

**METRONIDAZOLE NANO POLYMERS: PREPARATION,
CHARACTERIZATIONS AND RELEASE STUDY**

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The administration of drugs designed to be given as a single dose rather than multiple doses has recently been made possible using extended release formulation approach; the release of the drugs can be accomplished over long periods of time, enabling an almost constant level of the drug to be maintained in the bloodstream. Moreover, extended release formulations increase the clinical efficacy of drugs. The introduction of drug nanocomposites as extended release vehicles has provided a breakthrough in novel drug delivery systems in the field of pharmaceutical technology, for which nanopolymers are widely used for this purpose. This study aimed to achieve the preparation of new extended release formulation of metronidazole (MET) via loading of the MET onto nanopolymers in order to increase the residence time in the body by extended release.

Three nanocomposites were prepared using chitosan (CSNPs), alginate (AlgNPs) and chitosan-alginate (CS-AlgNPs) nanoparticles; MET-CSNPs, MET-AlgNPs and MET-CS-AlgNPs nanocomposites, respectively. The prepared nanocomposites were studied for their physiochemical properties, loading efficiency (LE), encapsulation efficiency (EE), and release.

The MET-CSNPs nanocomposites were prepared by mixing different concentrations of CS (0.5, 1, and 2 mg/mL) with TPP solutions (0.5, 1, 2.5 mg/mL) under controlled pH at 4.5 using NaOH. The product was centrifuged at 10000 rpm for 15 min and dried. The same procedure was repeated for the preparation of MET-CSNPs nanocomposites using different concentrations of MET (100, 200, and 400 mg).

The MET-AlgNPs were prepared by ionic gelation method between sodium alginate (1, 2 and 4 mg/mL) and cross-linking agent of CaCl₂ (0.5, 0.75, and 1% w/v) in the presence of MET (100, 200, and 400 mg).

MET-CS-AlgNPs nanocomposites were prepared using solutions of CS (0.5, 1 and 2 mg/mL), sodium alginate (2 and 4 mg/mL) and CaCl₂ (0.5 and 1%) at 100 mg MET concentration.

XRD spectra of MET-CSNPs showed two peaks at $2\theta=12^\circ$ and 23.7° , indicating amorphous forms due to cross-linkage with TPP. XRD spectra of MET-AlgNPs showed three diffraction peaks at 2θ values 14.1° , 21.8° and 39.1° . XRD patterns of MET-CS-AlgNPs showed overlap between patterns of CS and Alg, which lead to the appearance of peaks at $2\theta = 14.5^\circ$ and 20.6° .

The FTIR data for all nanocomposites prepared in this work showed the spectra of nanopolymers (CSNPs, AlgNPs and CS-AlgNPs) as well as the spectra of MET. This result indicates the incorporation of MET in the nanopolymers.

Correlation and multiple regression analyses were used in this work to examine the relationship between dependant variables (EE, LE, particle size and zeta potential) and independent variables

(concentrations of CS, TPP and MET) for all nanocomposites. At MET-CSNPs nanocomposites, the MET concentration had a significant effect on the EE, LE and particle size. The TPP concentration significantly affected the particle size and zeta potential. In addition, CS concentration only affected the LE and zeta potential.

In the case of MET-AlgNPs nanocomposites, the MET concentration only had a significant effect on the zeta potential. In addition, the variable CaCl_2 had a significant effect on the LE only. On the other hand, the Alg concentrations affected all dependant variables significantly except the zeta potential.

In regards to the MET-CS-AlgNPs nanocomposites, the independent variables were Alg, CaCl_2 and CS concentrations. The Alg concentrations significantly affected all dependant variables except EE. In addition, the CaCl_2 concentrations significantly affected all dependant variables except LE, whereas the CS concentrations significantly affected the EE and particle size.

Extended release study of MET from its respective nanocomposites was carried out using 0.1N HCl and showed that the release rate of MET from the MET-CSNPs nanocomposites was slower than MET-AlgNPs and MET-CS-AlgNPs. These results indicate extended release of the drug from its respective nanocomposites, and therefore these nanocomposites have good potential to be used as extended-release formulation of the drugs.

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This Thesis/Dissertation (**METRONIDAZOLE NANO POLYMERS: PREPARATION, CHARACTERIZATIONS AND RELEASE STUDY**) was successfully Defended and Approved on 29th May, 2018.

