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3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGR) from *Leishmania* donovani is indispensible for the parasites as depicted by gene knockdown studies

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*Leishmania*sis is one of the most diverse and complex of all vector borne diseases which are transmitted through the bite of infected female Phlebotomine sand flies. Existing anti*leishmania*l drugs are associated with toxicity, resistance issue, high prices and lack of quality during administration and long treatment length. Sterols are the important components of the cell membrane which are essential for cellular functions and maintain the cell structure. In humans, HMGR is a rate limiting enzyme of cholesterol biosynthesis and is a trans-membrane glycoprotein. In *Leishmania*, however HMGR exists as a soluble protein involved in ergosterol biosynthesis. The sterol biosynthetic pathway in *Leishmania* is considered to be an important drug target. In the present study, null mutants of LdHMGR were generated by homologous recombination and mutants were confirmed by PCR, western blotting and enzyme activity. The ergosterol level was quantified by HPLC method and found that the SKO LdHMGR parasite ergosterol level was low when compared to WT parasite and 99.14% reduction was observed in DKO LdHMGR. Growth curve analysis of SKO LdHMGR was found to be less with rapid reduction in growth rate of the DKO LdHMGR promastigotes as compared with WT promastigotes. Infectivity analyses showed decreased percentage of host cell line infection by null mutants of LdHMGR as compared to SKO LdHMGR and WT promastigote parasite. This data suggests that HMGR plays an essential role in growth and infectivity of parasite and it is an essential enzyme and can be utilized for future anti*leishmania*l chemotherapeutic intervention.

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