Phase transitions and charge transport properties of a novel ionic liquid with pharmacological applications [C_2OHmim][Ibu]

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The intrinsic combination of an ionic liquid (IL) with an active pharmaceutical ingredient (API) forming an IL-API, recently emerged as a strategy to overcome problems such as crystallization, polymorphs conversion, solubility, and bioavailability.[1] This IL-API combination allows to finely tune the physicochemical and biopharmaceutical properties, maintaining the bioactivity of the API or even undergo a novel effect over the precursor ion.[2] As long as the therapeutic activity is preserved, it is necessary to establish the experimental conditions that keep the substance in a stable state either crystalline or amorphous. Motivated by this problem that gained recently a growing interest in the pharmaceutical industry, a novel IL-API was prepared and its phase transformations and mobility were characterized.

The IL-API was synthetized by the appropriate combination of the ibuprofen anion (API) as sodium salt with the 1-(2-Hydroxyethyl)-3-Methyl-Imidazolium ([C_2OHmim]) cation.

Calorimetric studies showed that crystallization is circumvented in the IL-API upon cooling at 10 ºCmin^{-1} from 150 ºC down to -100 ºC, the material being easily vitrified. For the dried material, a glass transition temperature was detected at ~-24 ºC upon heating. Subsequently, two exothermal peaks are observed followed at higher temperatures by a bimodal endothermal peak. This behavior suggests the existence of two different crystalline forms allowing considering that the tested IL-API exhibits polymorphism. Measurements carried out with polarized optical microscopy also support this suspicion, but more studies must be done in order to assure these conclusions. The IL-API was dielectrically characterized over a wide frequency (10^{-1} to 10^6 Hz) and temperature range from -100 to 130 ºC. Additionally, mobility and diffusion coefficients were estimated revealing non-Arrhenius temperature dependence. Moreover, conductivity measurements revealed to be sensitive to the crystallization of the IL-API.

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References

(1) Hough, W. L.; Smiglak, M.; Rodríguez, H.; Swatloski, R. P.; Spear, S. K.; Daly, D. T.; Pernak, J.; Grisel, J.E.; Carliss, R. D.; Soutullo, M. D.; Davis, J. H.; Rogers, R. D. *New Journal of Chemistry* **2007**, 31, 1429-1436.

(2) V. Kumar, V. Malhotra Sanjay, in Ionic Liquid Applications: Pharmaceuticals, Therapeutics, and Biotechnology, American Chemical Society, Washington, DC, **2010**, 1-12.