

LIST OF FIGURES

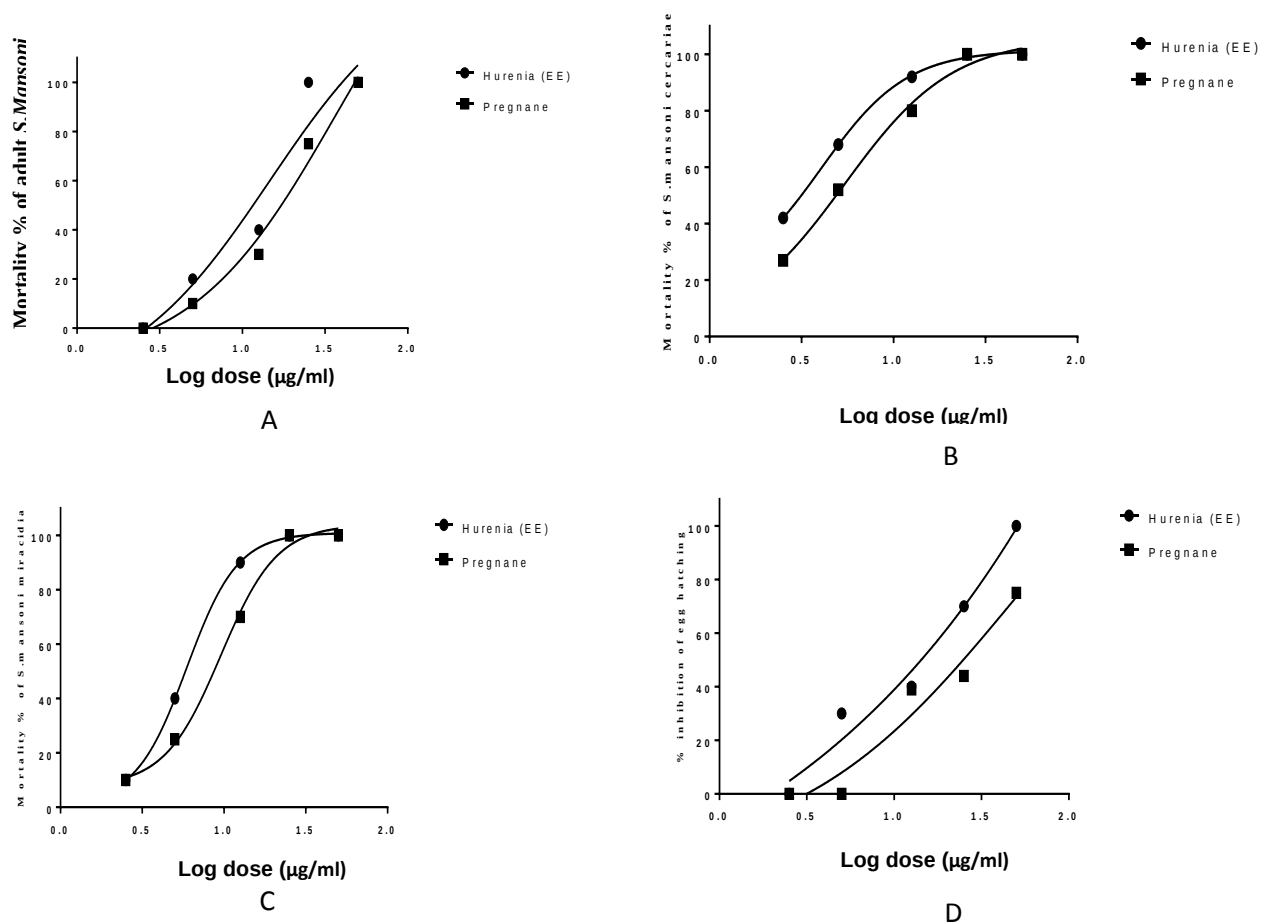


Figure S2 (A-D): **A:** Dose-response curve of % mortality of adult *S.mansoni* exposed to different concentrations of *H.saudi-arabica* ethanolic extract and pregnane glycoside respectively at 1hour. EC50 for *Hurenia* ethanolic extract was 14.36 while for pregnane glycoside it was 36.60. **B:** Dose-response curve of % mortality of *S.mansoni* cercariae exposed to different concentrations of *H.saudi-arabica* ethanolic extract and pregnane glycoside at 3hours. EC50 for *Hurenia* ethanolic extract was 4.037, while for pregnane glycoside it was 5.408. **C:** Dose-response curve of % mortality of *S.mansoni* miracidia exposed to different concentrations of *H.saudi-arabica* ethanolic extract and pregnane glycoside at 1/2h. EC50 was 5.923 while for pregnane glycoside it was 9.563. **D:** Dose-response curve of % inhibition of egg hatching of *S.mansoni* exposed to different concentrations of *H.saudi-arabica* ethanolic