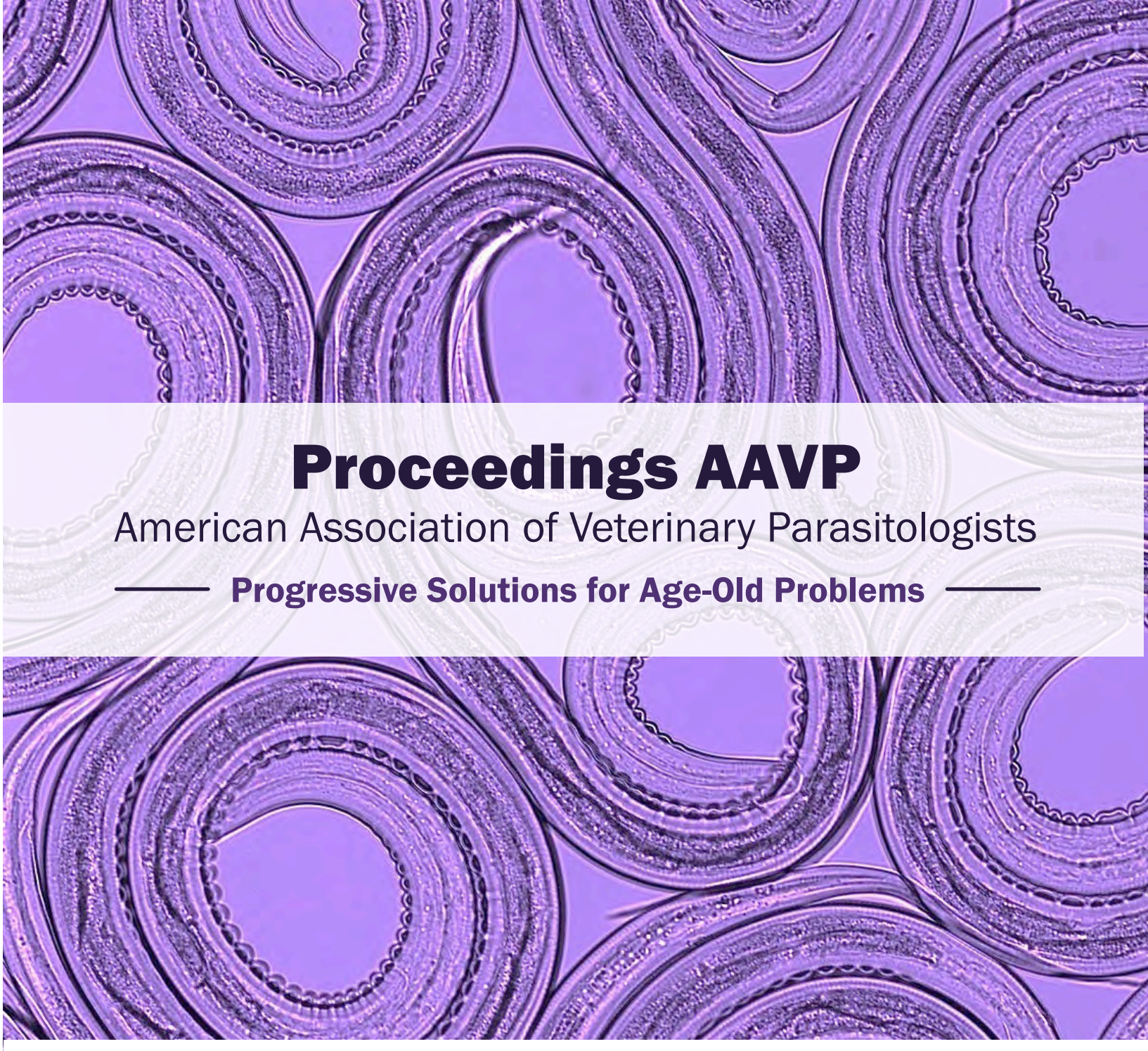

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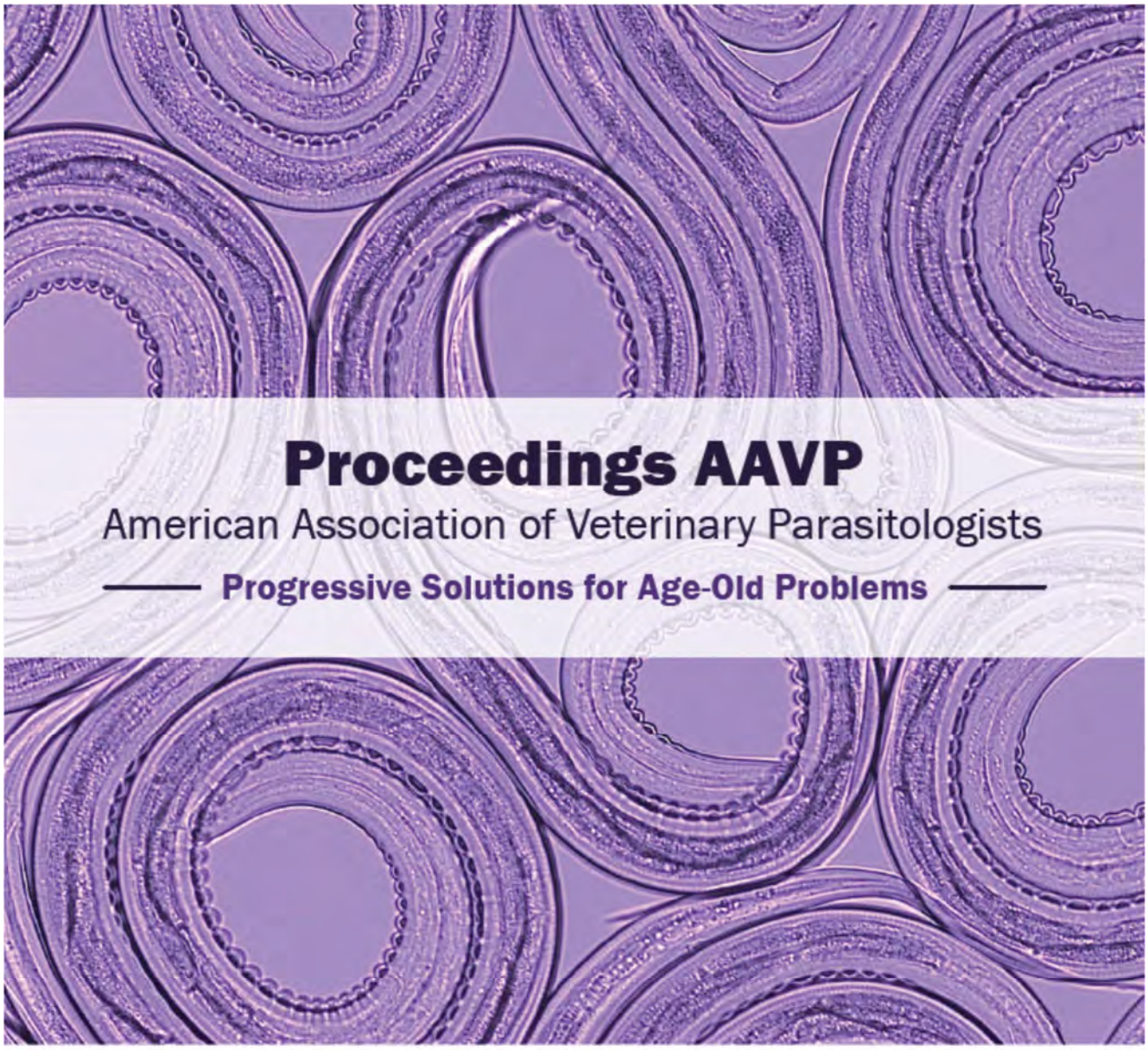

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molecular markers for further studies of Microphalloidea taxonomy, population genetics, and systematics.

127

Repurposing oxfendazole as a potential flukicidal compound

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Oxfendazole (OFZ) is a nematodicidal drug without flukicidal activity at its recommended therapeutic dose in sheep (5 mg/kg). However, flukicidal activity has been described when OFZ was used at a higher dose (30 mg/kg) both in sheep and pigs. The goals of this study were to characterize the OFZ/metabolites plasma disposition kinetics after OFZ administration at either 5 (OFZ_5) or 30 (OFZ_{30}) mg/kg dose to non-infected sheep (PK study), and to evaluate the dose-related pattern of *in vivo* accumulation of OFZ/metabolites into *F. hepatica* (Accumulation study). *Pk study*: sheep (n=12) were orally treated with OFZ at either 5 (OFZ_{TD}) or 30 (OFZ_{30}) mg/kg. Blood samples were collected over 96 h p.t. *Accumulation study*: *F. hepatica* infected animals (n=8) were orally treated with OFZ at either 5 or 30mg/kg. Animals were sacrificed by captive bolt in accordance with the Animal Welfare Policy (Act 087/02) of the Faculty of Veterinary Medicine, UNCPBA, Tandil, Argentina and internationally accepted animal welfare guidelines (AVMA, 2001). After sacrifice, samples of blood, bile, liver and adult liver flukes were obtained at different times. OFZ was the main analyte detected in plasma from OFZ treated sheep and its systemic exposure ($AUC_{0–LOQ}$) increased from 17.9 ± 3.71 (OFZ_5) up to 85.4 ± 22.6 (OFZ_{30}) µg.h/mL. The Cmax value was 4-fold higher in the OFZ_{30} group than that in OFZ_5 group. These differences were also reflected in the pattern of OFZ accumulation into *F. hepatica*, which was 332 % higher in group OFZ_{30} (4.28 µg/g) than OFZ_5 (0.99 µg/g). The OFZ dose increment was clearly associated with a higher plasma drug exposure and accumulation into the *F. hepatica*, which help to explain the OFZ flukicidal efficacy observed after a dose of 30 mg/kg. The reported pharmacological data may contribute to assess OFZ repurposing for a new use as flukicidal.