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Identification of the antimalarial artemisinin-naphthoquine phosphate as effective therapeutic combination against *Schistosoma haematobium*

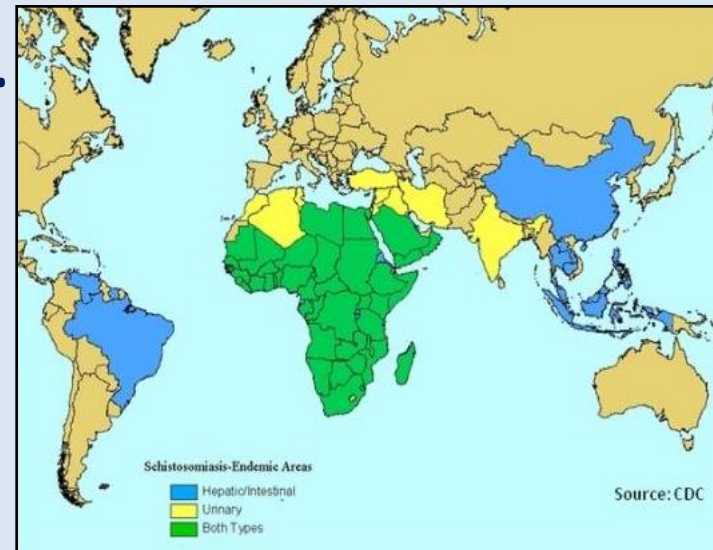
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BACKGROUND & OBJECTIVES

- Schistosomiasis is a worldwide public health challenge.
- *Schistosoma haematobium*- and *S. mansoni*-endemic areas.
- Praziquantel is the drug of choice.
- Efforts for testing existing drugs.
- Resistance with monotherapy.
- Effective drug combination.
- The compound naphthoquine phosphate tablet (CO-ArNp).



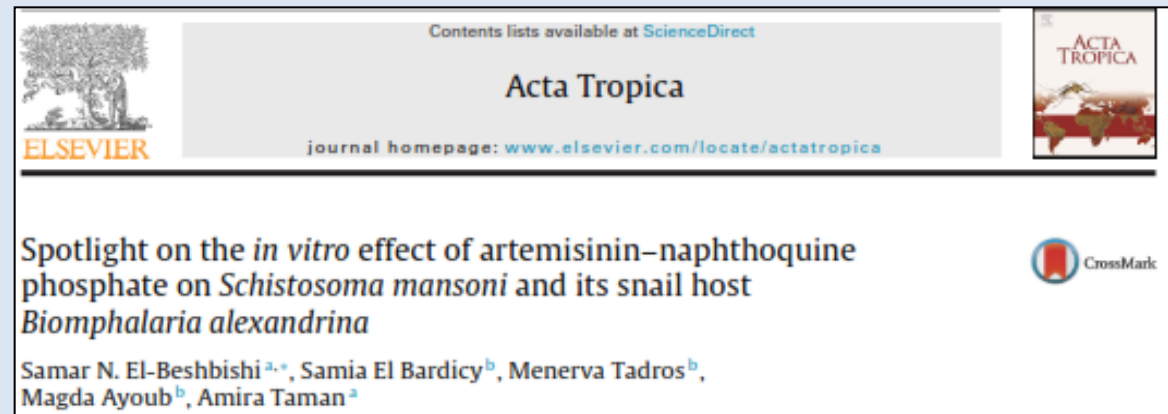
➤ **CO-ArNp significantly reduced worm burdens in *S. mansoni*-infected mice**

(El-Beshbishi *et al.*, 2013).



➤ **Potent *in vitro* effects of CO-ArNp against *S. mansoni* and its snail host**

(El-Beshbishi *et al.*, 2015).



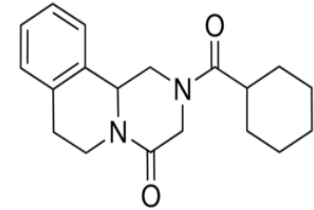
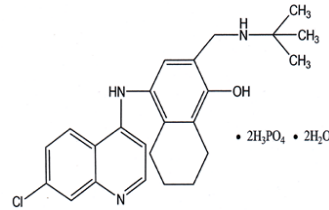
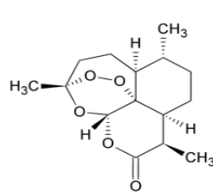
❑ **Examine CO-ArNp-similar *in vitro* efficacy on *S. haematobium*.**

