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AMMONIUM HEXAFLUOROSILICATES AS POTENTIAL ANTI-CARIES AGENTS: SYNTHESIS, STRUCTURES, SOLUBILITY, BIOLOGICAL ACTIVITY

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Ammonium hexafluorosilicates (AHFS) are a class of inorganic compounds widely used in modern technological practice and laboratory research [1, 2]. In recent years, AHFS have been actively studied as promising caries-preventive agents because of their certain advantages over traditional fluoride drugs. In the present communication the synthesis, structural characteristics, properties and biological activity of AHFS with heterocyclic and phenylammonium cations as potential anti-caries agents are discussed.

The crystalline salts with the composition $(LH)_2[SiF_6]$ (L^{1-3} = 2-, 3-, 4-carboxypyridine, **I-III**; L^{4-6} = 2-, 3-, 4-carboxymethylpyridine, **IV-VI**; L^{7-9} = 2-, 3-, 4-carboxyethylpyridine, **VII-IX**; L^{10} = 3-hydroxymethylpyridine, **X** (monohydrate); L^{11} = 4-hydroxymethylpyridine, **XI**; L^{12} = 2-amino-4,6-dihydroxypyrimidine, **XII**) were obtained by the interaction of hexafluorosilicic acid (45 %) with methanol solution of corresponding ammonium chlorides (LH)Cl or free base L. The amorphous salts $(L^{13})[SiF_6]$ (L^{13} = octenidine, **XIII**) and $(LH)_2[SiF_6]$ (L^{14-16} = 2-, 3-, 4-aminophenylacetic acid, **XIV-XVI**; L^{17-19} = 3-(3-aminophenyl)propionic, 3-(4-aminophenyl)propionic, 2-amino-2-phenylbutyric acid, **XVII-XIX**) were obtained in a similar way. All compounds were characterized by elemental analysis, ^1H, ^{19}F NMR, IR, mass-spectrometry, solubility data, and **III-XII** by X-ray crystallography. Based on X-ray diffraction data, interionic H-bonds are the main structure-organizing and stabilizing factor in the formation of structures of AHFS. The involvement of fluoride-ligands of the $[SiF_6]^{2-}$ anion in systems of inter-ionic H-bonds NH···F, H···F, OH···O and CH···F contacts of various strengths leads to a noticeable redistribution of the Si–F bond lengths. Analysis of XRD data allows us to underline the general tendency: as a rule, in the N–H···F–Si structural fragments, the Si–F and N···F distances are in the antibate dependence. Judging from the results of Hirschfeld surface analysis for complexes **VII-IX**, the dominant intermolecular contacts are H···F/F···H, H···H, H···O/O···H with percentages 33.3-34.5 %, 26.4-30.0 % and 16.0-21.8 % [3].

Assessment of solubility in water and organic solvents is a mandatory procedure for all drug candidates. The observed general tendency for a significant decrease in solubility of ionic AHFS when moving from solutions in highly polar water and DMSO solvents to less polar alcoholic media is generally to be expected, and the decrease in solubility of these salts in ethanol compared to methanol and water may reflect the relative “lipophilization" of the medium.

According to biological experiments (Wistar rats), all AHFS exhibit noticeable anti-caries activity with the simultaneous significant improvement in the biochemical parameters of dental pulp and the absence of hepatotoxic effects in a given dosing (with the exception of **XII**) [1-3]. Among the studied AHFS, complexes **VI** and **XII** exhibits the highest caries-preventive efficacy, which exceeds the analogous indicators for the reference drug, NaF, by 5 times. The results of determining the characteristics of acute toxicity of salts **VI** (LD_{50} = 481.28 mg/kg) and **XIII** (LD_{50} = 555.05 mg/kg) by the oral route of administration make it possible to classify this compounds as moderately toxic and slightly toxic compounds (hazard class III and IV, respectively).

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