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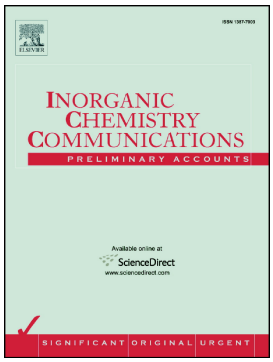

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Synthesis and characterization of novel trimethyltin(IV) and tributylltin(IV) complexes of anticoagulant, WARFARIN: potential DNA binding and plasmid cleaving agents

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Abstract: Novel trimethyltin(IV) (**1**) and tributyltin(IV) (**2**) derivatives of an anticoagulant drug warfarin (WR) have been synthesized and characterized through elemental analysis, FTIR studies, multinuclear NMR and ESI mass spectrometry and DFT calculation. Their DNA binding profile (mode and extent of binding with CT DNA) through UV-visible and fluorescence spectrophotometric titrations reveal their partial intercalation inside the base pairs of DNA, and the binding constant (K_b) calculated through UV-visible titration are in the order of 10^4 M^{-1}. Their partial intercalation has also been validated through a decrease in the viscosity of CT DNA with increasing the complex concentration. Both the complexes are potential concentration dependent plasmid cleaving agent which has been confirmed though gel electrophoresis of pBR322 plasmid. Both the organotin(IV) complexes have been found to exhibit a greater potential towards DNA binding and fragmentation in comparison to WR.

Keywords: Warfarin; organotin(IV); DNA-binding; partial intercalation; gel electrophoresis

Warfarin (WR) has been used widely as an oral anticoagulant drug after fourteen years of its crystallization by Karl Link in 1940 [1,2]. In 2006, it was estimated that in UK alone, ≈ 1% of the total population and ≈ 8% of population aged over 80 years are using WR as an oral anticoagulant drug [3]. Over the last two decades, a tremendous increase in its use can be traced due to its obvious effectiveness to prevent embolic strokes in patients with atrial fibrillation and valvular heart disease [4]. Besides, the ability of WR and other coagulants to decrease thromboembolic events, various reports in the literature suggest the possibility of their antitumor potential/efficacy [5-9]. The laboratory experiments and clinical trials on animals with WR,