❑ **The long term goal is to assess its potential use as broad-spectrum antischistosomal drug.**

MATERIALS & METHODS

1. Drugs

- CO-ArNp
- Praziquantel



2. Animals and parasites

- Male golden hamsters
- *Bulinus truncatus*



3. *In vitro* schistosomicidal activity

- CO-ArNp at 1-40µg/ml
- PZQ at 10µg/ml
- Medium without and medium with 0.8% DMSO



4. Scanning electron microscope study

- Inspect S, FEI Company, Holland



RESULTS

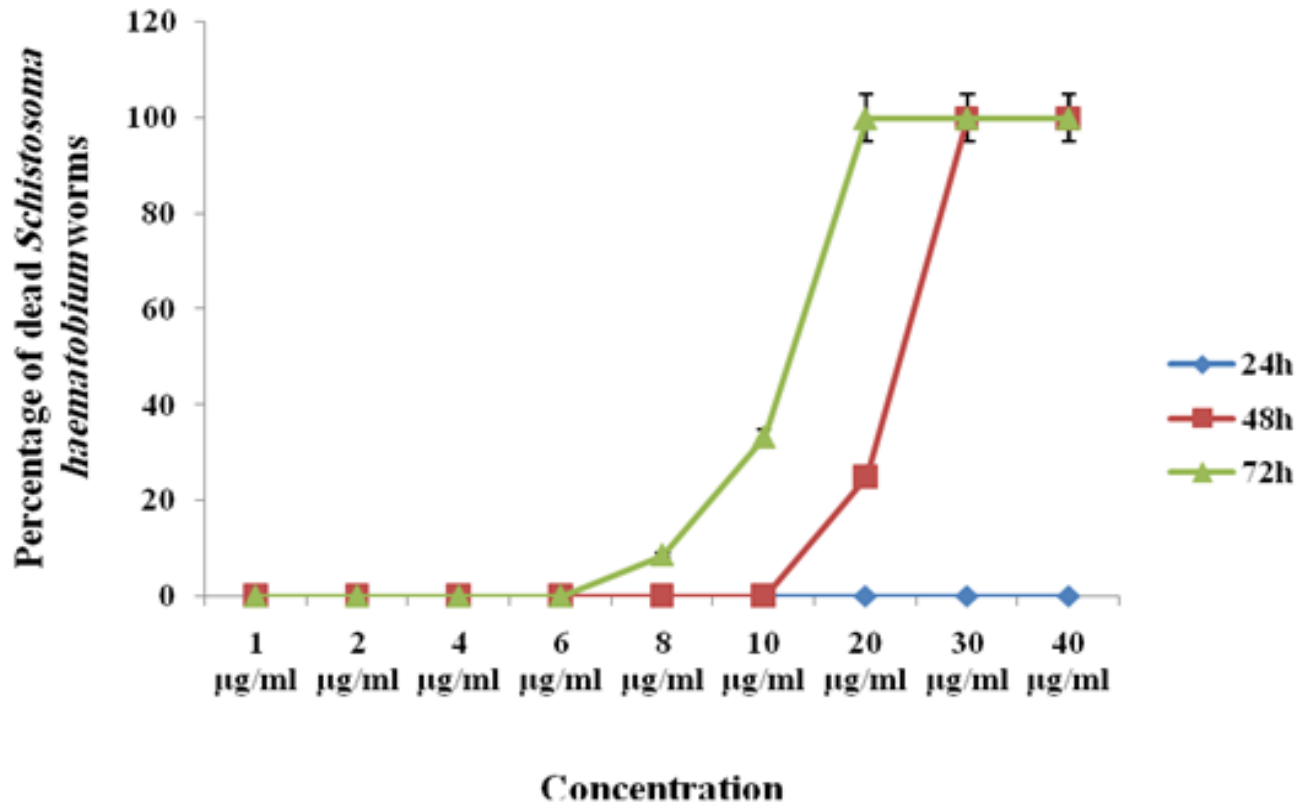


Fig.1. Dose- and time-response curves of adult *S. haematobium* exposed to CO-ArNp for 72 h.

Table 1. Motility scores of control and treated *S. haematobium* adult worms at different times post-incubation.

