2'-Hydroxyflavanone effects *in vitro* and *in vivo* against *Leishmania amazonensis*

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Leishmaniasis is a disease that deserves attention due to the wide variety of clinical manifestations and its high annual incidence. Pure compounds obtained from plants have significant antiprotozoal activity. 2'-hydroxyflavanone is a flavanone, currently known to inhibit metastasis, vascularization and induce apoptosis in many types of cancer cells. This study evaluated the effect of 2'- hydroxyflavanone on both forms of *L. amazonensis in vitro, in silico* pharmacokinetic analysis and its effect *in vivo*. Promastigotes were treated with different concentrations of 2'-hydroxyflavanone for 9 hours. 2'-hydroxyflavanone demonstrated a dose dependent inhibition profile from 3h of incubation with an IC50 of 11µM, reaching 80% of inhibition at the highest concentration (96µM). ROS levels and Mitochondrial membrane potential were measured showing na increase of ROS levels, reaching 1.8 fold to control and a depolarization of the mitochondrial membrane, reaching 69% (96µM). To evaluate antiamastogote activity, peritoneal macrophages were infected with *L. amazonensis* and incubated with 2'-hydroxyflavanone (3-12µM) for 72h. 2'-hydroxyflavanone demonstrated a decrease on infected index in a dosedependent manner with an IC50 of 3.4µM. All the tested concentrations were not toxic to macrophages, with and IC50 of 72µM and a selectivity index of 21.3. In silico analysis qualified 2'-hydroxyflavanone as a good candidate to oral treatment in vivo and fulfilled the Lipinski rule of five. Furthermore, oral treatment with 2'-hydroxyflavanone (50mg/kg/day) in BALB/c mice infected with L. amazonensis was able to control the lesion size and reduce the parasitic load. Toxicological analysis showed no change in biochemical and hematological parameters. The selective in vitro activity of 2'-hydroxyflavanone, together with excellent theoretical predictions of oral availability, clear decreases in parasite load and lesion size, and no observed compromises to the overall health of the infected mice encourage us to support further studies of 2'-hydroxyflavanone as a candidate for Leishmaniasis chemotherapy.

Supported by:CNPq; CAPES; FAPERJ; IOC/FIOCRUZ
Keywords:Leishmaniasis; 2'-hydroxyflavanone; chemotherapy