Stereochemistry and Anti-Inflammatory Inhibition: Asymmetry, And Complexes Of 4-Halogenated Mofebutazones Derivatives

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Abstract:

The role of halogens in racemic 4-hal-4-butyl (n-octyl)-1phenyl derivatives (hal: F, Cl, Br), of the cyclic pyrazoline(1,3)-diones in the solid state and in solution was determined [1]. Noncovalent interactions are observed for the F, Cl and Br derivatives between the halogen atom and the hydrogen atom of the nitrogen of the pyrazolidine ring, water hydrogens that interact either with the halogen atoms or with the carbonyl oxygen atoms very different from the none-halogenated pyrazoline-diones [2-5]. The 3d and 2d structures are stabilized by [H] and [H] interactions, intermolecular distances, and apolar forces between adjacently stacked phenyl rings. However, the R-or S-enantiomers or their water-stable complexes with Znmeglumine did not racemizes in aqueous dispersions [1,3]. Small-angle-, wide-angle x-ray scattering experiments, and molecular simulation reveal similar solution structure factors, S(Q), in the solid state and in solution [6,7]. The planes and their periodicities of the crystalline phases are preserved in the aqueous solution phase. There is also hydrogen bonding formed in the racemic and the R-enantiomeric n-octyl-1phenyl-1-Cl-pyrazoline-(1,3)-dione between the hydrogens of the water molecules and the halogens of the pyrazolidine ring: Cl forms a hydrogen bond to the water hydroxy group of a neighbouring molecule, which is hydrogen bonded to the chlorine of another molecule forming a 1-dimensional hydrogen-chloride bond network differently from hydrated cationic lipids or their polymorphs [8,9]. The n-octyl pyrazolidine approximant forms micelles in aqueous dispersions that selfassemble into quasicrystalline structures. The small-angle X-ray scattering experiments and the selected area electron diffraction pattern of thin films suggest that the micelle FCC phase transforms into a colloidal quasicrystalline phase with 12-fold symmetry that proceed through rearrangements of the micelles in the (111) layers of the FCC phase. The differences of the

halogenated cyclic and non-cyclic pyrazoline diones are related to biochemical changes in anti-inflammatory activities. The n-octyl compound reveal antimicrobial and antiviral (influenza) activities but no anti-inflammatory or analgesic activities.

Biography:

Prof. Henrich H. Paradies, FRSC & CC, MD, Ph.D., Ph.D., D.Sc. (h.c.) studied bioinspired, smart and multiscale materials with defined wettabilities of cationic lipids as components in antiviral, antibacterial, and anti-inflammatory ingredients, the inhibition of viral activities on the level of monomer or aggregated sizes (cyclic peptides), adherence for brushy surfaces by clinging to flaws and function of the organization on their specific head groups e.g. ammonium vs. phosphonium groups, Zn-cationic lipid-alendronate complexes or cyclic peptides with antimicrobial activities.

Publication of speakers:

1. Reichelt H., Paradies H.H. (2018) Structures and anti-inflammatory properties of 4-halogenatedmofeburazones. J. Mol. Structure, 1154: 204-218.
2. Paradies H.H., Ziedrich H.K., Flämig, H. H. (1990) Structural studies on mofebutazone derivatives and their in-vitro activities. J. Med. Chem. 25: 143-156.
3. Paradies H.H, (1987) Structure of phenylbutazone and mofebutazone in the crystalline state and in solution. J. Pharm.Sci.76:820-929.

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