INSTITUTO DE LA QUÍMICA Y METABOLISMO DEL FÁRMACO

CONICET

IQUIMEFA

CONSEJO NACIONAL DE INVESTIGACIONES CIENTÍFICAS Y TÉCNICAS
FACULTAD DE FARMACIA Y BIOQUÍMICA – UNIVERSIDAD DE BUENOS AIRES

DRUG DISCOVERY FOR NEGLECTED DISEASES INTERNATIONAL CONGRESS 2018

4th Scientific Meeting of the Research Network Natural Products against Neglected Diseases

DDNDIC 2018

ResNet NPND

Book of abstracts

4th – 6th December 2018

Facultad de Farmacia y Bioquímica – Universidad de Buenos Aires
Ciudad Autónoma de Buenos Aires, Argentina

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This event has been declared of interest by the Cámara de Diputados and the Cámara de Senadores de la Nación and has been additionally declared of sanitary interest by the Legislatura de la Ciudad Autónoma de Buenos Aires

Book of abstracts

ISBN: 978-987-47034-0-8

General coordination: Albertina Gladys Moglioni

Edited by Valeria Patricia Sülsen and Flavia del Carmen Redko

Drug Discovery for Neglected Diseases International Congress 2018: book of abstracts;
coordinación general de Albertina Gladys Moglioni ; editado por Valeria Patricia Sülsen; Flavia del Carmen Redko. - 1a ed . - Ciudad Autónoma de Buenos Aires: IQUIMEFA, 2018.
Libro digital, PDF

Archivo Digital: descarga y online
ISBN 978-987-47034-0-8

1. Lucha Contra las Enfermedades. I. Moglioni, Albertina Gladys, coord. II. Sülsen, Valeria Patricia, ed. III. Redko, Flavia del Carmen, ed.

CDD 540

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A murine model to assess anthelmintic resistance in *Fasciola hepatica*: preliminary study

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Fasciola hepatica (Fh) infection produce important loss in livestock industry, and is also an increasing concern for human public health [1]. Additionally, the spread of anthelmintic resistance (AR) lead to treatments failure [2], with a direct impact on humans' endemic regions[3]. Thus, advances in AR assessment are welcome, particularly those who allow a human´s extrapolation. The assessment of albendazole (ABZ), and triclabendazole (TCBZ) anthelmintic resistance in *Fh*, by a murine model.

15 Wistar rats were infected with 25 Fh metacercariae each, of an isolate resistant to ABZ and susceptible to TCBZ [2-4]. Twelve weeks later (day 0), the rats were assigned to five treatment groups (n=5 each): ABZ group, (ABZ 20 mg/kg PO by three consecutive days), TCBZ group (TCBZ 20 mg/kg PO by three consecutive days), and CONTROL group, without treatment. Twelve hours after the last dose, rats were bleed to quantify drug/metabolites plasma concentration by HPLC. Rats were slaughtered at day +7, to individually count the adult liver flukes. Post treatment *Fh* eggs per gram (EPG) were also measured. Both, mean flukes and EPG were compared among groups by Wilcoxon Rank Sum Test. Procedures were previously approved by animal welfare committee (CICUAL, FCV UNLP).

Mean flukes´ counts (SD) were 2.8 (1.9), 3.0 (1.4), y 3.2 (2.9), since Fh EPGs (SD), were 109.3 (97.6), 0.6 (0.8), y 102.6 (41.3), for the groups ABZ, TCBZ and CONTROL, respectively. Flukes´ counts were not different among groups, however, all the parasites recovered from TCBZ treatments were dead, whereas the flukes recovered from the other groups were alive. The mean (SD) plasma concentrations (µg/mL), were 0.48 (0.30), 1.52 (0.75), 4.51 (1.71) and 1.21 (0.65), for ABZ-sulphoxide (ABZSO), ABZ-sulphone ($ABZSO_2$), TCBZ y TCBZ-sulphone ($TCBZSO_2$), respectively.

The current evaluation confirmed the susceptibility/resistant status of the *Fh* isolate. It showed that TCBZ susceptibility can be demonstrated by this therapeutic schedule in rats. However, although ABZ´s flukes were alive, plasma concentrations of ABZSO in this assay were, comparatively, a half than those previously found in humans, after an ABZ dose of approximately 6 mg/kg [5]. The validation of this model will allow not only to reduce costs of resistance assays, but also, as rats are monogastric, would lead to a more reliable comparison to human's physiology. This would improve the current knowledge on prevalence of fasciolicides´ resistance in *Fh* from highly endemic regions.

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Keywords: Liver Fluke; benzimidazole; plasma concentration; efficacy; monogastric.

ISBN 978-987-47034-0-8