

7-(4-Chlorophenyl)-1-hydroxy-5-methylpyrido[3,4-*d*]pyridazin-4(3*H*)-one: synthesis, solvatomorphism, *in vitro* anti-inflammatory and cytotoxic activity studies and *in silico* analysis

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Streszczenie

The newly obtained compound 7-(4-chlorophenyl)-1-hydroxy-5-methylpyrido[3,4-*d*]pyridazin-4(3*H*)-one (**CPM**) was crystallized as two new variable solvates, namely, the dimethyl sulfoxide monosolvate, $C_{14}H_{10}ClN_3O_2 \cdot C_2H_6SO$ (**I**), and the sesquisolvate, $C_{14}H_{10}ClN_3O_2 \cdot 1.5C_2H_6SO$ (**II**), and their structures were confirmed by single-crystal X-ray diffraction analysis. In previous work, 1-hydroxy-5-methyl-7-phenylpyrido[3,4-*d*]pyridazin-4(3*H*)-one (**PM**) was found to display anti-cancer activity. In the next step of our studies, we synthesized a new derivative of **PM**, introducing a Cl atom into the **PM** structure, obtaining **CPM**, which showed not only anti-cancer but also anti-inflammatory activity. **CPM** and the new semi-products of each step of the synthesis were examined by 1H NMR, ^{13}C NMR and FT-IR spectroscopic analyses, and mass spectrometry. **CPM** forms (**I**) and (**II**) crystallize in the triclinic *P*1 and monoclinic *C*2/*c* space groups, respectively, and differ in the stoichiometry of the **CPM** and DMSO molecules in the crystal lattice, being 1:1 and 1:1.5 for (**I**) and (**II**), respectively. A powder X-ray diffraction analysis was performed only for solvate (**I**) due to the lack of stability of solvate (**II**). The potential cytotoxicity of **CPM** was evaluated against the normal cell lines L929 and RPTEC, as well as the cancer cell lines A172, AGS, CACO-2 and HepG2. The anti-inflammatory activity of **CPM** was also evaluated using colorimetric assay for the inhibition of COX-1 and COX-2. The same biological tests were carried out for **PM** to compare the activities of both compounds. The biological studies revealed that **CPM** does not exhibit more activity than **PM**. Moreover, *in silico* analysis of the bioavailability and molecular docking were performed.

Język	Słowa kluczowe
Angielski	pyrido[3,4-d]pyridazine derivatives, synthesis,
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