



Development and biological evaluation of protective effect of kidney targeted *N*-acetylated chitosan nanoparticles containing thymoquinone for the treatment of DNA damage in cyclophosphamide-induced haemorrhagic cystitis

Chaitali Prajapati^a, **Yogeeta O. Agrawal^{b,*}**, **Vinit V. Agnihotri^b**, Umesh B. Mahajan^a, Kalpesh R. Patil^a, Dipak D. Patil^c, Chandragouda R. Patil^{a,**}

^a Department of Pharmacology, R. C. Patel Institute of Pharmaceutical Education and Research, Dist. Dhule, Shirpur 425405, Maharashtra, India

^b Shri Vile Parle Kelavani Mandal's Institute of Pharmacy, Dhule 424001, Maharashtra, India

^c Department of Pharmaceutical Chemistry, H. R. Patel Institute of Pharmaceutical Education and Research, Dist. Dhule, Shirpur 425405, Maharashtra, India

ARTICLE INFO

Keywords:

Scanning electron microscopy
Cyclophosphamide
Thymoquinone
Nanoparticles
Cytokines
Comet assay
DNA fragmentation

ABSTRACT

Thymoquinone (TQ), the most prominent constituent of *Nigella sativa* seeds, essential oil, is reported to possess an organ protective effect via Nrf2 expression and activation of Phase-II antioxidant enzymes. Haemorrhagic cystitis is the sudden onset of haematuria combined with bladder pain and irritable bladder symptoms are the known toxic effects of cyclophosphamide (CYP) chemotherapy. The objective of the present study was to investigate and compare the protective effect of thymoquinone (TQ) and thymoquinone nanoparticles (TQ-NP) in the kidney against CYP-induced haemorrhagic cystitis. Primarily, TQ-NP was fabricated by synthesis of *N*-acetylated chitosan and nanoparticle preparation by the ionic gelation technique. They were characterized by particle size, polydispersive index (PDI), zeta potential, entrapment efficiency (EE), SEM, and dynamic scattering calorimetry (DSC). Moreover, fluorescein isothiocyanate (FITC) labeled NPs were prepared for biodistribution studies. The protective mechanisms of TQ-NP included its anti-inflammatory activity, inhibitory effects on cytokine levels, and protection against the DNA damage in the bladder epithelium. The cystitis was induced in rats by orally administering 200 mg/kg of CYP. The dose-dependent protective effect of the TQ-NP was determined by intravenously administering 1, 2, and 5 mg/kg of the TQ-NP to CYP-treated rats. The present study revealed that the TQ-NP prepared by ionic gelation method provides kidney targeted delivery of TQ as compared to TQ solution. The mean particle size, PDI, and %EE of TQ-NP were 272.6 nm, 0.216, 70.81 ± 0.12% respectively. The zeta potential of thymoquinone-loaded nanoparticles was found to be −20.7 mV and −22.6 mV respectively before and after lyophilization. SEM study also confirmed the small size and spherical shape. Pharmacokinetic studies revealed the improvement in half-life and prolonged action of the TQ-NP as compared to the TQ solution. Also, TQ-NP administration showed more protection against the characteristic histological alterations in the bladder in comparison to TQ solution. The present study indicates that TQ-NP exerts potent anti-oxidant, DNA protective and cytokine inhibitory activity at considerably lower concentrations as compared to plain TQ solution. The nano formulation of TQ using *N*-acetylated chitosan provides effective kidney targeted delivery of TQ, which in turn improves its retention and protective efficacy against CYP-induced haemorrhagic cystitis.

1. Introduction

Haemorrhagic cystitis causes damage to the urothelium of the

bladder mucosa, leading to dysuria and haematuria. It is an inflammatory condition originating from infectious or non-infectious causes [1]. Cyclophosphamide (CYP) is used as a chemotherapeutic agent in the

* Correspondence to: Y. O. Agrawal, Department of Pharmaceutics, Shri Vile Parle Kelavani Mandal's Institute of Pharmacy, Dist-Dhule, Dhule 424001, Maharashtra, India.

** Corresponding author.

E-mail addresses: goyaloyogita@rediffmail.com (Y.O. Agrawal), xplore.remedies@gmail.com (C.R. Patil).



Already have a manuscript? Use our Manuscript Matcher to find the best relevant journals!

[Find a Match](#)

Filters [Clear All](#)

- Web of Science Coverage
- Open Access
- Category
- Country / Region
- Language
- Frequency
- Journal Citation Reports

Refine Your Search Results

International Journal of Biological Macromolecules [Search](#) Sort By: Relevancy

Search Results

Found 8,027 results (Page 1) [Share These Results](#)

Exact Match Found

INTERNATIONAL JOURNAL OF BIOLOGICAL MACROMOLECULES

Publisher: ELSEVIER , RADARWEG 29, AMSTERDAM, Netherlands, 1043 NX
ISSN / eISSN: 0141-8130 / 1879-0003
Web of Science Core Collection: Science Citation Index Expanded
Additional Web of Science Indexes: Biological Abstracts | BIOSIS Previews | Current Contents Life Sciences | Essential Science Indicators

[Share This Journal](#) [View profile page](#)
* Requires free login.

Other Possible Matches

INTERNATIONAL JOURNAL OF AGRICULTURAL AND BIOLOGICAL ENGINEERING

Publisher: CHINESE ACAD AGRICULTURAL ENGINEERING , RM 506, NO 41, MAIZIDIAN ST, CHAOYANG DISTRICT, BEIJING, PEOPLES R CHINA, 100125
ISSN / eISSN: 1934-6344 / 1934-6352