

## Nanoparticulate delivery systems for liver targeting

A Thesis submitted for partial fulfillment of the requirements for the Degree of Doctor of Philosophy in Pharmaceutical Sciences (Pharmaceutics)

By

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# أنظمة توصيل نانونية لإستهداف الكبد ر سالة مقدمة من الماجستير / إيمان محد حامد المراكبي بكالوريوس العلوم الصيدلية 2004، جامعة عين شمس ماجستير الصيدلانيات 2010، جامعة عين شمس المدرس المساعد بقسم الصبدلانيات والصبدلة الصناعية ، كلية الصبدلة، جامعة عين شمس للإستيفاء الجزئي لمتطلبات الحصول على درجة دكتوراه الفلسفة في العلوم الصيدلية (صيدلانيات) تحت إشراف أ.د. ناهد داوود مرتضى أستاذ الصيدلانيات والصيدلة الصناعية- كلية الصيدلة - جامعة عين شمس أ.د. سمر منصور هليل أستاذ الصيدلانيات والصيدلة الصناعية- كلية الصيدلة - جامعة عين شمس أمد رانيا محد حتحوت أستاذ مساعد الصيدلانيات والصيدلة الصناعية- كلية الصيدلة - جامعة عين شمس قسم الصيدلانيات والصيدلة الصناعية

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# Dedication

I dedicate this thesis to my dear mother, father and my beloved daughter and son, Hala and Omar. Thank you.

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# List of Abbreviations

Abbreviation	Designation
ASH	alcohol-induced steatohepatitis
ANOVA	Analysis of variance
ASGP-receptor	Asialoglycoprotein receptor
CAC	Critical aggregation concentration
CAT	Catalase
CE%	Conjugation efficiency
CLs	Cationic liposomes
Соиб	Coumarin 6
CS	Chitosan
CV	Coefficient of variation
CytoMP	Cytomembrane
DLS	Dynamic light scattering
DMSO	Dimethyl sulfoxide
DoE	Design of experiments
DOX	Doxorubicin
DSC	Differential scanning colorimetry
EDC	N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide
	hydrochloride
EE%	Encapsulation efficiency
FA	Ferulic acid
FCM	Flow cytometry
FITC	Fluorescein isothiocyanate
FTIR	Fourier transform infrared spectroscopy
GA	Glycyrrhetinic acid
GL	Glycyrrhizin
h	Hour
<sup>1</sup> H NMR	Proton nuclear magnetic resonance
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
НС	Modified chitosan after 4 hours reaction

Abbreviation	Designation
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HO/BVR	Heme oxygenase/biliverdin reductase
HPLC	High performance liquid chromatography
HSA	Human serum albumin
HSC	Hepatic stellate cells
IC <sub>50</sub>	50% inhibitory concentration
ICH	International Conference on Harmonization
IV	Intravenous
КС	Kupffer cells
LOD	Limit of detection
LOQ	Limit of quantification
MC	Modified chitosan after 40 minute reaction
MDR	Multidrug resistance
min	Minute
ml	Milliliter
MTT	Tetrazolium
NASH	Non-alcoholic steatohepatitis
NBS	n-bromosuccinamide
NLC	Nanostructred lipid carrier
nm	Nanometer
NPs	Nanoparticles
O.D.	Optical density
OATP	Organic anion transporting polypeptides
°C	Degree celsius
P407	Poloxamer 407
PBC	Primary biliary cirrhosis
PBS	Phosphate buffer saline
PC	Purified chitosan
PDC	Polymer-drug conjugates
PDGF-β	Platelet derived growth factor β
PDI	Polydispersity index
PEG	Poly ethylene glycol

Abbreviation	Designation
PLGA/PEO	poly (D,L-lactide-co-glycolide)/polyethylene oxide
PS	Particle size
PSC	Primary sclerosing cholangitis
РТХ	Paclitaxel
$\mathbb{R}^2$	Coefficient of determination
RNS	Reactive nitrogen species
ROS	Reactive oxygen species
SD	Standard deviation
SE	Standard error
SEC	Sinusoidal endothelial cells
SOD	Superoxide dismutase
SRB	Sulforhodamine B
TEM	Transmission electron microscopy
Tg′	Glass transition temperature
TPP	Sodium tripolyphosphate
ZP	Zeta potential
λmax	Wavelength of maximum absorbance
μg	Microgram
μl	Microliter
2FI	Two factor interaction model