

# Comparison of curcumin, diacetylcurcumin and analogs as ligands for vanadyl, Ga(III) and In(III) complexes with therapeutic potential

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Vanadyl bis(ligand) complexes have been investigated extensively as possible insulin enhancing agents and also, more recently, for other medicinal applications, including as cancer chemotherapeutic agents. Ga(III) tris(maltolato) and tris(qinolinato) complexes have also shown anticancer potential. In this study, novel bis(1,7-diaryl-1,6-heptadiene-3,5-dione) complexes with the formula,  $ML_3$ , where M is Ga(III) or In(III), or of the formula,  $ML_2$  where M is  $[VO]^{2+}$ , were synthesized and characterized by ESI-MS, FTIR, UV/vis and EA. The ligand, L, is any of: curcumin (bis[4-hydroxy-3-methoxyphenyl]-1,6-heptadiene-3,5-dione, cur), demethoxycurcumin (DMC), bisdemethoxycurcumin (BDC), diacetylcurcumin (DAC), or diacetylbisdemethoxycurcumin (bis[4-acetyl-3-hydroxyphenyl]-1,6-heptadiene-3,5-dione, DABC, a new ligand). Cytotoxic potential of curcumin ligands and their metal complexes was tested in mouse lymphoma cells by MTT assay.  $VO(cur)_2$ ,  $VO(DMC)_2$  and  $VO(DAC)_2$  were screened as potential insulin mimetic agents in STZ- diabetic rats.

Neither the vanadyl complexes nor the ligands alone showed any glucose-lowering effect in acute i.p. testing. *In vitro*, vanadyl complexes were more cytotoxic than ligands alone (with the exception of DABC, which was not different from  $VO(DABC)_2$ ) but not significantly different from each other, with  $IC_{50}$ 's in the 5-10  $\mu M$  range, where  $IC_{50}$  values represent the concentration of a test compound that is required for 50% reduction of cellular growth.  $Ga(cur)_3$  and  $In(cur)_3$  addition to cell cultures resulted in  $IC_{50}$  values in the same range as for vanadyl complexes; however,  $Ga(DAC)_3$  and  $In(DAC)_3$  were much less cytotoxic ( $IC_{50} = 20-30 \mu M$ ) than  $Ga(cur)_3$  or  $In(cur)_3$ . Since both  $\beta$ -diketone and phenolic OH groups are known to contribute to the antioxidant potential of curcumin, one can speculate that in  $Ga(DAC)_3$  and  $In(DAC)_3$ , either or both of these functionalities may be hindered, causing a dramatic reduction in cytotoxic potential.