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*Research Article*

*Theme: Advancements in Amorphous Solid Dispersions to Improve Bioavailability*

# Sialic Acid Conjugated Chitosan Nanoparticles: Modulation to Target Tumour Cells and Therapeutic Opportunities

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***Abstract.*** Targeted delivery of therapeutics forestalls the dreadful delocalized effects, drug toxicities and needless immunosuppression. Cancer cells are bounteous with sialic acid and the differential expression of glycosyl transferase, glycosidase and monosaccharide transporter compared to healthy tissues. The current study entails the development and characterisation of sialic acid (SA)–labelled chitosan nanoparticles encapsulating gemcitabine (GEM). Chitosan (CS) was conjugated with SA using coupling reaction and characterised spectroscopically. Furthermore, different concentrations of chitosan and tripolyphosphate (TPP) were optimised to fabricate surface modified chitosan nanoparticles. SA conjugated chitosan nanoparticles encapsulating GEM (SA-CS_GEM NPs) of 232 ± 9.69 nm with narrow distribution (PDI < 0.5) and zeta potential of − 19 ± 0.97 mV was fabricated. GEM was successfully loaded in the SA-CS NPs, depicting prolonged and biphasic drug release pattern more elated at low pH. Pronounced cellular uptake (FITC tagged) and cytotoxicity ($IC_{50}$ 487.4 nM) was observed in SA-CS_GEM NPs against A549 cells. $IC_{50}$ for SA-CS_GEM NPs plunged with an increase in the time points from 24 to 72 h. Concentration-dependent haemolytic study confirmed significant haemocompatibility of SA-CS_GEM NPs. Pharmacokinetic study was performed on Sprague–Dawley rats and the kinetic parameters were calculated using PKSolver 2.0. Results demonstrated a consequential refinement of 2.98 times in modified SA-CS_GEM NPs with a significant increase in retention time, bioavailability and elimination half-life, and decrease in elimination rate constant and volume of distribution in comparison to CS_GEM NPs. Therefore, SA-CS shell core nanoparticles could be a beneficial approach to target and treat NSCLC (non-small cell lung cancer) and direct for research possibilities to target the other tumour cells.

**KEY WORDS:** A549 cell line; chitosan; nanoparticles; gem+citabine (GEM); PKSolver; sialic acid

## INTRODUCTION

Malignant oncogenic transformations are ascribed to the deviant glycosylation (1, 2). These anomalous glycosylations are resultant of conglomerate interactions from the substrate availability, gene expression (3), the ambience at cellular level (4) and the intrinsic protein structure (5). –O and –N linked (on proteins), glycosaminoglycans (on free as well as bound proteins), glycosphingolipids (on cell membrane) and glycosylphosphatidylinositol (on plasma membrane—glycolipids and glycans attached to proteins) are symphonic types of glycosylation (6). The heterogeneity of glycosylation at different glycosylation site renders the diverse 'glycoforms'. Tumour cells are witnessed with antigenic glycans delineated during foetal development (7, 8), modifying, clubbing and vaulting at the surfaces (9). In

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**Abbreviations:** *SA*, Sialic acid; *SAM*, Sialic acid mimetic; *CS*, Chitosan; *GEM*, Gemcitabine; *NPs*, Nanoparticles; *SA-CS_GEM*, Sialic acid conjugated chitosan nanoparticles encapsulating gemcitabine; *CS_GEM*, Chitosan nanoparticles encapsulating gemcitabine; *FT-IR*, Fourier-transform infrared spectroscopy; *UV-spectroscopy*, Ultraviolet spectroscopy; *HPLC*, High-pressure liquid chromatography; *MTT*, 3-(4, 5-Dimethyl thiazolyl-2)-2,5-diphenyltetrazolium bromide; *FITC*, Fluorescein isothiocyanate; *DMEM*, Dulbecco's modified eagle medium; *FBS*, Foetal bovine serum; *TPP*, Tripolyphosphate; *NSCLC*, Non-small cell lung cancer