extract and pregnane glycoside at 1/2h. EC50 for ethanolic extract was 6.212 while for pregnane glycoside it was 48.15. Where EC50 is the concentration of a drug that gives half-maximal response.

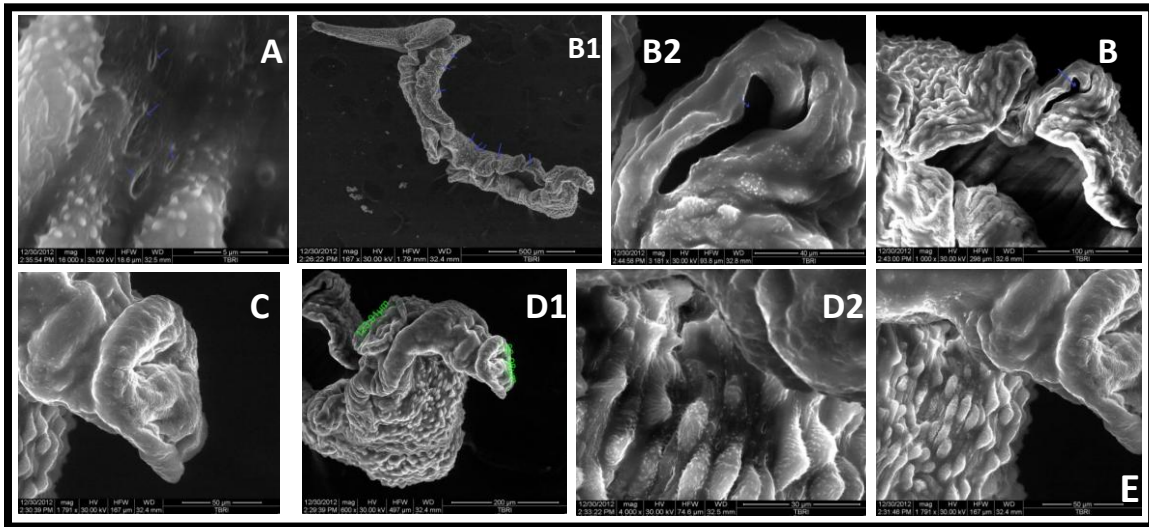


Figure S 3: SEM of *S.mansoni* adult male showing morphological changes of the male worms after 24 hrs exposure to a mixture of 2.5µg/ml, 2.6 µM of *H.saudii-arabica* ethanol extract and pregnane glycoside, respectively. Tegumental structures were heavily disturbed, oedematous with reduced numbers of tubercles and spines, among them multiple perforations (arrows) seen clearly in (A, B1, B2&B3). Remarkable thickening and shrinkage of the tegument mostly seen at the regions of suckers (C) The oral sucker was contacted, damaged and the tegumental surface appeared lacking tubercles, spongy with blebbing (D1&D2). The ventral sucker shows small blebs and perforations in between the remaining spines with loss of the tire-like appearance (E).

