CLINDAMYCIN NANO POLYMERS: PREPARATION, CHARACTERIZATIONS AND RELEASE STUDY

Prepared by

Yousef Rezek Almahamid

Supervised by

Dr. Samer Hasan Hussein-Al-Ali

A Thesis

Submitted to Faculty of Pharmacy as a Partial Fulfillment of The Requirements for Master's Degree in Pharmaceutical Sciences

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أشقـائـي الـذيـن أرى فـيـهم بـوضوح رحمة الله الـبـاقـيـة

..

رشا وديـمـا وريـمـا

شقـيـقـات قـلـبي وعطفه وحبه لـهذه الـحيـاة

..

هذه أجزاء روحي الـتي أهديـهـا كل عمري

.....

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COMMITTEE DECISION

This Thesis/Dissertation (**CLINDAMYCIN NANO POLYMERS: PREPARATION, CHARACTERIZATIONS AND RELEASE STUDY**) was successfully Defended and Approved on 15th April, 2019.

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CLINDAMYCIN NANO POLYMERS:PREPARATION,CHARACTERIZATIONS AND RELEASE STUDY

By

Yousef Rezek Almahamid

April, 2019

ABSTRACT

Conventional immediate release oral tablets and capsules products are formulated to release the active drug immediately after oral administration. This type of release generally results in relatively rapid drug absorption and onset of accompanying pharmacodynamics effects. Alternatively, conventional release containing lipophilic drugs, their absorption may be gradual due to slow dissolution in or selective absorption across the GI tract, thus resulting in a delayed onset time.

Recently modified-release dosage forms are deliberately changed from that of a conventional release dosage formulation to achieve a desired therapeutic objective or better patient compliance. Different types of modified-release drug products include delayed release (eg, enteric coated), extended release, and orally disintegrating tablets.

Extended-release drug products are a dosage form that allow at least a twofold reduction in dosage frequency as compared to that drug presented as a conventional immediate release dosage form. Examples of extended-release dosage forms include controlled-release, sustained-release, and long-acting drug products.

This study aimed to achieve the optimized preparation of new extended release formulation of Clindamycin (CLD) via loading of the CLD onto nanopolymers in order to increase the residence time in the body by extended release.

A nanocomposite (CS-Chondro-CLD) was prepared using Chondroitin sulfate (Chondro), and Chitosan (CS) polymer. The prepared nanocomposite was studied for their physiochemical properties, loading efficiency (LE), X-ray Powder Diffraction (XRD), Fourier-transform infrared spectroscopy (FT-IR), A scanning electron microscope (SEM), and release.

Full Factorial design was used in this work. The CS-Chondro nanocomposites were prepared by mixing different mass of CS (50, 100, and 200 mg) with Chondro solutions (50, 100, and 200 mg) under controlled pH of 5.0 using NaOH(0.1%). The product was centrifuged at 10000 rpm for 15 min and dried. The same procedure was repeated for the preparation of CS-Chondro-CLD nanocomposites using different concentrations of CLD (75, 150, and 300 mg).

XRD spectra of CS-Chondro and CS-Chondro-CLD showed two peaks at $2\theta=22.5^{o}$ and 40.7^{o}, indicating amorphous forms due to cross-linkage between CS and Chondro. The FTIR data for all nanocomposites prepared in this work showed the spectra of polymers (CS, and Chondro) as well as the spectra of CLD. This result indicates the incorporation of CLD in the nanopolymers.

Multiple regression analyses and stepwise method were used in this work to examine the relationship between dependant variables (loading efficiency, particle size and zeta potential) and independent variables with their interactions (concentrations of CS, Chondro and CLD) for all nanocomposites. Outlier reading was detected by using

Mahalanobis distance method. The data did not contain any outlier values for all experiments.

At LE response, the square (Chondro*Chondro and CLD*CLD) and 2-way interaction (CS*CLD) was excluded from the final equation; whereas other liner, square and 2-way interaction had a significant effect on the LE response.

At size response, 2-way interaction (Chondro*CLD) was excluded from the final equation; whereas other liner, square and 2-way interaction had a significant effect on the size response.

At zeta potential response, 2-way interaction (CS*Chondro) was excluded from the final equation; whereas other liner, square and 2-way interaction had a significant effect on the zeta potential response.

In vitro release study of CLD from its respective nanocomposites was carried out using PBS at pH of 4.8 and 7.4 and showed that the release rate of CLD from the optimized nanocomposites at pH 4.8 start after 10 hours; whereas at pH 7.4 after 2 hours.

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LIST OF ABBREVIATIONS

CLD	Clindamycin
DOE	Design Of Experiments
CS	Chitosan
Chondro	Chondroitin
CS-Chondro	Chitosan-Chondroitin Nanoparticles
CS-Chondro-CLD	Chitosan -Chondroitin -Clindamycin Nanoparticles
LE	Loading Efficiency
EE	Encapsulation Efficiency
DLS	Dynamic Light Scattering
SEM	Scanning Electron Microscope
TEM	Transmission Electron Microscope
DSC	Differential Scanning Calorimetric
XRD	X-Ray Diffraction
FT-IR	Fourier-Transform Infrared Spectroscopy
PBS	Phosphate Buffered Saline
UV-Vis	Ultraviolet–Visible Spectroscopy
ANOVA	Analysis of Variance
SS	Sums of Squares
PDI	Polydispersity Index
R	Correlation of Coefficient
R^2	Coefficient of Determination
MS	Mean Square
MSE	Mean Square Error
SPSS	Statistical Package For The Social Sciences