OPTIMIZATION OF METHOTREXATE NANOCOMPOSITES FORMULATIONS USING FULL FACTORIAL DESIGNS

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جامعة الاسراء

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Dedication

This project is lovingly dedicated to my sweet **Father and Mother,** whose love, affection, encouragement and whose prays of night and day support me to get such tonor and success. Without their support this research would not have made possible. Many thanks for you to teaching me to believe in God, in myself and in my dreams.

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OPTIMIZATION OF METHOTREXATE NANOCOMPOSITES FORMULATIONS USING FULL FACTORIAL DESIGNS

ABSTRACT

In general, the importance of using nanoparticles as carriers of drug was duo to high carrier capacity, high stability, probability of incorporation of both lipophilic and lipophobic drugs, and probability of various routes of administration, including inhalation rout and oral rout. The cyclodextrins (CD_s) as drug delivery system are used to solve the problem of hydrophobicity of drugs. Therefore, methotrexate (MTX) as hydrophobic drug was incorporated into β-CD/Alg nanoparticles to forming MTX-β-CD/Alg nanocomposites. The independent variable was beta-cyclodextrin, sodium alginate and calcium chloride, whereas the dependent variable was loading efficiency, Encapsulation efficiency and particle size, using full factorial design Minitab 18 software.The analysis of the model was carried out using graphical analysis such as Pareto chart, surface and contour plots, main effect plots, interaction plots, normal probability plot of the residuals and residuals versus corresponding predicted values plots. Analysis of variance (ANOVA) is structured to obtain the significant independent variables affecting on the dependent response by using P value lower than 0.05.The β-CD/Alg nanoparticlessamples were prepared by using different amounts of β-CD (50, 100, 200 and 500 mg) with sodium alginate at different amounts (25, 50, 100, 150 and 200 mg)

and calcium chloride (30,45,60 and 75 mg) under pH at 10 with constant mass of MTX at 50 mg. The final product of nanocomposites was separated via centrifugation at 11000 rpm for 20 min and then dried. The final nanocomposites was characterized by Fourier transform infrared(FTIR), X-ray diffraction (XRD) and in vitro release. FTIR test was used to evaluate the functional groups of MTX loaded β-CD/Alg nanocomposites.While XRD pattern was used to explain the interaction between MTX and its carrier (β-CD/Alg) nanoparticles. This result could be clarified bythe strong interaction which destroyed the close packing for beta cyclodextrin for the formation of crystallites between methotrexate and beta cyclodextrin.After *in vitro* release study of MTX from final formulation, the results suggested that the MTX exhibited prolongedrelease from nanocomposites of formulation.

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LIST OF ABREVIATIONS

MTX	Methotrexate
B-CD	B-cyclodextrin
$CaCl_2$	Calcium Chloride
CDs	Cyclodextrins
UV-vis	Ultraviolet-visible spectrophotometer
DLS	dynamic light scattering
XRD	X-Ray Diffraction
DMSO	Dimethyl Sulfoxide
CD	Cyclodextrin
SA	Sodium alginate
HCl	Hydrochloric acid
DHFR	Dihydrofolate reductase
THF	Tetrahydrofolates
RNA	Ribonucleic acid
DNA	Deoxyribonucleic acid
pH	Power of hydrogen
W/V	Weight per volume
mg	Milligram
ml	Milliliter
min	Minutes
%	Percentage
°C	Celsius
IC50	Half maximal inhibitory concentration
5-FU	5-Flurouracil
M	Molarity
rpm	Rounds per minute
EE	Encapsulation efficiency
LE	Loading efficiency
FTIR	Fourier Transform Infrared Spectroscopy
λ_{max}	Lambda max
nm	Nanometer
TGA	Thermo-gravimetric
R	Correlation of Coefficient
R^2	Coefficient of Determination