Groups	Percentage of worms in each motility score post-incubation								
	24 h			48 h			72 h		
	3	1.5	0	3	1.5	0	3	1.5	0
Control	100			100			100		
PZQ	54.55	45.45				100			100
CO-ArNp									
1 µg/ml	100			100			100		
2 µg/ml	100			100			100		
4 µg/ml	100			100			100		
6 µg/ml	100			100			100		
8 µg/ml	100			100			91.31		8.69
10 µg/ml	100			100			66.66		33.33
20 µg/ml	100			75		25			100
30 µg/ml	100					100			100
40 µg/ml	100					100			100

Motility scores: 3, complete body movement; 1.5, partial body movement; 0, die

Table 2. *In vitro* effect of PZQ and CO-ArNp on the mortality of male & female *S. haematobium* worms under culture conditions.

Groups	Percentage of dead worms post-incubation					
	24 h		48 h		72 h	
	male	female	male	female	male	female
PZQ	60	14.28	100	100	100	100
CO-ArNp						
1 µg/ml	0	0	0	0	0	0
2 µg/ml	0	0	0	0	0	0
4 µg/ml	0	0	0	0	0	0
6 µg/ml	0	0	0	0	0	0
8 µg/ml	0	0	0	0	6.66	12.5
10 µg/ml	0	0	0	0	25	50
20 µg/ml	0	0	0	50	100	100
30 µg/ml	0	0	100	100	100	100
40 µg/ml	0	0	100	100	100	100

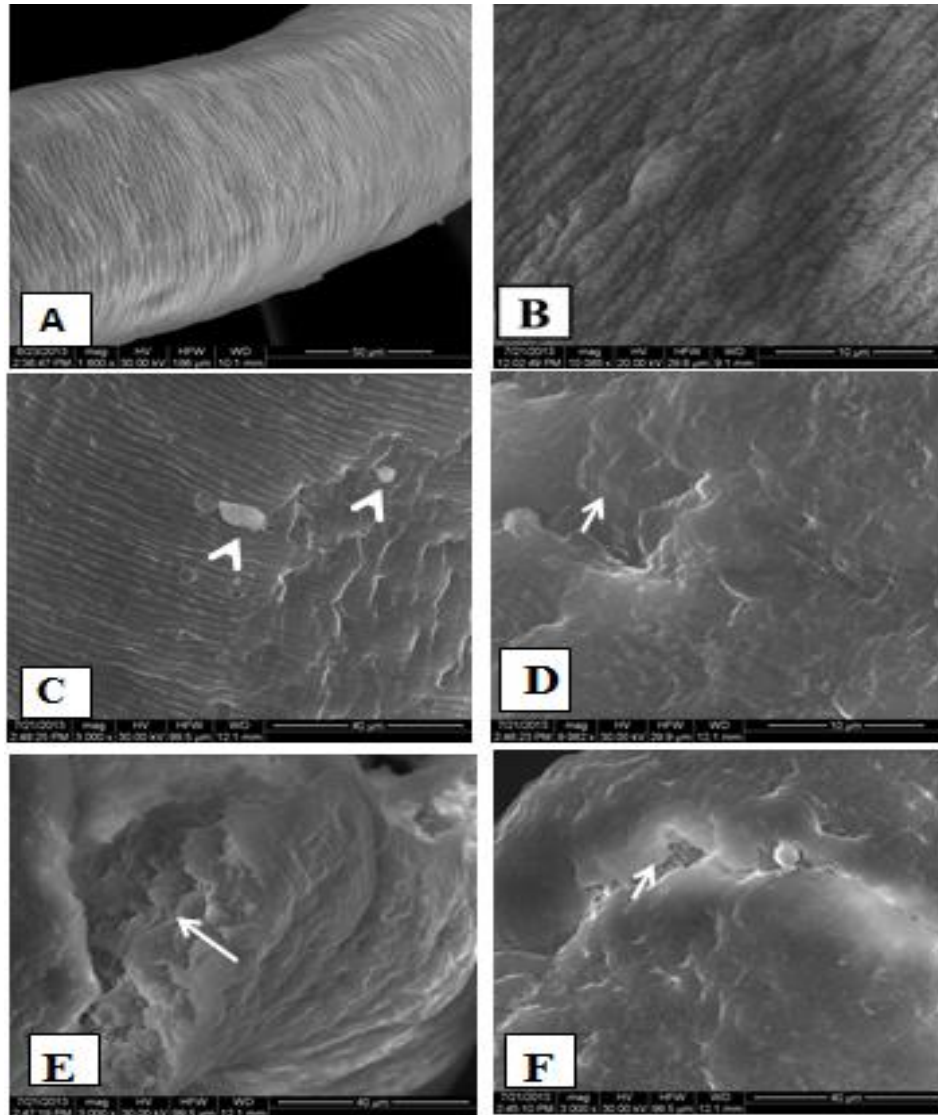


Fig. 2. SEM of middle part of female *S. haematobium*, 48 h post-incubation.

