

CONTROLLED PRECIPITATION OF HYDROPHOBIC PHARMACEUTICALS IN SUBCRITICAL WATER

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Subcritical water has received attention as an ideal green fluid for extraction, purification, separation and, more recently, rapid precipitation processes. Subcritical liquids are substances that have been heated and pressurized beyond their boiling points, and below the critical points whilst still in a liquid state. The versatility of subcritical water as a dissolution fluid comes from the ability to tune the polarity of water by manipulating temperature. Between 100oC and 250oC the polarity of water changes from being equivalent to dimethylsulfoxide (DMSO) to being equivalent to acetone. Within the aforementioned temperature range, a vast number of hydrophobic compounds with antioxidant and other therapeutic properties have been dissolved. Dissolution of these compounds was accomplished without loss of the therapeutic activity.

The aim of this work was to dissolve a number of common active pharmaceutical ingredients (APIs) in subcritical water and then examine the effect and potential of subcritical water to rapidly precipitate these APIs. Griseofulvin, naproxen, budesonide and pyrimethamine were the APIs selected for this study. Rapid precipitation of APIs was accomplished by rapidly cooling the solution, which allowed the polarity of water to decrease fast enough to allow particles of narrow size distribution to form. Product characteristics and morphology were in some cases dependant on the pre-injection temperature of the solution. Micronization was possible for griseofulvin and pyrimethamine down to 500nm with uniform crystalline morphologies. Processed products retained their crystalline morphology and active chemical structure, which was determined by infrared spectroscopy and thermogravimetric analysis.