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Supercritical antisolvent co-precipitation of rifampicin and ethyl cellulose

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ABSTRACT:

Rifampicin-loaded submicron-sized particles were prepared through supercritical anti-solvent process using ethyl cellulose as polymeric encapsulating excipient. Ethyl acetate and a mixture of ethyl acetate/dimethyl sulfoxide (70/30 and 85/15) were used as solvents for both drug and polymeric excipient. When ethyl acetate was used, rifampicin was crystallized separately without being embedded within the ethyl cellulose matrix while by using the ethyl acetate/dimethyl sulfoxide mixture, reduced crystallinity of the active ingredient was observed and a simultaneous precipitation of ethyl cellulose and drug was achieved. The effect of solvent/CO2 molar ratio and polymer/drug mass ratio on the co-precipitates morphology and drug loading was investigated. Using the solvent mixture, co-precipitates with particle sizes ranging between 190 and 230 nm were obtained with drug loading and drug precipitation yield from respectively 8.5 to 38.5 and 42.4 to 77.2% when decreasing the ethyl cellulose/rifampicin ratio. Results show that the solvent nature and the initial drug concentrations affect morphology and drug precipitation yield of the formulations. In vitro dissolution studies revealed that the release profile of rifampicin was sustained when co-precipitation was carried out with the solvent mixture. It was demonstrated that the drug to polymer ratio influenced amorphous content of the SAS co-precipitates. Differential scanning calorimetry thermograms and infrared spectra revealed that there is neither interaction between rifampicin and the polymer nor degradation of rifampicin during co-precipitation. In addition, stability stress tests on SAS co-precipitates were carried out at 75% relative humidity and room temperature in order to evaluate their physical stability. SAS co-precipitates were X-ray amorphous and remained stable after 6 months of storage. The SAS co-precipitation process using a mixture of ethyl

acetate/dimethyl sulfoxide demonstrates that this strategy can be successful for controlling rifampicin delivery.