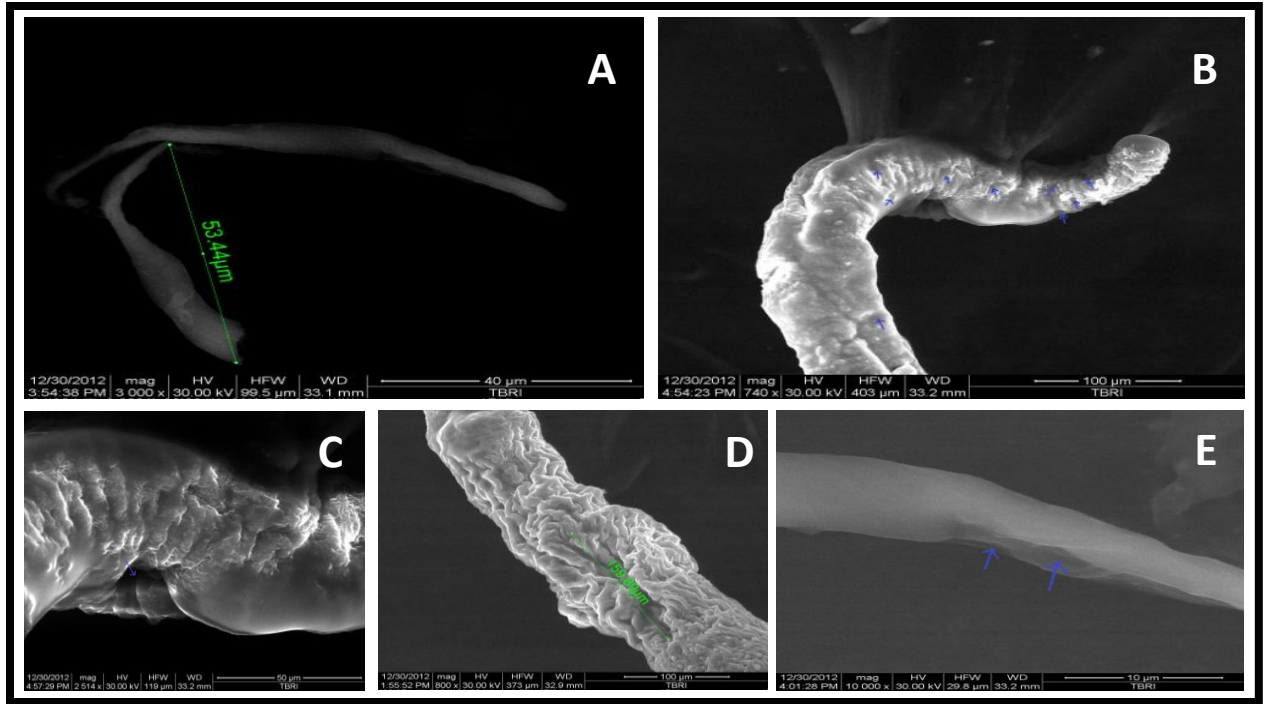


Figure S4: SEM of *S.mansoni* adult female showing morphological changes of the female worms after 24 hrs exposure to a mixture of 2.5μg/ml, 2.6μM of *H.saudi-arabica* ethanol extract and pregnane glycoside respectively. The tegument is shrunken, oedematous with numerous small protuberances. Multiple wide holes (arrows) are clearly evident at the region of the oral and ventral suckers which appear deformed (A&B). Deep grooves appear at the area of the retracted ventral sucker with loss of the tyre-like appearance(C&D). Erosions of the tegument are seen clearly in (E).

