THESIS TITLE : EFFECTS OF ARTESUNATE ON *OPISTHORCHIS VIVERRINI IN VITRO* AND *IN VIVO*

AUTHOR : MR. THEWARACH LAHA

THESIS ADVISORY COMMITTEE :

.....Chairman

(Associate Professor Smarn Tesana)

.....

(Associate Professor Dr.Paiboon Sithithaworn)

.....

(Associate Professor Dr.Jintana Sattayasai)

ABSTRACT

In this study, *in vitro* and *in vivo* effects of artesunate, a derivative of qinghaosu, on immature and mature stages of *Opisthorchis viverrini* were investigated. (Effects of praziqauntel on mature worms were used as a positive control.)

In vitro experiments revealed that exposure of the mature worms to 1 μg/ml of artesunate for 168 hours resulted in a slightly decrease in motility of parasite. No motile worms were observed when they were incubated

with either 50, 100, 150 or 200 μg/ml of artesunate for 120, 48, 48 or 24 hours, respectively. Exposure to artesunate induced morphologic changes characterized by vacuolization of the tegument and atrophy of testis and vitelline glands. No differences on the number of egg released by the worms were observed after exposure to various concentrations of artesunate.

Similar results were observed in immature worms treated with artesunate. However, no motile worms were observed after 48 hours of incubation with either 50, 100, 150 or 200 μg/ml.

All mature worms exposed to 1μg/ml of praziqauntel were immobilized within 1 hour of incubation, whereas, immediate effects were seen when exposed to higher concentrations (50 - 200 μg/ml) of praziqauntel. The effects of praziqauntel on tegument, testis and vitelline glands were qualitatively similar to those of artesunate. Nevertheless, the number of egg released was significantly decreased in praziqauntel - treated group when compared to control.

In vivo experiments were carried out by using hamsters infected with 50 metacercariae of *Opisthorchis viverrini* for 3 (immature stage) or 8 (mature stage) weeks. Worm reduction rates in hamsters infected with immature stage of *Opisthorchis viverrini* after treatment with a single dose of artesunate at either 100, 200, 300 or 400 mg/kg were 0, 3.56, 0 and 50.77 %, respectively. No evidence of cure was observed.

Effect of artesunate treated in animals infected with mature worms were examined by giving drug in either a single dose of 100, 200, 300 and 400 mg/kg or 200

mg/kg/day for 2, 4 and 6 consequtive days. A single dose of 100, 200, 300 or 400 mg/kg of artesunate resulted in cure rates of 0,0, 16.67 and 42.86 % and worm reduction rates of 0.37, 58.4, 86.73 and 91.98 %, respectively. No complete cure with a worm reduction rate of 51.80 % was observed in animals received 200 mg/kg/day of artesunate for 2 day. A hundred percent of cure rate and worm reduction rate were observed in animals received 200 mg/kg/day of artesunate for either 4 or 6 days. Faecal egg output, expressed as egg per gram of faeces and egg per day, was significantly different between pre - and post - treatment in each treated group.

Treatment with a single dose of praziqauntel at either 100, 200, 300 or 400 mg/kg. In animals infected with mature stage of *Opisthorchis viverrini* showed cure rates of 28.57, 14.28, 100 and 100 % and worm reduction rates of 87.07, 90.15, 100 and 100 %, respectively. Faecal egg output was significantly decreased after treatment when compared to those before treatment.

In conclusion, the effects of artesunate on *Opisthorchis viverrini* are comparable to those of praziqauntel in both *in vitro* and *in vivo* experiments. However, on the amount of drug used in this study, artesunate seems to be less effective than praziqauntel against *Opisthorchis viverrini*.