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## Supercritical antisolvent co-precipitation of Rifampicin and Ethyl cellulose

Rania Djerafi<sup>a</sup>, Andri Swanepoel<sup>b</sup>, Christelle Crampon<sup>a</sup>, Lonji Kalombo<sup>b</sup>, Philip

Labuschagne<sup>b</sup>, Elisabeth Badens<sup>a</sup>, Yasmine Masmoudi<sup>a</sup>

<sup>a</sup> Aix Marseille Univ, CNRS, Centrale Marseille, M2P2, Marseille, France

<sup>b</sup> Polymers & Composites, Council for Scientific & Industrial Research (CSIR), PO Box 395, Pretoria, South Africa

### 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/CO<sub>2</sub> 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 190-230 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

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