The antihelminthic effects of a plant-derived compound, plumbagin (5-hydroxy-2-methyl-1,4-naphthoquinone), against Fasciola gigantica and Schistosoma mansoni

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Fasciolosis and schistosomiasis by the trematodes in Fasciola and Schistosoma spp. are recognized as major global parasitic diseases that cause health problems in animals and humans as well as economic losses worldwide. At present, effective vaccines are not yet available; therefore, anthelmintic drugs including triclabendazole (TCZ) and praziquantel (PZQ) are the main method of control of the infections. However, resistances to these drugs have emerged and may pose a serious problem as no other effective drugs are yet available. Plumbagin (5-hydroxy-2-methyl-1,4-naphthoquinone; PB) is a compound derived from the roots of many plants, especially those in the Plumbaginaceae family, which is used as a traditional medicine for the treatments of several ailments including parasitic infections. However, there are only a few scientific reports of its potential and no data of its mechanism as an anthelmintic agent. The objective of this study was to investigate the in vitro anthelmintic activities of PB against Fasciola gigantica and Schistosoma mansoni, and its effect on the structure of the tegument and associated structures by light (LM), scanning (SEM), and transmission electron microscopy (TEM).

Based on the measurements of relative motility and survival index, PB showed more antihelminthic effect than TCZ and PZQ. When examined by LM and SEM, PB caused more damage in the tegument on male than female flukes. PB caused similar tegumental alterations as those observed in TCZ or PZQ treatments, but with greater severity, comprising of swelling, blebbing and rupturing of the tegument, loss of spines, and eventually erosion, lesion and desquamation of the tegument. When observed by TEM, PB-treated flukes exhibited markedly swollen mitochondria, followed by disruption of the apical plasma membrane, dilatation of basal infolds, depolymerization of microtrabecular and cytoskeletal networks, and formation of vacuoles throughout the tegument syncytium, followed by the breaking-down and detachment of the whole tegument. Over a long periods of incubation, the tegumental cell bodies, subtegumental musculature, and surrounding parenchymal tissue showed degeneration and necrotic changes, while TCZ and PZQ showed less effect at comparable doses and times. A test by MTT assay indicated that PB reduced mitochondrial activity, thus this may be the initial tripping point that triggered the cascade of structural changes in the tegument and underlying structures that eventually lead to parasites’ death.

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Fig. 1: Light micrographs (LM) of (a) untreated and (b) 100 μg/ml PB-treated 4-week-old juveniles of F. gigantica at 24 h. (c) untreated and (d) 10 μg/ml PB-treated adult S. mansoni at 3h.

Fig. 2: Scanning electron micrograph (SEM) of the tegumental surfaces of adult male S. mansoni from untreated control group.

Fig. 3: Transmission electron micrographs of the 4-week-old juveniles of F. gigantica in untreated group after 24 h incubation in 0.1% DMSO.

Fig. 4: Newly excysted juvenile liver fluke (NEJ) of Fasciola hepatica after in vitro incubated with (A) 0.1% DMSO as control, and (B) the purple formazan granules appeared throughout the tissues of control NEJ incubated 4 hour with MTT (Magnification approximately 300x).