MOLECULAR INSIGHT OF THE SOLUBILITY OF TWO ANTI-INFLAMMATORY DRUGS WITH SIMILAR STRUCTURE IN CO_2-EXPANDED SOLVENTS BY IR SPECTROSCOPY

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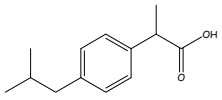
Precipitation techniques from CO_2-expanded solvents are eco-efficient one-step processes for the straightforward preparation of micro and nano sized powders of polar pharmaceutically active materials, with a highly homogeneous crystalline structure [1]. The selection of the most appropriate precipitation procedure depends on the solubility behaviour of the drug in a given CO_2 expanded solvent. The solubility behaviour of the two Non-Steroidal Anti-Inflammatory Drugs (NSAIDS), ibuprofen (**1**) and naproxen (**2**), is similar in CO_2-expanded ethanol at 10 MPa and 308 K, showing that for both compounds CO_2 acts as a co-solvent in a wide concentration range. In marked contrast, under the same pressure and temperature conditions in CO_2-expanded acetone, the role of CO_2 appears different for the two drugs. In naproxen/acetone/CO_2 solution, the CO_2 exhibits a strong anti-solvent character whereas it behaves as a co-solvent in the mixture "ibuprofen/acetone/CO_2" until high values of the CO_2 concentration are reached [2]. Therefore, the DELOS process [3] is the most suitable precipitation procedure for ibuprofen diluted in "acetone-CO_2" and "ethanol-CO_2" solvent mixtures. For naproxen, although a gas anti-solvent [4] process is preferable to precipitate it from "CO_2-expanded acetone", the DELOS process remains the best adapted for its precipitation from "CO_2-expanded ethanol".



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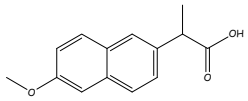

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Based on the experience gained in our previous investigations [5], we have used in this work mid-IR spectroscopy in order to understand at a molecular level the different solubility behaviour in CO_2-expanded solvents of these two anti-inflammatory drugs having similar molecular structure.

References

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