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Pharmaceutical and immunological evaluation of mucoadhesive nanoparticles based delivery system(s) administered Intranasally

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Chitosan (CS) has attracted sizeable attention for mucosal vaccine delivery systems as it possesses the favorable biological properties such as biocompatibility, biodegradablility, mucoadhesive properties, and permeation enhancing ability. In spite of all its superior properties, chitosan has a major drawback that at physiological pH, chitosan lose its ability to enhance drug permeability and absorption. In contrast, trimethyl chitosan (TMC) shows high solubility, bioadhesive properties and ability to enhance permeability over a wide pH range. Nevertheless, TMC synthesis also accompanies synthesis dependent polymer chain scission, which may influence the carrier and adjuvant properties of TMC.

In this study, Trimethyl chitosan (TMC-M) was synthesized using milder method, which also limits the chain scission as reported in case of TMC synthesized using conventional method. The TMC-M, TMC and CS were characterized on the basis of their molecular weight and viscosity. The HBsAg was used as candidate antigen and nanoparticles were formulated using Polyelectrolyte complexation method. The developed nanoparticles based delivery system(s) were compared and characterized in-vitro on the basis of particles size, morphology, antigen loading and antigen release and in-vivo on the basis on nasal clearance, nasal uptake and immune induction following nasal immunization.

It was observed that the TMC-M had higher molecular weight as compared to TMC. This indicates that TMC-M synthesis did not cause any synthesis related chain scission. The CS, TMC and TMC-M nanoparticles were approximately 200 nm in size and smooth in morphology. It was observed that lyophilization did not affect the particles size, zeta potential or potency of the TMC-M, TMC and CS based nanoparticles. The TMC-M particles demonstrated higher surface zeta potential as compared to TMC and CS particles. TMC-M nanoparticles showed the lowest nasal clearance rate and higher nasal uptake when compared with chitosan (CS) and TMC nanoparticles. The immunogenicity of nanoparticles based delivery system(s) was assessed by measuring anti-HBsAg antibody titer in mice serum and secretions after intranasal administration. The alum based HBsAg vaccine injected subcutaneously was used as positive control.

Results indicated that alum based HBsAg induced strong humoral but negligible mucosal immunity. However, TMC-M nanoparticles induced stronger immune response at both of the fronts as compared to generated by CS or TMC nanoparticles. Present study demonstrates that TMC-M can be a better carrier adjuvant for nasal subunit vaccines.

Biography

He (Sharad Mangal) did Master's Degree in Pharmacy in 2008 from Dr. H.S. Gour University, Sagar, MP, INDIA. He received many prestigious awards that includes "Nagarjuna Gold Medal" and "Dal Chand Jain Award" by Dr. H.S. Gour University. Currently he is working in the field Application of Biomaterial and Nanotechnology for vaccine delivery. These studies have resulted in with the contribution of several publications and some more are in the formulation phase. He has published 10 international publications (5 Original Research, 5 Comprehensive Review) in the peer reviewed journals of high impact and repute in the field of vaccine delivery.