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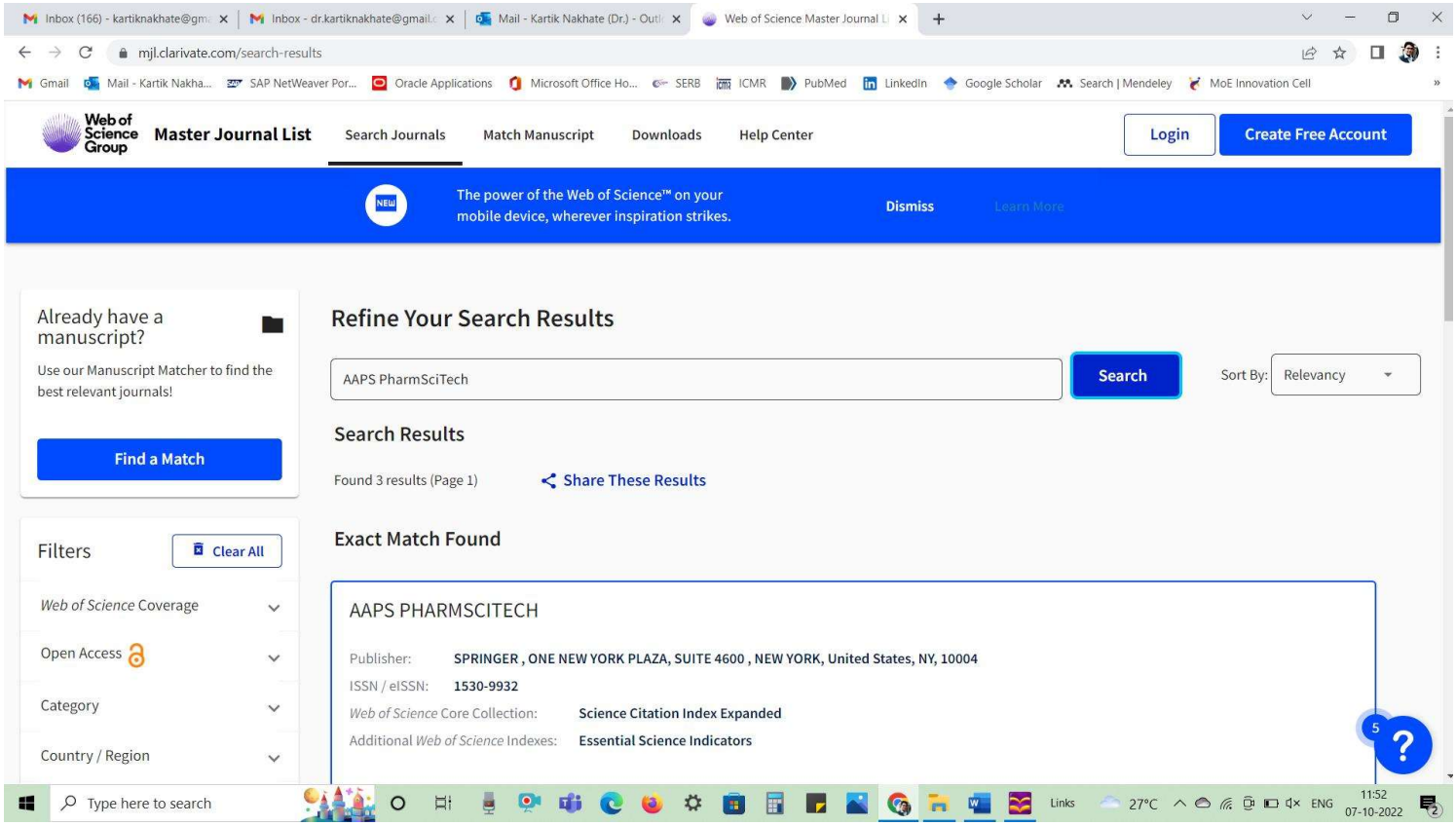
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