Strategies for overcoming tropical disease by ruthenium complexes with purine analog : application against *Leishmania spp.* and *Trypanosoma cruzi*.

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Streszczenie

Tropical diseases currently constitute a major health problem and thus a challenge in the field of drug discovery. The current treatments show serious disadvantages due to cost, toxicity, long therapy duration and resistance, and the use of metal complexes as chemotherapeutic agents against these ailments appears to be a very attractive alternative. Herein, we describe three newly synthesized ruthenium complexes with a bioactive molecule, the purine analogue 5,6,7-trimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine (tmtp): *cis,fac*-[$RuCl_2(dmso)_3(tmtp)$] (**1**) , *mer*-[$RuCl_3(dmso)(H_2O)(tmtp)]\cdot 2H_2O$ (**2**) and *fac,cis*-[$RuCl_3(H_2O)(tmtp)_2$] (**3**). Their structures were characterized using X-ray and spectroscopic methods (IR, NMR or EPR). The stability of the synthesized complexes **1**–**3** in various buffered solutions (pH = 3–7.4) was monitored using conventional and stopped-flow techniques. The *in vitro* antiproliferative activity of all ruthenium complexes against promastigote forms of *Leishmania spp*. (*L. infantum*, *L. braziliensis*, and *L. donovani*) and epimastigote forms of *Trypanosoma cruzi* was investigated. Notably, the results showed that the activity of **1** against *L. brasiliensis* was more than three-fold higher than that of glucantime, and **1** showed no appreciable toxicity towards J774.2 macrophages. Additionally, **2** displayed even 141-fold lower toxicity against host cells than glucantime, demonstrating significantly higher selectivity than the reference drug. Therefore, **1** and **2** appear to be excellent candidates for further development as potential drugs for the effective treatment of leishmaniasis and Chagas disease. All novel complexes were also shown to be potent inhibitors of Fe-SOD in the studied species, while their effects on human CuZn-SOD were very low.

Adres publiczny

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