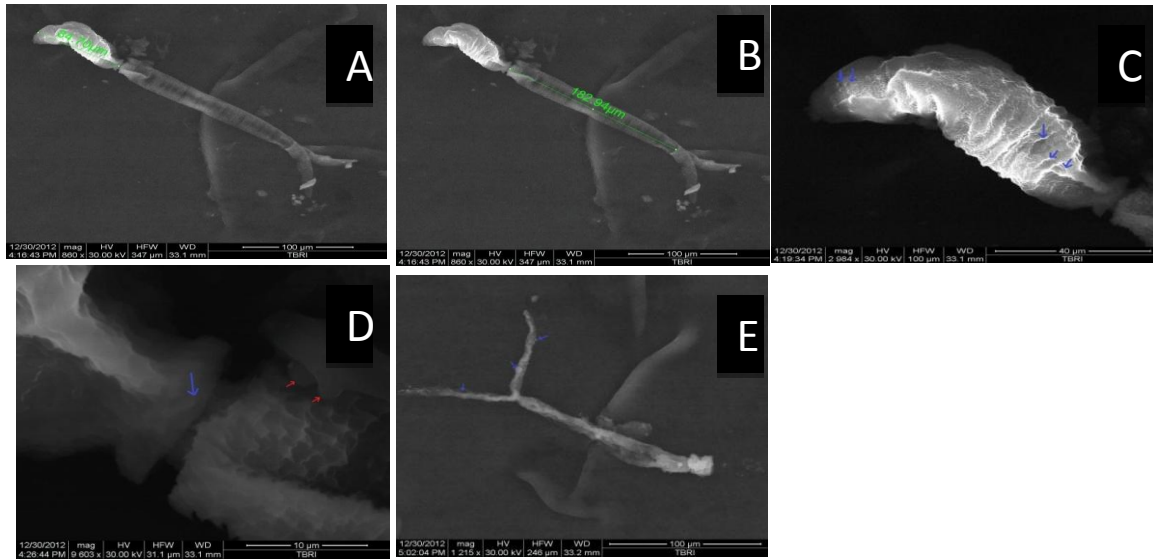


Figure S5: SEM of *S.mansoni* cercariae after 4hrs exposure to a mixture 12.5μg/ml, 13μM of both *H.saudi-arabica* ethanol extract and pregnane glycoside, respectively. Morphological changes in both body and tail were visible in the form of shrinkage and thickening of the tegument clearly seen in (A&B). There is extensive contraction, wrinkling and bending of the body with erosions of the tegument (arrows) seen in (C).The collar-like region seen in (D) shows fusion of ridges and loss of spines (blue arrow) while vesicles are seen in the tail region just below the body (red arrow).The distal bifid part of the tail shows vesicles/blebs and erosions of the tegument as seen in (E).

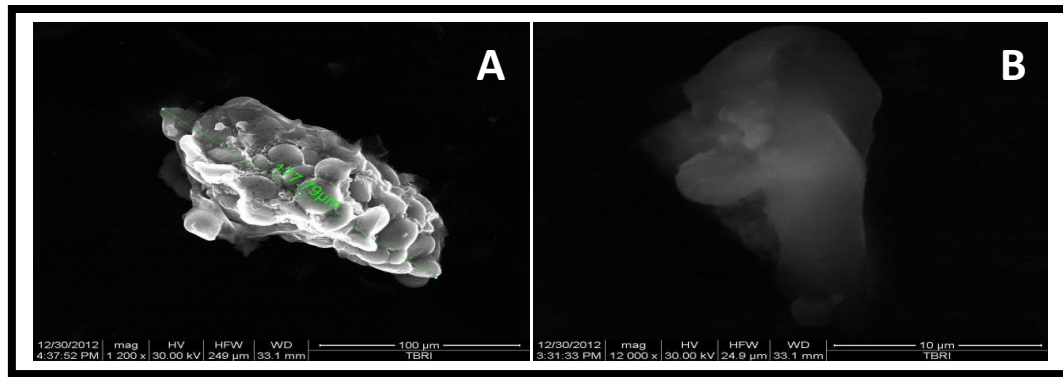


Figure S6: Shows morphological changes of *S.mansoni* miracidium 2 hrs after exposure to a mixture 5μg/ml, 5.2μM of both ethanolic extract of *H.saudi-arabica* and its isolate; pregnane glycoside. (A) swellings, vesiculation, formation of blebs that completely masking the ciliated surface with preservation of the apical cone.(B) shows completely disfigured miracidium with complete loss of ciliae and apical cone.

