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Fabrication and evaluation of rifampicin-loaded Solid Lipid Microparticles (SLMs) based on structurally modified phytolipid from *Irvingia wombolu*

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Edible phytolipids from *Irvingia wombolu* (IW) combined with Phospholipon 90H (P90H) formed structurally modified lipids as a vehicle for the delivery of a BCS class II drug, rifampicin, offering increased pay load of drug in addition to increased physical stability. Rifampicin-loaded Solid Lipid Microparticles (SLMs) using structurally modified lipid matrices based on IW Fats (IWF) and P90H were formulated. The rifampicin-loaded SLMs were prepared using P90H and IWF at optimized concentrations of 1:2 and 1:3, respectively, and characterised in terms of particle size and morphology, pH, Encapsulation Efficiency (EE), thermal stability and stability in Simulated Gastric Fluid (SGF, pH 1.2), *in vitro/in vivo* release and antimicrobial susceptibility studies. The particle size ranged from 32±7.64 to 55±26.46 µm, pH was stable over 3 months and EE range of 84 to 91.6 % were obtained. Rifampicin-loaded SLMs had about 21.2% degradation at 4 h in SGF, while rifampicin pure sample had 63.9% degradation. SLMs had about 66.2 to 81.1% release in Simulated Intestinal Fluid (SIF, pH 7.4) at 12 h and also exhibited significantly higher *in vivo* absorption of rifampicin than the reference commercial sample ($p<0.05$). Rifampicin-loaded SLMs also exhibited good activities against *Staphylococcus aureus, Bacillus subtilis, E. coli* and *Klebsiella pneumonia*. The formulated rifampicin-loaded SLMs had good *in vitro* and *in vivo* properties and also exhibited sustained release properties for once daily administration. Method of SLM preparation adopted is straightforward and the produced SLMs indicated sustained drug release, better *in vivo* bioavailability, prevention of acidic degradation of rifampicin and good antimicrobial properties.

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Simulation study of the mechanism of uptake of cell pentrating peptides in cancer cells

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It is somehow easy to understand why it is still so controversial the mechanisms of cellular uptake of Cell-Penetrating Peptides (CPP). Although there is evidence that these peptides are capable of directly crossing the plasma membrane without any intermediate step, still several researchers claim that endocytosis is an intermediate step required for entry into the cells. It is well known that ionic interactions play a critical role for the binding to the plasma membrane and translocation of CPPs. A simulation of the interaction between Arginine-Glycine (RG)5 and Histidine-Glutamic Acid (HE)5, as well as with DOPC of the lipid bilayer was conducted in order to calculate the free binding energy. The results supported the data obtained in the *in vitro* release, cell uptake and cytotoxicity studies. The absolute value of binding energy of (RG)5 with (HE)5 was the highest, however a decrease in the pH was found to diminish this strong bond. Interestingly, the conjugation of (RG)5 to PEG-PLA copolymer increased the binding energy to DOPC. In summary, the peptides tend to interact with the cell membrane which facilitates the uptake in an energy and receptor independent manner as postulated by many researchers.

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