Customized Bioactive β-Glucan Conjugated Polymeric Nanoparticles Targeting Inflammatory Macrophages in Pancreatitis Treatment

*Archana Karole[1], Yirivinti Hayagreeva Dinakar[1], Poonam Sagar[2], Shabi Parvez[1], Shyam Lal Mudavath[3,] **

[1]Infectious Disease Biology Laboratory, Chemical Biology Unit, Institute of Nano Science and Technology, Knowledge City, Sector-81, Mohali-140306 (Punjab) India.

[2]Department of Food and Nutrition, National Agri-Food Biotechnology Institute, Knowledge City, Sector 81 Mohali, Punjab, India.

[3]Department of Animal Biology, School of Life Sciences, University of Hyderabad, Prof. C.R. Rao Road, Gachibowli Hyderabad 500046, Telangana, India.

shyamlal_absls@uohyd.ac.in, shavs0502@gmail.com

Macrophage polarization plays vital role in inflammatory disease condition, M1 macrophages worsens the disease by releasing Pro-inflammatory cytokines. The Dectin-1 receptors are overexpressed on M1 macrophages and M cells of Intestinal Lymphatic System (ILS) which are the potential target for treating various inflammatory disease. Pancreatitis is rare condition involving inflammation to the pancreas, further inflamed pancreas are overfilled with proteolytic enzyme trypsin making it potential stimulus to release the drug by trypsin mediated cleavage[1,2]. In this work we developed enzyme responsive, biocompatible and orally administrable β-Glucan-conjugated PLGA nanoparticles (GNPs) targeting Dectin-1 receptor for maximum accumulation of GNPs. The GNPs makes its way into the inflamed pancreas through Dectin-1 receptor. We synthesized and characterized GNPs exhibiting significant (25%) drug loading for AMX. The in-vitro studies revealed that AMX-loaded GNPs (AMX-GNPs) release the drug in the presence of trypsin and showed potential anti-inflammatory activity by modulating macrophage polarization and reducing cytokine release from M1 polarized macrophages. We observed that GNPs follow the oral route and release the drug primarily in the inflamed pancreas via the intestinal lymphatic system (ILS). Further, the in-vivo efficacy assessments in acute and chronic pancreatitis animal models demonstrated that AMX-GNPs effectively inhibit the inflammatory cytokines and activate anti-inflammatory mediators through regulating NF-κB activation pathways and M1macrophage polarization. The development of GNPs shows promising potential for treatment of pancreatitis due to its efficient binding and internalization through Dectin-1 receptor and active targeting of proinflammatory mediators by trypsin mediated drug release.

References:

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