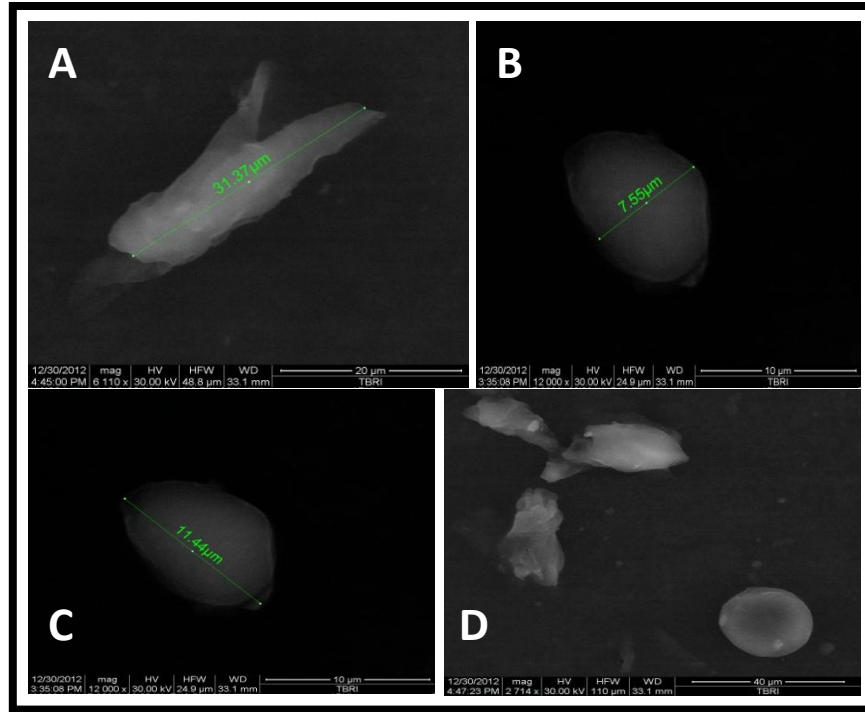


Figure S7: SEM of *S.mansoni* ova exposed to a mixture 25μg/ml and 26μM of both ethanolic extract of *H.saudi-arabica* and its isolate; pregnane glycoside, respectively for 2 hrs. Some ova show elongation with shrinkage of the shell clearly seen in (A). Others become oedematous, swollen with loss of the lateral spines as seen in (B&C). There is complete loss of the microspicules-like chitinous minute projections of the egg shell surface that is clearly seen in (D).

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Table S1: ^1H and ^{13}C NMR (400MHz, 100MHz) In CDCl_3 of isolated compound CI

