International Journal of Biological Macromolecules 263 (2024) 130517

Contents lists available at ScienceDirect

International Journal of Biological Macromolecules

journal homepage: www.elsevier.com/locate/ijbiomac

Transporter targeted-carnitine modified pectin-chitosan nanoparticles for inositol hexaphosphate delivery to the colon: An in silico and in vitro approach

Nidhi Mishra [a], Madhu Sharma [b], Pooja Mishra [c], Raquibun Nisha [a], Priya Singh [a,3], Ravi Raj Pal [a], Neelu Singh [a], Samipta Singh [a], Priyanka Maurya [a,1], Suyash Pant [d], Prabhat Ranjan Mishra [b], Shubhini A. Saraf [a,2,*]

[a] Department of Pharmaceutical Sciences, Babasaheb Bhimrao Ambedkar University, Vidya Vihar, Raebareli Road, Lucknow 226025, Uttar Pradesh, India
[b] Division of Pharmaceutics and Pharmacokinetics, CSIR-Central Drug Research Institute, Lucknow 226031, Uttar Pradesh, India
[c] Department of Horticulture, Babasaheb Bhimrao Ambedkar University, Vidya Vihar, Raebareli Road, Lucknow 226025, Uttar Pradesh, India
[d] Department of Pharmacoinformatics, National Institute of Pharmaceutical Education and Research, Kolkata, India

ARTICLE INFO

Keywords:
Transporter-targeting
Bio-polymeric nanoparticles
Colon targeting

ABSTRACT

Orally targeted delivery systems have attracted ample interest in colorectal cancer management. In this investigation, we developed Inositol hexaphosphate (IHP) loaded Tripolyphosphate (Tr) crosslinked Pectin (Pe) Chitosan (Ch) nanoparticles (IHP@Tr*Pe-Ch-NPs) and modified them with L-Carnitine (CE) (CE-IHP@Tr*Pe-Ch-NPs) to improve uptake in colon cells. The formulated CE-IHP@Tr*Pe-Ch-NPs displayed a monodisperse distribution with 219.3 ± 5.5 nm diameter and 30.17 mV surface charge. Cell-line studies revealed that CE-IHP@Tr*Pe-Ch-NPs exhibited excellent biocompatibility in J774.2 and decreased cell viability in DLD-1, HT-29, and MCF7 cell lines. More cell internalization was seen in HT-29 and MCF7 due to overexpression of the OCTN2 and $ATB^{0,+}$ transporter (CE transporters) compared to DLD-1. The cell cycle profile, reactive oxygen species, apoptosis, and mitochondrial membrane potential assays were performed to explore the chemo-preventive mechanism of CE-IHP@Tr*Pe-Ch-NPs. Moreover, the in-silico docking studies revealed enhanced interactive behavior of CE-IHP@Tr*Pe-Ch-NPs, thereby proving their targeting ability. All the findings suggested that CE-IHP@Tr*Pe-Ch-NPs could be a promising drug delivery approach for colon cancer targeting.

1. Introduction

Cancer is a major burden disease worldwide that annually takes a toll on several lives. Worldwide, the prevalence and mortality are still rising substantially despite enormous attempts to address the issue. The incidence of colorectal cancer (CRC), the third largest cause of cancer mortality worldwide, is swiftly escalating in developing countries [1,2]. Cancer treatment burns holes in the patient's pocket, as well as the side effects of cancer therapy worsen the quality of life of a cancer patient. It has been demonstrated that 30–40 % of malignancies might be prevented with a simple diet change that includes increasing fruit and vegetable intake, retaining a healthy body weight, abstaining from alcohol, and engaging in consistent physical activity [3,4]. Natural dietary agents are known to control the genesis and course of malignancies owing to their low or no toxicity, notable multiple-site efficacy, oral ingestion, recognized mechanisms of action, competitive prices, and human acceptance. The utilization of natural products for CRC management is very promising because diet plays a significant role in the

* Corresponding author at: Pharmaceutical Education and Research (NIPER), Raebareli, Transit Campus: NIPER-Raebareli, Bijnor- Sisendi Road, Sarojini Nagar, Near CRPF Base Camp, Lucknow 226002, Uttar Pradesh, India.
E-mail address: shubhini.saraf@gmail.com (S.A. Saraf).
[1] Present Address: Faculty of Pharmacy, Babu Banarasi Das Northern India Institute of Technology, Sector II, Dr. Akhilesh Das Nagar, Faizabad Road, Lucknow-226028, Uttar Pradesh, India.
[2] Present Address: National Institute of Pharmaceutical Education and Research (NIPER), Raebareli, Transit Campus: NIPER-Raebareli, Bijnor- Sisendi Road, Sarojini Nagar, Near CRPF Base Camp, Lucknow-226002, Uttar Pradesh, India.
[3] Present Address: School of Pharmacy, GITAM (Deemed-to-be) University, Rudraram, Patancheru Mandal, Hyderabad, 502329, Telangana, India.

https://doi.org/10.1016/j.ijbiomac.2024.130517
Received 6 June 2023; Received in revised form 23 February 2024; Accepted 27 February 2024
Available online 28 February 2024