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A step towards a safer efficient antituberculosis therapy: Formulation and assessment of Rifampicin targeted inhaled nanocomposite

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Rifampicin, despite of being the most effective antitubercular drug; its efficacy encounter obstacles mainly; poor bioavailability and therapeutic activity is concentration-dependent. Nanocrystals, a new carrier-free colloidal drug delivery system, is thought as a viable drug delivery strategy to develop the poorly soluble drugs. Rifampicin nanosuspensions were fabricated using the anti-solvent precipitation technique. The impact of solvent type and flow rate, stabilizer type and concentration, stirring time and apparatus together with the solvent-antisolvent volume ratios on this controlled nanocrystallization have been evaluated. Nanocrystals were characterized by TEM, particle size and zeta potential analysis, solubility and dissolution profiles. The compatibility between RIF and the stabilizer were investigated via FTIR and the DSC techniques. The shelf-life stability of the optimized nanosuspension was assessed within a period of three months at different storage temperatures. Cell cytotoxicity was evaluated using MTT assay on lung epithelial cells.In addition, design of an inhaled targeted nanocomposite based carbohydrate was performed and their aerosolization performance was assessed. The results obtained highlighted that polyvinyl alcohol at 0.4% w/v, 1:15 methanol to deionized water volume ratio and 30 min sonication were the optimal parameters for RIF NS preparation. Nanocrystals were obtained with a particle size (101 nm) and zeta potential (-26 mV) additionally, exhibited 50 folds enhancement in rifampicin solubility and 97% of RIF was dissolved after 10 minutes. The prepared nanosuspension was stable at 4±0.5°C with no significant change in particle size or zeta potential. The MTT cytotoxicity assay of rifampicin nanosuspension demonstrated a good safety profile, reduction in cell cytotoxicity with IC50 values of 0.5 and 0.8 mg/mL for rifampicin powder and optimized nanocrystals, respectively. With aid of some carbohydrates, nanocrystals were transformed into decorated microparticles, which is suitable for inhalation therapy. The formulated nanocomposite was able to deliver the drug to the infected alveoli. Novel rifampicin-loaded nanocomposite could be followed as an approach for enhancing rifampicin therapeutic outcomes which initiate the generation of a wave for an efficient strategy for safe targeted delivery of such a poorly soluble drug to the lung.

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Pharmaceutical & drug delivery technologies for effecient pain management

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Breakthrough pain in cancer patients is a transitory exacerbation of pain experienced for a short period of time by the patient who has relatively stable and adequately controlled baseline pain. Transmucosal drug delivery through intranasal, sublingual, and buccal mucosa are considered an attractive routes to deliver breakthrough pain management medications. It avoids the hepatic first-pass clearance, which results in enhanced bioavailability and faster onset of drug action. The *in-vivo* pharmacokinetics of three breakthrough pain drugs has been evaluated in rabbis. Conscious rabbits were used, because anesthesia could impair the nasal mucociliary clearance and thereby allowing the formulations to remain in contact with the nasal mucosa for a longer time than would be normally expected without anesthesia. The same apply for the sublingual delivery to mimic the transient time in clinical use. In two separate experiments, the sublingual administration of Fentanyl and Oxycodone showed promising kinetic profiles, resulting in a rapid absorption with acceptable absolute bioavailability up to 82%. Factors such as formulation viscosity and drug moieties of salt versus free base were also evaluated in light of its effect on absolute bioavailability. Furthermore, Tetrahydrocannabenol (THC) intranasal delivery, also showed acceptable bioavailability comparable to the currently marketed soft gelatin capsules formulations, but irritation to nasal mucous membranes requires further drug formulation efforts to overcome this problem. With the increase demand on enhancing the quality of cancer patients' life, transmucosal delivery offers compelling opportunities to bring new safe and effective drugs to the market.

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