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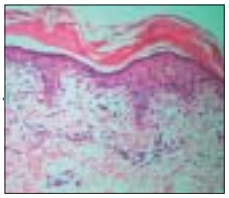

Hypothesis: The potential utility of topical eflornithine against cutaneous leishmaniasis

Sir,

The trypanothione biosynthetic pathway is common to the trypanosomatid family of protozoa, which includes *Leishmania* and *Trypanosoma,* and is absent in the host systems. This pathway constitutes an important target for

chemotherapy against leishmaniasis. The trypanothione pathway combines two metabolic pathways: the glutathione and the polyamine biosynthetic pathways, to produce trypanothione, a glutathione-spermidine conjugate.[1]

The levels of trypanothione are increased in the Leishmania parasite selected for resistance to the heavy metal, arsenic. The levels of putrescine and spermidine were increased in resistant mutants. This increase is mediated by overexpression of ornithine decarboxylase, the rate-limiting enzyme in polyamine biosynthesis.[2] Fluorinated analogues of L-ornithine are powerful inhibitors of ornithine decarboxylase and inhibit the cell growth of *L. infantum* promastigotes.[3]

Eflornithine was originally used orally in the treatment of childhood hyperactivity.[4] It was used as an anti-cancer drug in 1970[5] and was later used intravenously in the treatment of African sleeping sickness.[5,6] Interestingly, hair loss was observed as an adverse effect of this treatment.[5,7] Eflornithine hydrochloride cream (13.9%) is the first topical preparation approved by the FDA in August 2000 for the reduction of facial hirsutism in women.[5] It is a potent inhibitor of ornithine decarboxylase. A topical formulation of this agent has been used for treatment of hirsute women as inhibition of ornithine decarboxylase delays the initiation of anagen and keeps hair in telogen. Therefore, eflornithine does not remove the excess hair but it causes slowing of excessive hair growth.

Given the important role of ornithine decarboxylase in the trypanothione biosynthetic pathway, eflornithine could prove to be effective against leishmaniasis. Combining this agent with glucantime could potentiate the therapeutic response of the latter and break the resistance of the resistant strains against it. Clinical studies on this subject are warranted.

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