Interaction of methotrexate, an anticancer agent, with copper(II) ions : coordination pattern, DNA-cleaving properties and cytotoxic studies.

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Streszczenie

The acid–base properties and the Cu(II) binding processes of methotrexate (MTX) were characterized by selected spectroscopic techniques and potentiometric measurements. The pH titration data showed that MTX behaves as a triprotic ligand. The deprotonation constants were determined for a-COOH and c-COOH groups and (N1)H? from the pteridine ring. Taking all the obtained results into consideration, a coordination pattern was proposed. The DNA-cleaving activity and reactive oxygen species (ROS) generation were investigated for both MTX and the Cu(II)–MTX system. The complex displayed a promising nuclease activity toward plasmid DNA in the presence of hydrogen peroxide. Interestingly, the induction of ROS, such as hydroxyl radicals, superoxide anions or singlet oxygen, was excluded and a different mechanism of DNA degradation was proposed. As MTX is now commonly used in anticancer therapy i.e. against lung cancer, basic cell-based studies were carried out to establish if its Cu(II) complex exhibits higher cytotoxic properties than the ligand alone. Activities of both compounds were also tested against colon carcinoma. Moreover, the determined values of IC50 were confronted with the cytotoxic activity of cisplatin.

Słowa kluczowe

Methotrexate, Copper(II) complexes, Plasmid DNA damage, Cytotoxic studies

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