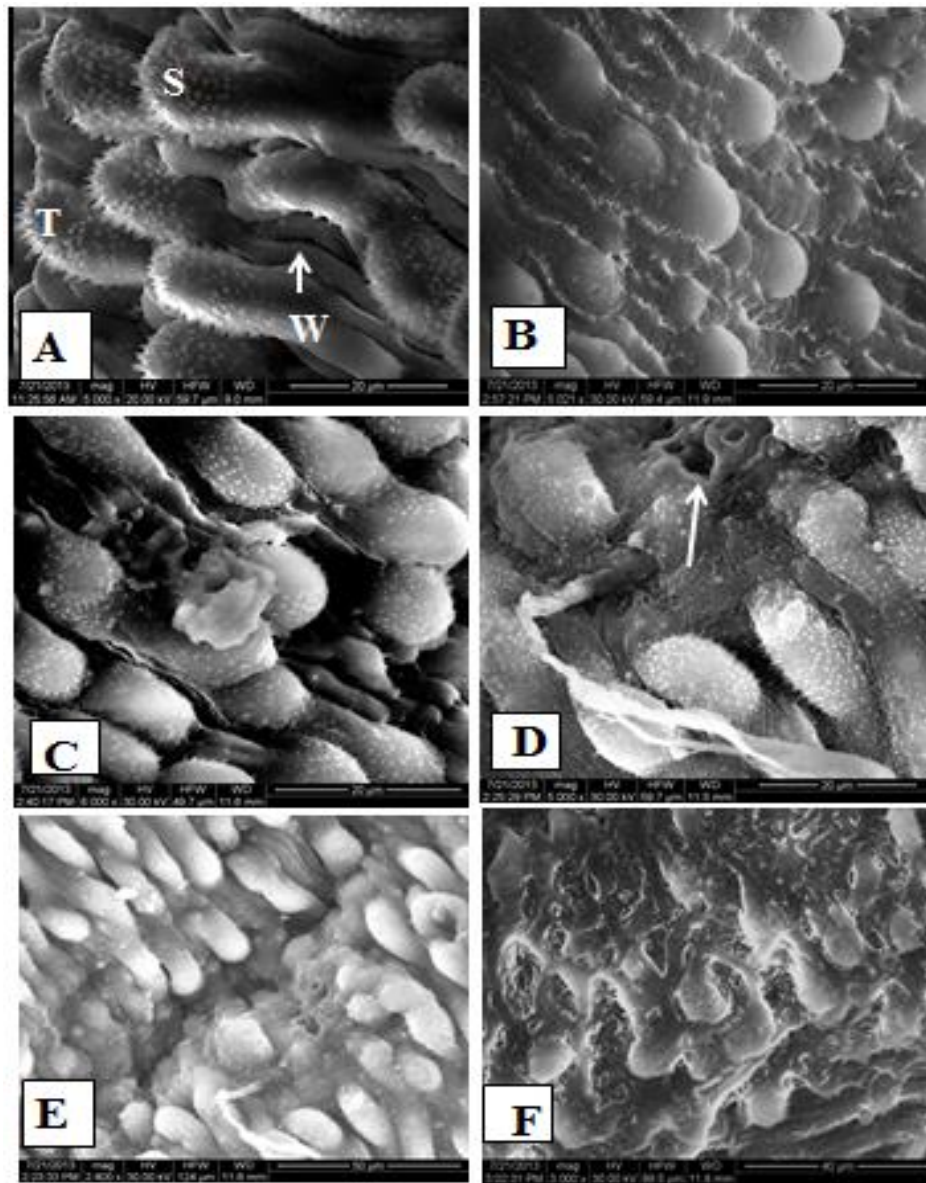


Fig. 3. SEM of middle part of male *S. haematobium*, 48 h post-incubation.

