High Pressure NMR studies of triacetyl-β-cyclodextrin/drug inclusion complexes in super critical CO_2

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Many drug formulations use cyclodextrins, CDs, since their cavities provide microenvironments where drug molecules can enter and form inclusion complexes for drug delivery. In the last years there has been an increasing research devoted to CD derivatives, in particular triacetyl-β-CD (TA-β-CD), since its hydrophobicity decreases the solubility of the guest molecule providing a longer and controlled release of the drug. Supercritical (sc) CO_2 is a very attractive medium for the preparation of CDs inclusion complexes, as alternative to aqueous and organic solvents. In contrast to β-CD, which is insoluble in $scCO_2$, its per-acetylated derivative exhibits melting point reduction and solubility in dense CO_2, since the acetyl groups are accessible to Lewis acid:base interactions[1-5]. A few papers report the use of this CD derivative to form inclusion complexes. However significant conformational distortions induced by the acetylation of β-CD have also been detected in solid state and in solution leading to self-closure of the molecular cavity from both sides of its conical structure by the acetyl chains[6,7]. In this work a high-pressure apparatus especially designed for high-pressure NMR studies[8] was used to obtain information on the molecular structure and dynamics of TA-β-CD dissolved in $scCO_2$ and thus allow to discuss the feasibility of preparing host-guest inclusion complexes of this CD derivative in $scCO_2$.

High resolution ^1H and ^{13}C NMR and two-dimensional NOESY (Nuclear Overhauser Effect SpectroscopY) and ROESY (Rotating-frame Overhauser Effect SpectroscopY) experiments were performed for TA-β-CD in $scCO_2$. We will present and discuss preliminary results that show that at 40ºC in $scCO_2$, TA-β-CD presents structural distortions which compromise the inclusion of a guest molecule into the cavity.

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