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FULL PAPER

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Synthesis and structural and DNA binding studies of mono- and dinuclear copper(II) complexes constructed with —O and —N donor ligands: Potential anti-skin cancer drugs

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Mononuclear and dinuclear copper(II) complexes with thiophenecarboxylic acid, [Cu(3-TCA)$_2$(2,2′-bpy)] (**1**), [Cu(3-Me-2-TCA)$_2$(H_2O)(2,2′-bpy)] (**2**), [Cu(5-Me-2-TCA)$_2$(H_2O)(2,2′-bpy)] (**3**) and [Cu_2(2,5-TDCA)(DMF)$_2$(H_2O)$_2$(2,2′-bpy)$_2$](ClO_4)$_2$ (**4**) (where 3-TCA = 3-thiophenecarboxylic acid; 3-Me-2-TCA = 3-methyl-2-thiophenecarboxylic acid; 5-Me-2-TCA = 5-methyl-2-thiophenecarboxylic acid; 2,5-TDCA = thiophene-2,5-dicarboxylic acid; 2,2′-bpy = 2,2′-bipyridyl; DMF = *N*,*N*-dimethylformamide), were synthesized. Compounds **1**–**4** were extensively characterized using both analytical and spectroscopic methods. Additionally, the solid-state structures of **1** and **4** were unambiguously established from single-crystal X-ray diffraction studies. The hexacoordinated Cu(II) centre in **1** (CuO_4N_2) is a distorted octahedral geometry whereas the pentacoodinated **4** (CuO_3N_2) has distorted square pyramidal geometry. Compounds **1** and **4** exhibit intermolecular hydrogen bonding which leads to the formation of two- and three-dimensional supramolecular architectures, respectively. Spectrophotometric and computational investigations suggest that these compounds bind with DNA in minor groove binding such that $K_b = 4.9 \times 10^5\ M^{-1}$ and $K_{sv} = 3.4 \times 10^5\ M^{-1}$, and binding score of −5.26 kcal mol^{-1}. The binding affinity of these complexes to calf thymus DNA is in the order **2** > **3** > **4** > **1**. Methyl-substituted thiophene ring increases the DNA binding affinity whereas unsubstituted thiophene ring DNA binding rate is reduced. The methyl group on the thiophene ring would sterically hinder π–π stacking of the ring with DNA base pairs, and subsequently they are involved in hydrophobic interaction with the DNA surface rather than partial intercalative interaction. Compounds **1**–**4** show pronounced activity against B16 mouse melanoma skin cancer cell lines as measured by MTT assay yielding IC_{50} values in the micromolar concentration range. The compounds could prove to be efficient anti-cancer agents, since at a concentration as low as 2.1 μg ml^{-1} they exerted a significant cytotoxic effect in cancer cells whereas cell viability was not affected in normal cells.