Position	CI	
	δ_{H} (mult, J in Hz)	δ_{C}
1	1.15, <i>m</i> , 1.85, <i>m</i>	36.6, <i>t</i>
2	1.90, <i>m</i> 1.54, <i>m</i>	29.3, <i>t</i>
3	3.55, <i>m</i>	76.2, <i>d</i>
4	2.36, <i>m</i> 2.16, <i>m</i>	38.2, <i>t</i>
5	-	138.9, <i>s</i>
6	5.46, <i>br</i> (<i>d</i> , 5.4)	121.8, <i>d</i>
7	1.90, <i>m</i> 2.24, <i>m</i>	26.9, <i>t</i>
8	1.85, <i>m</i>	36.1, <i>d</i>
9	1.35, <i>m</i>	42.7, <i>d</i>
10	-	36.8, <i>s</i>
11	1.85, <i>m</i> 1.64, <i>m</i>	25.7, <i>t</i>
12	4.83, <i>dd</i> , (12.0, 4.0)	78.0, <i>d</i>
13	-	51.3, <i>s</i>
14	-	84.7, <i>s</i>
15	1.67, <i>m</i> 1.84, <i>m</i>	31.7, <i>t</i>
16	1.56, <i>m</i> 1.90, <i>m</i>	24.6, <i>t</i>
17	2.06, <i>m</i>	49.5, <i>d</i>
18	1.16, <i>s</i>	9.4, <i>q</i>
19	1.04, <i>s</i>	19.0, <i>q</i>
20	4.94, (<i>br q</i> , 5.5)	72.9, <i>d</i>
21	1.09, (<i>d</i> , 6.0)	19.1, <i>q</i>
Acetyl		
CH ₃	2.05, <i>s</i>	21.3, <i>q</i>
C=O	-	169.7, <i>s</i>
Benzoyl		
1	-	165.6, <i>s</i>
2	-	122.2, <i>s</i>
3,7	7.49, (<i>t</i> , 7.5)	132.9, <i>d</i>
4,6	7.69, (<i>t</i> , 7.5)	116.2, <i>d</i>
5	-	161.4, <i>d</i>
Cym		
1'	4.83, (<i>d</i> , 9)	95.5, <i>d</i>
2'	1.44(<i>m</i>), 1.95(<i>m</i>)	35.5, <i>t</i>
3'	3.71, <i>m</i>	76.7, <i>d</i>
4'	3.20, <i>m</i>	82.0, <i>d</i>
5'	3.78, <i>m</i>	68.2, <i>d</i>
6'	1.19, (<i>d</i> , 6)	18.0,
OMe	3.32, <i>s</i>	57.8, <i>q</i>
Cym		
1''	4.66, (<i>d</i> , 9.5)	99.2, <i>d</i>
2''	1.45(<i>m</i>), 2.00(<i>m</i>)	35.7, <i>t</i>
3''	3.68, <i>m</i>	76.6, <i>d</i>
4''	3.16, <i>m</i>	82.1, <i>d</i>
5''	3.70, <i>m</i>	67.9, <i>d</i>
6''	1.20, (<i>d</i> , 6)	18.0
OMe	3.31, <i>s</i>	57.9, <i>q</i>
Glc		
1'''	4.44, (<i>d</i> , 7.5)	104.8, <i>d</i>
2'''	2.94, <i>m</i>	73.7, <i>d</i>
3'''	3.08, <i>m</i>	76.8, <i>d</i>
4'''	3.00, <i>m</i>	70.2, <i>d</i>
5'''	3.17, <i>m</i>	76.6, <i>d</i>
6'''	3.42, <i>m</i> , 3.68 <i>m</i>	61.4

Table S2: ^1H and ^{13}C NMR (400MHz, 100MHz) of isolated compounds CII, CIII.

