

LOADING OF PRAZIQUANTEL IN NANOCARRIER AS A NEW THERAPEUTIC APPROACH TOWARDS SCHISTOSOMIASIS MANSONI: AN EXPERIMENTAL STUDY

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

(وقل أعملوا فليس لله
عملكم ورسول الله والمؤمنون)

صَدَقَ اللَّهُ الْعَظِيمُ

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Objective:

The use of nanoparticles (NPs) as a drug carrier can improve today's therapies. The main objective of this work focuses on the preparation of chitosan and mesoporous silica nanoparticles loaded with praziquantel (PZQ-Cs and PZQ-Si, respectively) in order to enhance the therapeutic efficacy and overcome the drawbacks of conventional praziquantel (PZQ) therapy.

Methodology:

After preparation of PZQ-Cs and PZQ-Si, detailed physicochemical characterization was carried out. Mice were experimentally infected with *S. mansoni* and treated 6 weeks post-infection with PZQ in different doses either via oral or intraperitoneal (IP) routes. PZQ in the same doses orally administered to *S. mansoni* infected mice was used as a drug control and infected and non-infected non-treated mice served as positive and negative controls, respectively.

Results:

PZQ-Si exhibited the best physicochemical attributes in terms of small uniform size (105 nm), spherical shape

and PZQ entrapment efficiency (83%). A maximum antischistosomal effect was achieved using orally administered PZQ-Si as reflected by total worm burden, tissue egg count, oogram pattern and hepatic granuloma count and diameter. The biomarkers related to liver oxidative stress status and immunomodulatory effect (serum TNF- α and IL-10) were significantly improved. Data obtained implied that IP route was less efficacious for the delivery of PZQ-Si. Encapsulation of PZQ permits the reduction of the used therapeutic dose of PZQ. Only improvement of infection induced inflammatory and hepatic oxidative stress reactions were achieved with PZQ-Cs. Hepatic DNA fragmentation, measured by comet assay, was significantly improved in infected mice treated with a maximum dose of PZQ loaded in prepared nanoparticles as compared to positive or PZQ control groups.

Conclusion:

The results indicate that mesoporous silica NPs are promising safe nanocarriers for PZQ potentiating its antischistosomal effect, with antioxidant, immunomodulatory and anti-inflammatory action in animal model infected with *S. mansoni*. From a practical standpoint, PZQ-Si using a lower dose of PZQ could be suggested for effective PZQ antischistosomal mass chemotherapy.

Keywords: Chitosan nanoparticles, Mesoporous silica nanoparticles, *Schistosoma mansoni*, liver, histopathology, oxidative stress, genotoxicity.

List of Abbreviations

Abbreviation	Full name
A_{blank}	: Absorbance of blank
A_{sample}	: Absorbance of the sample
A_{standard}	: Absorbance of the standard
AgNPs	: Silver NPs
ANOVA	: Analysis of variance
A.U.	: Arbitrary unit
CCA	: Circulating anodic antigen
CD4	: Cluster of differentiation
C_{free}	: Free drug concentration
C_i	: Initial concentration
CsNPs	: Chitosan nanoparticles
Cs-TPP	: Chitosan- sodium tri-poly-phosphate
DLS	: Dynamic Light Scattering
DMSO	: Dimethyl sulfoxide
DNA	: Deoxy ribonucleic acid
DTNB	: 5, 5` di-thio bis- 2-nitrobenzoic acid
EDTA	: Disodium ethylene-diamine-tetra-acetic acid
EE	: Encapsulation efficiency
ELISA	: Enzyme linked immunosorbent assay
EPR	: Enhanced permeability and retention
FDA	: Food and Drug Administration
gm	: Gram

List of Abbreviations

.....

GTPase	: Guanosine triphosphatase
GSH	: Reduced glutathione
HBV	: Hepatitis B virus
HCV	: Hepatitis C virus
HRP	: Horseradish Peroxidase
Hx and E	: Hematoxylin and Eosin
IFN- γ	: Interferon-gamma
IgE	: Immunoglobulin E
IgM	: Immunoglobulin M
IgG	: Immunoglobulin G
IHA	: Indirect haemagglutination
IL-	: Interleukin
ILARC	: International Labor Rights Case Law
IP	: Intraperitoneal
Kg	: Kilogram
LSD	: Least significant difference
M	: Mole
MDA	: Malondialdehyde
MSNPs	: Mesoporous silica nanoparticles
min	: Minute
mg	: Milligram
ml	: Milliliter
mV	: Millivolt
mM	: Millimole
MSP₁₀	: Merozoite surface protein 10

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NaCl	: Sodium Chloride
NaOH	: Sodium Hydroxide
NEDA	: 1-naphthyl Ethylene-diamine
nm	: Nanometer
nmol	: Nanomole
NO	: Nitric oxide
NODCAR	: National Organization for Drug Control and Research
NPs	: Nanoparticles
NSCP	: National Schistosomiasis Control Program
PBS	: Phosphate buffered saline
PCR	: Polymerase chain reaction
PEG	: Polyethylene glycol
pg	: Picogram
PLGA	: Poly d, l-lactic-coglycolic acid
PMMA	: Poly-methyl-methacrylate
P-value	: Probability
PZQ	: Praziquantel
PZQ-Cs	: Praziquantel-loaded chitosan nanoparticles
PZQ-NPs	: Praziquantel-loaded nanoparticles
PZQ-Si	: Praziquantel-loaded mesoporous silica nanoparticles
RBCs	: Red blood cells
RNS	: Reactive nitrogen species

List of Abbreviations

ROS	: Reactive oxygen species
rpm	: Round per minute
S.	: <i>Schistosoma</i>
SCGE	: Single cell gel electrophoresis
SD	: Standard deviation
SEA	: Soluble egg antigen
SH	: Thiol group
SLN	: Solid Lipid Nanoparticles
spp.	: Species
SWA	: Soluble worm antigen
SWAP	: Soluble worm antigenic preparation
TBRI	: Theodor Bilharz Research Institute
TEM	: Transmission electron microscopy
Th1	: T-helper lymphocyte type 1
Th2	: T-helper lymphocyte type 2
US EPA	: United States Environmental Protection Agency
V: V	: Volume: volume
WBCs	: White blood cells
WHO	: World Health Organization
ZP	: Zeta Potential
18s rRNA	: 18s ribosomal ribonucleic acid
μm	: Micrometer
μmol	: Micromole

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