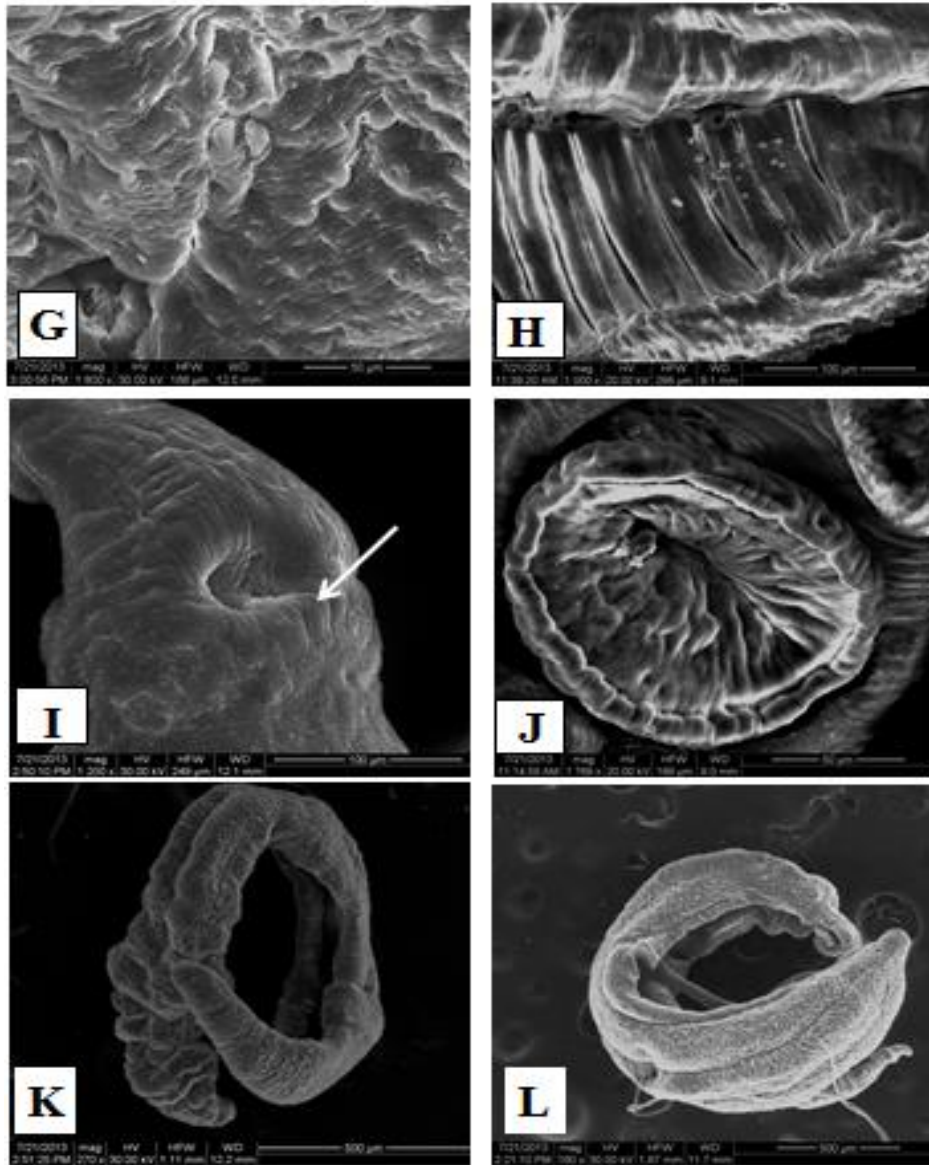


Fig. 3. SEM of of male *S. haematobium*, 48 h post-incubation.

SUMMARY & CONCLUSION

- ✓ Assessment of the anti-malarial; CO-ArNp on *S. haematobium*.
- ✓ The lethal effect of CO-ArNp on *S. haematobium*.
- ✓ A 100% mortality at 20 µg/ml after 72h.
- ✓ A 100% mortality rate at 30 µg/ml after 48h.
- ✓ SEM revealed marked tegumental alterations.
- ✓ **CO-ArNp has important potential as a novel schistosomicidal.**

RECOMMENDATION

- ❑ Effects on other schistosomes and snail hosts.
- ❑ Possible mechanism/s of action.
- ❑ Studies in humans with current antimalarial dose.
- ❑ Assess its value to eradicate both parasitic diseases.
- ❑ **Develop the most feasible & cost-effective strategies for the different endemic areas.**

Thank you

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