Position	CII		CIII	
	δ_{H}	(mult, J in Hz) δ_{C}	δ_{H} (mult, J in Hz)	δ_{C}
2	-	164.3, <i>s</i>	-	158.5, <i>s</i>
3	6.76, <i>s</i>	103.7, <i>d</i>	-	135.6, <i>s</i>
4	-	181.7, <i>s</i>	-	179.4, <i>s</i>
5	-	161.4, <i>s</i>	-	159.3, <i>s</i>
6	6.21, (<i>d</i> , 1.0)	98.9, <i>d</i>	6.32, (<i>d</i> , 1.0)	100.0, <i>d</i>
7	-	163.3, <i>s</i>	-	166.0, <i>s</i>
8	6.46, (<i>d</i> , 1.0)	93.9, <i>d</i>	6.42, (<i>d</i> , 1.0)	94.9, <i>d</i>
9	-	157.3, <i>s</i>	-	163.0, <i>s</i>
10	-	103.7, <i>s</i>	-	105.6, <i>s</i>
1'	-	124.1, <i>s</i>	-	123.1, <i>s</i>
2'	7.50, <i>s</i>	113.4, <i>d</i>	7.7, <i>s</i>	117.4, <i>s</i>
3'	-	147.4, <i>s</i>	-	145.4, <i>s</i>
4'	-	148.3, <i>s</i>	-	149.8, <i>s</i>
5'	7.18, (<i>d</i> , 7.5)	115.7, <i>d</i>	6.89, (<i>d</i> , 8.5)	116.0, <i>s</i>
6'	7.47, (<i>d</i> , 7.5)	118.2, <i>d</i>	7.65, (<i>d</i> , 8.5)	123.5, <i>d</i>
C-5(OH)	12.93(chelated)		12.35(chelated)	
Glc				
1''	5.24, (<i>d</i> , 7.5)	97.9, <i>d</i>	5.13, (<i>d</i> , 7.5)	104.5, <i>d</i>
2''	3.47, <i>m</i>	77.3, <i>d</i>	3.50, <i>m</i>	75.3, <i>d</i>
3''	3.38, <i>m</i>	76.8, <i>d</i>	3.45, <i>m</i>	78.8, <i>d</i>
4''	3.21, <i>m</i>	70.4, <i>d</i>	3.58, <i>m</i>	74.4, <i>d</i>
5''	3.58, <i>m</i>	76.9, <i>d</i>	3.45, <i>m</i>	77.1, <i>d</i>
6''	3.45, <i>m</i> 3.66, <i>m</i>	62.9, <i>d</i>	3.31, <i>m</i> 3.46, <i>m</i>	68.9, <i>t</i>
Rha				
1'''	5.17, <i>br s</i>	100.5, <i>d</i>	4.54, <i>br s</i>	102.5, <i>d</i>
2'''	3.38, <i>m</i>	70.5, <i>d</i>	3.09, <i>m</i>	71.5, <i>d</i>
3'''	3.21, <i>m</i>	69.6, <i>d</i>	3.51, <i>m</i>	72.2, <i>d</i>
4'''	3.20, <i>m</i>	72.0, <i>d</i>	3.07, <i>m</i>	73.6, <i>d</i>
5'''	3.78, <i>m</i>	68.6, <i>d</i>	3.30, <i>m</i>	69.6, <i>d</i>
6'''	1.10, (<i>d</i> , 5.5)	18.0, <i>q</i>	1.14, (<i>d</i> , 5.5)	17.8, <i>q</i>

Measured in CD₃OD

Table S3: Percent mortality of adult *S.mansoni* exposed to different concentrations of *H.saudi-arabica*

	1h	2h	3h	4h	6h	12h	24h	48h
PZQ 10 µg/ml(+ve control)	70	90	100	100	100	100	100	100
Medium with 1% DMSO (-ve Control)	0	0	0	0	0	0	0	0
EE	2.5 µg/ml	0	10	20	30	65	90	100
	5 µg/ml	20	45	65	90	100	100	100
	12 µg/ml	40	65	90	100	100	100	100
	25 µg/ml	100	100	100	100	100	100	100
	50 µg/ml	100	100	100	100	100	100	100
CI	2.5 µg/ml(2.6 µM)	0	0	0	10	30	80	100
	5 µg/ml(5.2 µM)	10	15	35	60	85	95	100
	12 µg/ml(13 µM)	30	65	90	100	100	100	100
	25 µg/ml(26 µM)	100	100	100	100	100	100	100
	50 µg/ml(52µM)	100	100	100	100	100	100	100

EE= ethanolic extract of the aerial parts of *H.saudi-arabica*;CI=compound I; pregnane glycoside

Table S4: Percent mortality of *S.mansoni* cercariae exposed to different concentrations of *H.saudi-arabica*

