Poster Presentation

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Structure Determination of LASSBio-1289: A New Antihypertensive Lead-Compound

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Hypertension is considered a multi-factorial disease being an important worldwide public-health challenge due to its high frequency and concomitant risks of cardiovascular and other diseases. It has been identified as the leading risk factor for mortality, and is ranked as the third cause of disability-adjusted life-years[1]. The LASSBio-1289 compound was designed from the lead compound LASSBio-294 through the use of medicinal chemistry strategy of bioisosteric replacement of aromatic rings[2]. Many factors are involved in the task of describing the relationship between chemical structure and pharmacological activity of a prototype of a new drug. Among these factors the study of atomic-level structure can be included. The aim of this work is to carry out the structural characterization of LASSBio-1289, in solid-state. Since many NAH derivatives, as LASSBio-1289, do not form single crystals for proper structure determination, this task was overcome by using X-ray powder diffraction data and an ab initio simulated annealing procedure. This study can contribute to better understand the full pharmacodynamic profiles and physicochemical properties of this class of compounds. The LASSBio-1289 compound was synthesized following the procedure described in literature[3]. The sample was sofly hand-grinded in an agate mortar in order to get a fine powder suitable for X-ray powder diffraction analysis. The final refined values for the unit-cell parameters after the Rietveld fit were: a = 14.5119(3) Å, b = 12.1375(2) Å, c = 7.5498(1) Å, β = 91.113(1) Å, Z = 4, Z' = 1 and ρcalc = 1.44039(5) g.m-3. The goodness-of-fit indicator and R-factors were: χ2 = 1.290, RBragg = 1.749%, Rwp = 4.903%, Rexp = 3.802% and Rp = 3.661%. The crystal structure of LASSBio-1289 compound consists of four formula units per unit cell (Z = 4), accommodating one molecule in the asymmetric unit (Z' = 1). The sample was indexed as monoclinic space group (P21/c).

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