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TABLE OF CONTENTS

	Page
ABSTRACT	II
COMMITTEE DECISION	VI
ACKNOWLEDGEMENT	VII
LIST OF TABLES	XI
LIST OF FIGURES	XII
LIST OF ABBREVIATIONS	XIV
CHAPTER	
1 INTRODUCTION	1
1.1 Background of study	1
1.2 Problem Statement	2
1.3 Objectives	3
2 LITERATURE REVIEW	4
2.1 Nanoparticles	4
2.2 Metronidazole	4
2.2.1 The mechanism of action for metronidazole	5
2.3 Alginate	6
2.3.1 Structure of sodium alginate	6
2.3.2 Application of sodium alginate	6
2.3.3 Basic properties of sodium alginate	7
2.3.4 Preparation of alginate nanoparticles	8
2.3.5 Application of alginate nanoparticles	8
2.4 Chitosan	9
2.4.1 Structure of chitosan	9
2.4.2 Application of chitosan	10
2.4.3 Basic properties of chitosan	11
2.4.4 Preparation of chitosan nanoparticles	12
2.5 Studies on loading metronidazole on others carriers	15

2.6	Extended release	16
2.7	Burst release	17
2.8	Kinetic models	17
3	METHODOLOGY	19
3.1	Materials	19
3.2	Preparation of nanoparticles and nanocomposites	19
3.2.1	CSNPs and MET-CSNPs nanocomposites	19
3.2.2	AlgNPs and MET-AlgNPs nanocomposites	20
3.2.3	CS-AlgNPs and MET-CS-AlgNPs nanocomposites	21
3.3	Physio-chemical analysis and characterizations	21
3.3.1	Powder X-Ray Diffraction	21
3.3.2	Infrared spectroscopy	21
3.3.3	The metronidazole loading and encapsulation efficiency	22
3.3.4	The particle size and zeta potential of particles	23
3.3.5	Extended release study of the metronidazole from the respective nanocomposites	24
4	RESULTS AND DISCUSSION	25
4.1	Characterization of CSNPs nanoparticles and MET-CSNPs nanocomposites	25
4.1.1	XRD for MET-CSNPs nanocomposites	25
4.1.2	FTIR spectroscopic analysis of MET-CSNPs nanocomposites	26
4.1.3	Effect of CS, MET and TPP concentrations on encapsulation efficiency and loading efficiency of MET-CSNPs nanocomposites	28
4.1.4	The Effect of CS, MET and TPP concentrations on particle size and zeta potential of MET-CSNPs nanocomposites	31
4.1.5	Release study of MET from MET-CSNPs nanocomposites	36
4.2	Characterization of AlgNPs nanoparticles and MET-AlgNPs nanocomposites	38

4.2.1	XRD for MET-AlgNPs nanocomposites	38
4.2.2	FTIR spectroscopic analysis of AlgNPs and MET-AlgNPs	39
4.2.3	Effect of Alg, MET and CaCl ₂ concentrations on encapsulation efficiency and loading efficiency of MET-AlgNPs nanocomposites	40
4.2.4	The Effect of Alg, MET and CaCl ₂ concentrations on particle size and zeta potential of MET-AlgNPs nanocomposites	43
4.2.5	Release study of MET from MET-AlgNPs nanocomposites	47
4.3	Characterization of CS-AlgNPs nanoparticles and MET-CS-AlgNPs nanocomposites	48
4.3.1	XRD for MET-CS-AlgNPs nanocomposites	48
4.3.2	FTIR spectroscopic analysis of CS-AlgNPs and MET-CS-AlgNPs	49
4.3.3	Effect of Alg, CaCl ₂ and CS concentrations on encapsulation efficiency and loading efficiency of MET-CS-AlgNPs nanocomposites	50
4.3.4	The Effect of Alg, CaCl ₂ and CS concentrations on particle size and zeta potential of MET-CS-AlgNPs nanocomposites	51
4.3.5	Release study of MET from MET-CS-AlgNPs nanocomposites	53
5	CONCLUSIONS AND RECOMMENDATION FOR FURTHER RESEARCH	55
6	REFERENCES	57
7	APPENDICES	69

