TITLE: BACTERIAL REVERSE MUTATION TEST (AMES TEST) FOR EVALUATION OF MUTAGENICITY OF METAL COMPLEX OF VANADIUM

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The demonstration that the Ames *Salmonella*/microsome assay (Ames test) is effective at identifying potentially carcinogenic chemicals led its immediate adoption, and requirement, by regulatory authorities world-wide. When a chemical is determined to be a mutagen in the Ames test it has the potential of also being a carcinogen based on the somatic mutation theory of carcinogenesis. Thus, a drug candidate that is active in a mutagenicity test or that produces mutagenic metabolites by activation in a microsomal enzyme system will generally be discarded in favor of a backup candidate. Therefore, the aim of this study was to investigate the mutagenic activity of the metal complex of vanadium with orotic acid bioactive ligand (OV001) to guarantee its safe use in humans. The Ames test uses bacteria as sensitive indicators of DNA damage, and a rat liver homogenate (S9 microsomal fraction) for metabolic conversion of carcinogens to their active mutagenic forms. In the present study, the Ames test was performed using TA98, TA100, TA97 and TA102 strains of *Salmonella typhimurium* in the absence (-S9) and presence (+S9) of metabolic activation system in five concentrations, varying from 6.25 to 50 µg/ plate. The results obtained showed that OV001 did not induce any increase in the number of revertant colonies relative to the negative control, indicating the absence of mutagenic activity. The absence of mutagenic effects in bacterial systems is encouraging, because although many compounds have considerable pharmacological activities, some undesirable properties such as mutagenicity, carcinogenicity and toxicity may restrict their use as therapeutic agent. In this context, it is important to continue the pharmacological and toxicological investigations of OV001 in order to determine the mechanism(s) of action to guarantee their safer and more effective application to human health.

Keywords: metal complex, Ames test, mutagenicity

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