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A multienzyme response is involved in the phenomenon of resistance to triclabendazole on *Fasciola*

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The trematode *Fasciola hepatica* is the producer of a parasitic zoonosis known as fasciolosis. Triclabendazole (TCBZ) is the most widely used fasciolicide anthelmintic. Today, its indiscriminate use has led to the expression of anthelmintic resistance. Our previous studies over the *Sligo* strain (TCBZ-R) confirmed in the Phase I of detoxification, an overexpression of Flavin-Monooxygenases. This phenomenon should not be the only response that the trematode has and should not rule out the involvement of other processes of detoxification of Phase I or II. In the processes of detoxification in Phase I, the Carboxylesterase (CE) is a serine esterase-dependent with broad substrate specificity. This family of enzymes are involved in many metabolic functions including detoxification of xenobiotics. In Phase II exists a system using the Glutathione (GSH). It is a sequence of certain enzymes that culminate adding reduced GSH to xenobiotic increasing its water solubility and facilitating their excretion. Glutathione addition plays an important role in antioxidant defense in different tissues catalyze the reduction of oxidized to reduced GSH which will be utilized by GST to reduce the peroxide and lipoperoxide, which they are reactive oxygen species. This process involves Glutathione Peroxidase (GPx), Glutathione Reductase (GSR) and Glutathione S-Transferase (GST). In the present work, we evaluate, *in vitro*, the cytosolic activity of different xenobiotic metabolizing enzymes of Phase I: CE and Phase II: GST, GPx and GSR in adults of *F. hepatica* TCBZ susceptible (TCBZ-S) and TCBZ resistant (TCBZ-R), respectively *Cullompton* strain and *Sligo* and *Oberon* strains. In the TCBZ-R *Sligo* and *Oberon* strains, the GST activity was 1277 ± 32 and 1216 ± 16 nmol/min/mg protein, respectively, higher than that in the TCBZ-S *Cullompton* strain 800 ± 60 nmol/min/mg protein. Regarding the GPx activity in the *Sligo* and *Oberon* strains, TCBZ-R was 83 ± 3.41 and 81 ± 2.45 nmol/min/mg protein, respectively, higher than that in the TCBZ-S *Cullompton* strain 49 ± 2.58 nmol/min/mg protein. The GSR activity in *Sligo* and *Oberon* strains was 38 ± 2.07 and 41 ± 1.25 nmol/min/mg protein, respectively, higher than that in the TCBZ-S *Cullompton* strain 29 ± 1.22 nmol/min/mg protein, whereas CE activity did not differ between the different strains tested. In this work, a multienzyme response involving at all the family of enzymes GSH dependent is detected. Carboxylesterase expressed no significant differences not being involved in the resistance phenomenon. These results contribute to the understanding of the mechanisms referred to the phenomenon of resistance to TCBZ.

Biography

Vanesa Fernández is a Veterinary Doctoral Student at the National University of Central Buenos Aires and CONICET scholarship.

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