LIST OF TABLES

Table 4.1	The effects of chitosan to TPP mass ratio on the encapsulation efficiency and loading efficiency	31
Table 4.2	The effects of chitosan to TPP mass ratio on the size of MET-CSNPs nanocomposites	34
Table 4.3	The SPSS data analysis for MET-CSNPs nanocomposites	35
Table 4.4	The correlation coefficients (R^2) obtained by fitting the MET release data from MET-CSNPs nanocomposites in 0.1N HCl.	37
Table 4.5	The SPSS data analysis for MET-AlgNPs nanocomposites	45
Table 4.6	The correlation coefficients (R^2) obtained by fitting the MET release data from MET-AlgNPs nanocomposites in 0.1N HCl	47
Table 4.7	Comparison between MET-CS-AlgNPs and MET-AlgNPs nanocomposites at different parameters	52
Table 4.8	The SPSS data analysis for MET-CS-AlgNPs nanocomposites	53
Table 4.9	The correlation coefficients (R^2) obtained by fitting the MET release data from MET-CS-AlgNPs nanocomposites in 0.1N HCl	54

LIST OF FIGURES

Figure 2.1	Chemical structure of metronidazole	5
Figure 2.2	Chemical structure of sodium alginate	6
Figure 2.3	Chemical structures of chitin and chitosan	10
Figure 2.4	Preparation chitosan nanoparticles by reverse micellar method	13
Figure 2.5	Preparation chitosan particles by Sieving method	14
Figure 2.6	Preparation chitosan nanoparticles by ionic gelation method	15
Figure 4.1	XRD diffraction spectra of MET (A), CSNPs (B) and MET-CSNPs (C)	26
Figure 4.2	FTIR spectra of n-CS (A) , CSNPs (B) , MET (C) and MET-CSNPs (D)	27
Figure 4.3	Effect of CS, MET and TPP concentrations on encapsulation efficiency and loading efficiency	29
Figure 4.4	Effect of CS, MET and TPP concentrations on particle size and zeta potential	33
Figure 4.5	<i>In vitro</i> release behaviours of MET from MET-CSNPs nanocomposites in 0.1N HCl	37
Figure 4.6	XRD diffraction spectra of MET (A), AlgNPs (B) and MET-AlgNPs (C)	38
Figure 4.7	FTIR spectra of n-Alg, AlgNPs, MET and MET-AlgNPs	40
Figure 4.8	Effect of Alg, MET and CaCl ₂ concentrations on encapsulation efficiency and loading efficiency for MET-AlgNPs	42
Figure 4.9	Effect of Alg, MET and CaCl ₂ concentrations on particle size and zeta potential	44
Figure 4.10	<i>In vitro</i> release behaviours of MET from MET-AlgNPs nanocomposites in the 0.1N HCl	47
Figure 4.11	XRD diffraction spectra of MET (A), CS-AlgNPs (B) and MET-CS-AlgNPs (C)	48

Figure 4.12	FTIR spectra of MET (A), CS-AlgNPs (B) and MET-CS-AlgNPs (C)	49
Figure 4.13	Effect of Alg, CaCl ₂ and CS concentrations on encapsulation efficiency and loading efficiency of MET-CS-AlgNPs	50
Figure 4.14	Effect of Alg, CaCl ₂ and CS concentrations on particle size and Zeta potential of MET-CS-AlgNPs	51
Figure 4.15	<i>In vitro</i> release behaviours of MET from MET-CS-AlgNPs nanocomposites in the 0.1N HCl.	54

LIST OF ABBREVIATIONS OR SYMBOLS

MET	Metronidazole
CSNPs	Chitosan nanoparticles
AlgNPs	Alginate nanoparticles
CS-AlgNPs	Chitosan-Alginate nanoparticles
MET-CSNPs	Metronidazole-Chitosan nanoparticles
MET-AlgNPs	Metronidazole-Alginate nanoparticles
MET-CS-AlgNPs	Metronidazole-Chitosan-Alginate nanoparticles
CS	Chitosan
Alg	Sodium alginate
LE	Loading efficiency
EE	Encapsulation Efficiency
HPLC	High-performance liquid chromatography
TPP	Tri-Poly-Phosphate
NaOH	Sodium hydroxide
CaCl ₂	Calcium Chloride
XRD	X-ray diffraction
FTIR	Fourier-transform infrared spectroscopy
PBS	Phosphate Buffered Saline
UV-Vis	Ultraviolet-visible spectroscopy
DLS	Dynamic light scattering
BSA	Bovine serum albumin
PDI	Polydispersity index
R	Correlation of coefficient
R ²	Coefficient of determination
SPSS	Statistical Package for the Social Sciences