	1h	2h	3h	4h	6h	12h
PZQ 10 µg/ml(+ve control)	60	80	95	100	100	100
Medium with 1% DMSO (-ve Control)	0	0	0	0	0	0
EE 2.5 µg/ml	0	22	42	78	100	100
EE 5 µg/ml	16	48	68	95	100	100
EE 12 µg/ml	33	71	92	100	100	100
EE 25 µg/ml	72	83	100	100	100	100
EE 50 µg/ml	81	96	100	100	100	100
CI 2.5 µg/ml(2.6 µM)	0	10	27	40	100	100
CI 5 µg/ml(5.2 µM)	12	23	52	78	100	100
CI 12 µg/ml(13 µM)	31	52	80	93	100	100
CI 25 µg/ml(26 µM)	56	77	100	100	100	100
CI 50 µg/ml(52µM)	75	89	100	100	100	100

EE= ethanolic extract of the aerial parts of *H.saudi-arabica*; CI=compound I;pregnane glycoside

Table S5: Percent mortality of *S.mansoni* miracidia exposed to different concentrations of *H.saudi-arabica*

	½ h	1h	1½h	2h	4h
PZQ 10 µg/ml (+ve control)	90	100	100	100	100
Dechlorinated water with 1% DMSO (-ve control)	0	0	10	30	80
EE	2.5 µg/ml	10	30	70	95
	5 µg/ml	40	65	90	100
	12 µg/ml	90	100	100	100
	25 µg/ml	100	100	100	100
	50 µg/ml	100	100	100	100
	2.5 µg/ml(2.6 µM)	10	20	55	75
CI	5 µg/ml(5.2 µM)	25	45	70	90
	12 µg/ml(13 µM)	70	90	100	100
	25 µg/ml(26 µM)	100	100	100	100
	50 µg/ml(52µM)	100	100	100	100

EE=ethanolic extract of the aerial parts of *H.saudi-arabica*; CI=compound I;pregnane glycoside

Table S6: Percent inhibition of egg hatching after exposure to different concentrations of *H.saudi-arabica*

		½ h	1h	1½h	2h	4h
	PZQ(10 µg/ml)	30	55	87	100	100
	Dechlorinated water with 1% DMSO (-ve control)	0	0	0	0	0
EE	2.5 µg/ml	0	10	30	55	70
	5 µg/ml	30	45	60	76	87
	12 µg/ml	40	58	70	85	90
	25 µg/ml	70	90	100	100	100
	50 µg/ml	100	100	100	100	100
	2.5 µg/ml(2.6 µM)	0	0	15	35	50
CI	5 µg/ml(5.2 µM)	0	17	38	59	80
	12 µg/ml(13 µM)	39	50	64	77	90
	25 µg/ml(26 µM)	44	60	75	87	95
	50 µg/ml(52µM)	100	100	100	100	100

EE= ethanol extract of the aerial parts of *H.saudi-arabica*; CI=compound I; pregnane glycoside

TableS7. Results of cytotoxic activity of the ethanol extract of the aerial parts of *H.saudi-arabica*

Tested Human cell line		IC ₅₀ µg/ml	
		Doxorubicin	Ethanollic extract
Liver carcinoma	HEPG2	4.58	14.84
Breast carcinoma	MCF-7	5	8.48
Colorectal adenocarcinoma	CACO-2	4.43	24.1

Table S8: Cytotoxicity of the ethanol extract of the aerial parts of *H.saudi-arabica* on liver (HEPG2), Breast (MCF-7) and Colorectal adeno (CACO-2) carcinoma cell lines.

Conc. (µg/ml)	Mean of surviving fraction					
	HEPG2		MCF-7		CACO-2	
	Mean	SD	Mean	SD	Mean	SD
0.000	1.000	0.046	1.000	0.038	1.000	0.020
5.000	0.723	0.035	0.551	0.042	0.689	0.116
12.500	0.535	0.069	0.453	0.030	0.631	0.050
25.000	0.362	0.051	0.428	0.037	0.490	0.055
50.000	0.375	0.044	0.366	0.041	0.436	0.047

Conc= concentration