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Amorphous Ibuprofen Confined in Nanostructured Silica Materials: A Dynamical Approach

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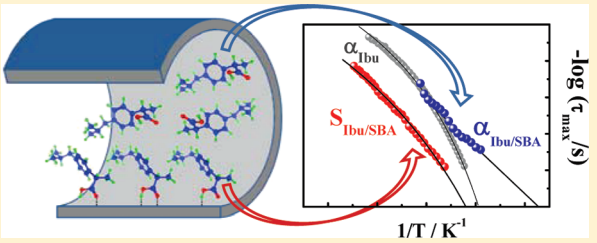
ABSTRACT: The molecular mobility of condensed matter confined to nanometer dimensions can be dramatically changed from those of the bulk state in such a way that, when the guest is a drug, it can be advantageously used in pharmaceutical applications. We show by dielectric relaxation spectroscopy that the molecular mobility of the important ibuprofen drug embedded in nanoporous SBA-15 is significantly influenced by the confinement. An evidence of the existence of two families of molecules with different molecular mobilities is provided and investigated in their temperature dependence. One family is due to molecules close to the pores' center with a higher mobility compared with the bulk at low temperatures, and another family with slower dynamics originated from molecules interacting with the pore walls. The work reports the simultaneous manifestation of true confinement and surface effects in this nanostructured silica host for a drug. For future applications in drug delivery systems, the dynamics determined by the guest−host interplay and the one of the bulklike molecules can be tuned to achieve a desired release profile.



INTRODUCTION

Pharmaceutical compounds in their amorphous form can play a crucial role concerning the therapeutic activity.[1−4] Recently, confinement of drugs in nanoporous host systems emerged as a strategy to stabilize the otherwise unstable glassy/supercooled state and to manipulate the crystalline state of pharmaceuticals.[5,6] Moreover, it is well known that the glass transition and the glassy dynamics (α-relaxation, dynamic glass transition) of guest molecules is affected by confining it in nanoscaled geometries, which tend to lower the glass transition temperature T_g.[7−10] This is called the confinement effect.[8] Even the molecular motions responsible for the α-relaxation can change dramatically for pore sizes lower than a critical value, which allows estimating a minimal length scale for cooperativity.[8] In addition to this scenario, molecular dynamics in a confining space is also determined by surface effects resulting from interactions of the guest molecules with the walls of the porous host. These interactions take place at the interface of both and slow down the molecular dynamics.[8,11,12] Surface effects become important for small pores and strong surface interaction as has been shown for systems forming hydrogen bonds between the guest molecules and the inner pore wall.[13−16] As a result, the molecular dynamics of molecules confined to nanoporous hosts is controlled by a counterbalance between confinement and surface effects.

Among the different nanoporous matrices, mesoporous silica-based materials attract a great interest due to their particular physical properties, such as their biocompatibility, ordered pore network, high internal surface area, silanol-containing surface, and chemical and mechanical stability.[17,18]

Small organic molecules have been confined to such matrices[19−23] and pharmaceutics as well[24−29] from which particular relevance was given to the analgesic, antipyretic, and anti-inflammatory poorly water-soluble model drug, ibuprofen, as a potential drug delivery system.[30−33]

The crystallization of bulk ibuprofen (racemic form) can be easily circumvented on cooling from the melt,[34−36] which allowed some of us to investigate the molecular mobility in the supercooled and the glassy state[35] using dielectric relaxation spectroscopy (DRS),[37] over a wide frequency and temperature range. Multiple relaxation processes were identified: the main α-relaxation associated with the dynamic glass transition, a β_{JG} Johari−Goldstein process taken as the precursor of the α-relaxation, and a more localized secondary γ-relaxation. Moreover, in the supercooled liquid state ($T > T_g$), an additional relaxation mode with a Debye-like shape (D-process) was found assigned to the dynamics of hydrogen-bonded aggregates.

Regarding the molecular mobility in confinement, NMR showed that ibuprofen, when confined to MCM-41[38−41] and SBA-15,[27] is extremely mobile and it is not in a crystalline or glassy state. Nevertheless, most of these studies were carried out at room temperature. Therefore, it is necessary to investigate the molecular mobility in a much wider temperature and frequency range. DRS is a powerful tool to get a detailed knowledge regarding the molecular mobility of guests, among which only few studies refer to organic low-molecular-weight materials confined

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