SYNTHESIS AND PHYSICOCHEMICAL CHARACTERIZATION OF TITANIUM(IV)-FLAVONOID COMPLEXES AS ANTICANCER AGENTS

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ABSTRACT

After platinum-based chemotherapy has proven effective in treating cancer, titanium(IV) complexes were the first to be developed and tested in clinical trials. The poor efficacy to toxicity ratio and formulation issues in the potential drugs, however, caused all candidates to fail the trials. The complexes hydrolyse quickly, resulting in the production of several unclear aggregates and making them difficult to isolate and identify the specific active species and thus the exact cellular target(s) [1]. In spite of that, these compounds still have considerable potential in the field of pharmaceuticals, due to the fact that in biological environments hydrolysis produces safe and inert titanium dioxide. Being cognizant of the existing literature and the arisen problems with potential titanium drugs in cancer chemotherapy, we have chosen a different approach. In that respect, the primary goal of this undertaken research has been to develop hydrolysis-resistant titanium(IV) complex forms that can be employed as metallodrugs to treat metabolic and cancer disorders or even prevent them altogether. Consequently, incorporation of antioxidant, anti-inflammatory, and anti-cancer property-bearing species,[2] involving organic ligands seeking complexation to select metal ions, has been pursued in our Lab as a very promising alternative to the already existing complexes. To that end, titanium(IV)-flavonoid systems have been investigated synthetically, using chrysin and quercetin in both binary and ternary systems, complemented with 1,10-phenanthroline as an auxiliary ternary aromatic chelator. The newly emerging materials, revealed for the first time in our Lab, in binary and ternary systems, have been fully characterized in the solid state and in solution through Elemental analysis, Fourier Transform Infrared spectroscopy (FT-IR), Nuclear magnetic resonance (^{1}H, ^{13}C NMR) and Electron Spray Ionization (ESI-MS). Further delineation of their 3D structure was verified through single crystal X-Ray Crystallography and their luminescence properties where investigated in the solid state. The collective results reveal a well-defined physicochemical profile on the hybrid Ti(IV)-organic species that supports their ensuing investigation in in vitro cell cultures of distinct cancer cell tissues, thereby meriting substantive consideration in future therapeutics.

KEYWORDS: Flavonoids, Titanium, Anticancer activity, Metal-organic complex, Crystal structure

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