EFFECT OF HYPUSINATION INHIBITION IN THE GROWTH AND DIFFERENTIATION OF *LEISHMANIA AMAZONENSIS*

Souza, A. R.; Santos, F. R.; Ferraz, D. B.; Costa-Neto, C. M.; Ramalho-Pinto, F. J.
FMRP-USP, Departamento de Bioquímica e Imunologia, SP

Hypusination is a chemical reaction catalyzed firstly by deoxyhypusine synthase, and further, by deoxyhypusine hydroxylase, in which spermidine is covalently bound to the lysine^{50} on the eIF5A, generating the amino acid hypusine. The eukaryotic initiation factor eIF5A is a protein that participates in eukaryotic cell growth and/or differentiation. The compound N1-guanil-1,7-diaminoheptano (GC7), blocks the hypusination of eIF5A. In order to determine the role of eIF5A in the life cycle of *Leishmania amazonensis*, we have investigated the effect of GC7 on the *in vitro* growth and differentiation of promastigotes. We report that GC7, at concentration range of 12.5 to 500 mM, do not interfere with the growth of promastigotes. However, concentrations of 1 to 5 mM of this inhibitor were able to promote a significant decrease of parasite replication. In the differentiation assay for *in vitro* transformation of amastigotes to promastigotes, GC7 did not affect parasite differentiation even at concentrations of 1 to 5 mM. Our results indicate that *L. amazonensis* is quite resistant to the inhibitory effect of GC7, with only very high concentrations of the inhibitor (1 to 5 mM), being able to interfere with the growth of promastigotes. However, the GC7 does not interfere with the process of amastigote to promastigote differentiation.

Supported by CNPq, CAPES and FAPESP
Key words: GC7, hypusination, *Leishmania amazonensis*