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BACKGROUND:
Schistosomiasis is a parasitic disease caused by trematodes of the genus Schistosoma. Five species of Schistosoma are known to infect humans, out of which S. haematobium is the most prevalent, causing the chronic parasitic disease schistosomiasis that still represents a major problem of public health in many regions of the world and especially in tropical areas, leading to serious manifestations and mortality in developing countries. Since the 1970s, praziquantel (PZQ) is the drug of choice for the treatment of schistosomiasis, but concerns about relying on a single drug to treat millions of people, and the potential appearance of drug resistance, make identification of alternative schistosomiasis chemotherapies a high priority. Alkylphospholipid analogs (APLs), together with their prototypic molecule edelfosine (EDLF), are a family of synthetic antineoplastic compounds that show additional pharmacological actions, including antiparasitic activities against several protozoan parasites.
METHODOLOGY/PRINCIPAL FINDINGS:
We found APLs ranked edelfosine> perifosine> erucylphosphocholine> miltefosine for their in vitro schistosomicidal activity against adult S. mansoni worms. Edelfosine accumulated mainly in the worm tegument, and led to tegumental alterations, membrane permeabilization, motility impairment, blockade of male-female pairing as well as induction of apoptosis-like processes in cells in the close vicinity to the tegument. Edelfosine oral treatment also showed in vivo schistosomicidal activity and decreased significantly the egg burden in the liver, a key event in schistosomiasis.
CONCLUSIONS/SIGNIFICANCE:
Our data show that edelfosine is the most potent APL in killing S. mansoni adult worms in vitro. Edelfosine schistosomicidal activity seems to depend on its action on the tegumental structure, leading to tegumental damage, membrane permeabilization and apoptosis-like cell death. Oral administration of edelfosine diminished worm and egg burdens in S. mansoni-infected CD1 mice. Here we report that edelfosine showed promising antischistosomal properties in vitro and in vivo.