**Sorafenib-loaded Chitosan-Lipid Hybrid Nanoparticles for Sustained Drug Release and Improved Oral Bioavailability**

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**Background and aims.** Sorafenib (SRF) is a kinase inhibitor used to treat advanced renal cell, hepatocellular and differentiated thyroid carcinomas. However, its poor aqueous solubility results in low and variable oral bioavailability, high doses, side effects, and suboptimal therapeutic effects. We aimed to develop SRF-loaded solid lipid nanoparticles coated with chitosan (CS-SRF-SLNs) to improve oral bioavailability of SRF.

**Methods.** SRF-SLNs were first prepared with nanoemulsion template method using stearyl alcohol as a solid lipid and Myrj 52/Tween 80/Span 80 as a surfactants mixture. SRF-SLNs were subsequently coated with chitosan using electrostatic deposition technique to form CS-SRF-SLNs, and were assessed for their physicochemical properties, morphology, thermal and crystalline behaviours, *in vitro* drug release, and *in vivo* oral pharmacokinetics in rats.

**Results.** The optimized CS-SRF-SLNs showed small particle size (124.6 nm), low PDI (0.148), positive surface charge (+21.2 mV) and high encapsulation efficiency (91%) with spherical and smooth surface morphology. DSC and PXRD results confirmed successful incorporation of SRF in amorphous state in the lipid core, and FTIR study confirmed chitosan deposition on the surface of SRF-SLNs. Chitosan coating resulted sustained SRF release from SRF-SLNs in simulated gastric and intestinal fluids. Furthermore, CS-SRF-SLNs demonstrated significantly enhanced oral bioavailability in rats (3.9- and 2-times higher) compared to SRF dispersion and uncoated SRF-SLNs, respectively. CS-SRF-SLNs also showed adequate stability upon storage and in rat serum.

**Conclusion/Discussion.** SRF was formulated as SRF-SLNs followed by successful coating with cationic chitosan through electrostatic interactions with anionic lipid core as revealed by FTIR results and surface charge inversion from -18.6 mV (SRF-SLNs) to +21.2 mV (CS-SRF-SLNs). The substantial improvement in bioavailability suggests that CS-SRF-SLNs could be a useful carrier system for the oral delivery of SRF.

**References:**

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