were of analytical grade.

Method

The DADS loaded nanoparticles were prepared by nanoprecipitation method using acetone as a solvent. Briefly, PLGA (75:25) and DADS were dissolved in 5 ml of acetone. The prepared solution was added drop-wise with syringe (G¼22) into 20 ml of distillated water under magnetic stirrer at room temperature. The resulting solution was stirred for complete evaporation of the organic solvent. The nanoparticles were collected by centrifugation and further freeze dried. The effect of independent variables viz. change in stirring speed, polymer to drug ratio, ratio of volume of outer water phase to the organic phase and concentration of surfactant was studied on particle size and entrapment efficiency(dependent variables). The optimized formulation was selected by application of Box Behnken design using Design expert software.

RESULTS AND DISCUSSION:

A Box-Behnken design was applied for optimization of NPs formulation. The optimized formulation of NPs were selected on the basis of criteria of attaining the maximum value of encapsulation efficiency while minimizing the particle size with numerical point prediction optimization method using Design Expert software®. Scanning electron microscopic images have showed that the nanoparticles have regular and uniform shape (Figure 1). The average particle size of nanoparticles was found to be 108nm. The zeta potential of NPs were found to be + 31.5mV ± 2mV, which indicated the physical stability of the formulation. The value of polydispersity index was found to be 0.206. The optimized formulation has shown entrapment efficiency of 77.24%. The in-vitro drug release have shown initial burst release and then prolonged drug

release with cumulative drug release of 74.54%. The release kinetics was studied by applying zero order kinetic model, first order kinetic model, Higuchi model and Korsmeyer-Peppas. According to the highest correlation (R^2) value it is evident that the optimized formulation of DADS nanoparticles follows the Higuchi model.

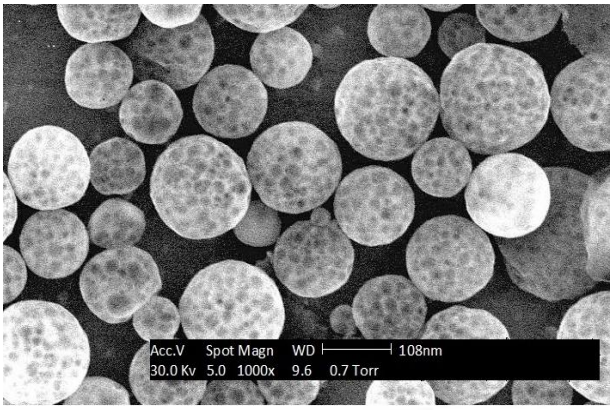

Figure 1: Scanning electron microscopic image of nanoparticles

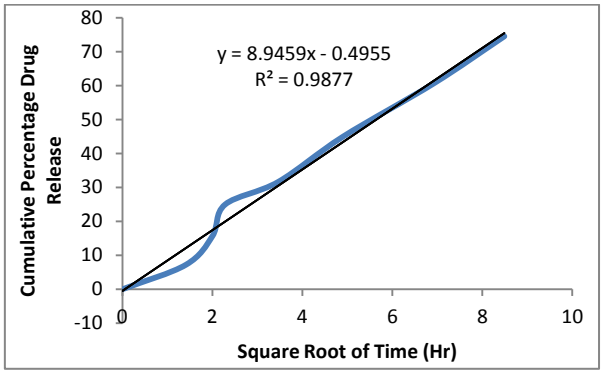

Figure 2: Drug release kinetics of nanoparticles

CONCLUSION:

The result of the study has shown physical stability, good encapsulation efficiency and prolonged rate of drug release from nanoparticles. Thus, it can be concluded that the PLGA nanoparticles containing DADS could provide a promising strategy for treatment of colon cancer with enhanced bioavailability with further cytotoxicity and *in-vivo* studies.

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