بسم الله الرحمن الرحيم

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تم رفع هذه الرسالة بواسطة / مني مغربي أحمد

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

ملاحظات: لا يوجد

Faculty of Pharmacy

Biocompatible Nanocarriers for Enhanced Therapeutic Efficiency of an Antibacterial Drug

A Thesis

Submitted in Partial Fulfillment of the Requirements for the

Master Degree

In Pharmaceutical Sciences

(Pharmaceutics)

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2022

Acknowledgments

First of all, thanks to God for helping me achieving this work. I would like to refer that the realization of this dissertation has been a major learning experience, not only for the academic and scientific knowledge but mainly for the personal experience.

Then, I would like to express my deepest appreciation and my sincere gratitude to **Prof.dr.Ahmed Shawaky Mohamed Geneidi**, Professor of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Ain Shams University for setting a unique model to what a sincere professor, scientist, and advisor should be. I am deeply grateful for his support, encouragement and continuous advice.

Words are not enough to express my profound gratitude to **Prof.dr Mona Mohamed Abdel Mottelab**, Professor of Pharmaceutics and Industrial Pharmacy. Faculty of Pharmacy, Ain Shams University to whom I owe so much for her extensive efforts, continuous discussions and guidance. She is a truly a role model for a professor.

Finally, I would like to deeply thank my family who supported me always, giving me hope, power, and motivation to make my dreams come true.

Lina K.M Abdel Salam

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الملخص العربي……١

List of Abbreviations

Area under the curve	AUC
Central nervous system	CNS
Cerebrospinal fluid	CSF
Entrapment effciency percent	EE%
Gama-amino butyric acid	GABA
Gastrointestinal	GI
Hours	Hr
Large unilamellar vesicles	LUV
Minmum effective concentration	MIC
Minutes	Min
Multi-lamellar vesicles	MLV
Particle size	PS
Penentration enhancer nanovesicles	PEVs
Pentration enhancer	PE
Phase transition temperature	Tc
Polydispersity index	PDI
Proniosomal gel	PG
Reticulocyte endothelial system	RES
Small unilamellar vesicles	SUV
Stratum corenum	SC
The critical packing parameter	CPP
The hydrophilic-lipophilic balance	HLB

Transdermal drug delivery	TDD
Transition temperature	Tm
Zeta potentail	ZP

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Abstract

Biocompatible Nanocarriers for Enhanced Therapeutic Efficiency of an Antibacterial Drug

The therapeutic efficacy of a locally applied drug depends mainly on its ability to penetrate and permeate the skin. Therefore, there is a continuous need to develop new drug delivery systems that can overcome the skin barrier (brick and mortar-like structure). Vesicular systems are among the most commonly used systems to achieve such purpose. The use of nanocarriers such as penetration enhancer nanovesicles, proniosomes, and proniosomal gels are examples of formulation techniques that have shown enhanced dermal delivery of drugs.

Levofloxacin is a third generation member of fluoroquinolones with potent antibacterial effect and broad spectrum of activity against different types of bacterial strains. It is the first choice for treatment of many complicated infectious diseases. Also, it can effectively be used in attacking resistant strains causing complicated urinary tract infections involving inflammation of prostate gland, polynephritis and skin, and soft tissue infection.

Therefore, the aim of the study is to formulate and evaluate biocompatible nanocarrier systems loaded with levofloxacin for dermal drug delivery such as penetration enhancer nanovesicles and proniosomal gels loaded with levofloxacin followed by an assessment of the selected optimized formulations aiming to enhance its therapeutic effect and to increase the patient adherence to drug therapy with minimum side effects.

In the first chapter of work, penetration enhancer nanovesicles loaded with levofloxacin were prepared using the film hydration method. Five different hydrophilic and lipophilic penetration enhancers were selected and used to

formulate levofloxacin-loaded penetration enhancer containing vesicles namely: polyethylene glycol 400, propylene glycol, limonene, transcutol, and cineole. The concentration of the pentration enhancers were studied as a variable affecting different formulation characteristics. The prepared penetration enhancer nanovesicles loaded with levofloxacin were characterized in terms of the particle size , polydisperity index, zeta potentail , entrapment efficiency , in vitro release and ex-vivo permeation. Limonene (L1-LV) pentration enhancer nanovesicles displayed the smallest particle size among the other formulations.The lipophillicity and the hydrophillicity of the penetration enhancers greatly affect the entrapment effciency values. Polyethylene glycol (PEG3-LV) pentration enhancer nanovesicles displayed the highest entrapment efficiency. The selected formulae for the ex-vivo permeation data were propylene glycol and transcutol penetration enhancer nanovesicles. It was found that maximum drug deposited in the skin was for transcutol PEVs (T3-LV) in comparison to propylene glycol PEVs (PG 2-LV).

In the second chapter of work , coacervation phase separation method was used for the preparation of proniosomal gels. The proniosomal gels were prepared utilizing safe and convenient different non-ionic surfactants like spans and tweens assembled with measured quantities of cholesterol and lecithin. The effects of concentration of non-ionic surfactants, cholesterol, and lecithin were studied. The observed depandent variables were the particle size, polydisperity index, zeta potential, entrapment efficiency, in vitro release, and ex vivo permeation. Span 20 proniomal gel formulation had the smallest vesicle size. Proniosomal gel formulation loaded with span 20 exhibited the highest encapsulation efficiency in comparison to others prepared by tween. Levofloxacin proniosomal gels showed

relatively high permeation on the basis that non-ionic surfactant present in these formulation acts as permeation enhancers. Span 80 based formulations exhibited a higher percentage of drug permeation and deposition across various skin layers after 6 hours as compared to tween 80.

To conclude, the dermal application of the investigated penetration enhancer nanovesicles and proniosomal gel formulations showed promising results as successful nanocarriers for levofloxacin.

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General Introduction