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# Anthelmintic activity of antioxidants: *in vitro* effects on the liver fluke *Opisthorchis felineus*

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*Background*: Currently, pharmacologists and medical parasitologists are searching for new agents against foodborne trematodiases. Redox metabolism is important for parasites as far as long-lived adult parasites inside a mammalian host are exposed to redox challenges. Thus, parasite survival may depend on the ability to maintain the necessary balance between oxidation and antioxidation. The importance of redox metabolism for parasites is underscored by the number of relevant genes in helminth genomes, levels of expression of these genes, and the presence of relevant proteins in the secretome. Antioxidants have been poorly studied as anthelmintic agents, in particular against the foodborne trematodes.

*Methods and Algorithms*: Study of *in vitro* anthelmintic activity of nonenzymatic natural and synthetic antioxidants of various chemical structures was performed using standard motility and mortality assays against juvenile and adult *Opisthorchis felineus* worms. Kaplan–Meier survival curves were built using the 'survival' (v.2.38) R package. Four-parameter logistic regression was utilized to calculate IC50 and standard error (SE) values ('drc 3.0-1 ' R package). The ANOVA lack-of-fit test was performed to assess the hypothesis that a proposed regression model fits the data well. Hematoxylin and eosin staining was performed to analyze the tegument structure of adult flukes after SkQ1 treatment.

*Results*: Promising agents have been found among both natural and synthetic compounds. The mitochondria-targeted antioxidant SkQ1 [10-(6'-plastoquinonyl) decyltriphenylphosphonium] in motility assays was as effective (half-maximal inhibitory concentration [IC50] 0.6–1.4 μM) as officinal terapeutic agent praziquantel (IC50 0.47–1.4 μM). Moreover, SkQ1 was significantly more effective than praziquantel in mortality assays. Furthermore, extensive tegument damage of the adult fluke was revealed after SkQ1 treatment. Flavonoids manifested potency too, with IC50 values in a micromolar range (5.1–17.4 μM). Other natural and synthetic compounds tested against helminths were significantly less effective than praziquantel.

*Conclusion*: Results of our study indicate that SkQ1 and flavonoids have high anthelmintic activities against the liver flukes. We propose that structure–activity relationship research might be worthwhile based on the structures of the most effective substances.

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