Effect of Artemisinin and Its Derivatives on Germination and Seedling Growth of Three Weed Species

Mona M. G. Saad, Muhammad A. Algamal and Samir A. M. Abdelgaleil Department of Pesticide Chemistry and Technology, Faculty of Agriculture, 21545-El-Shatby, Alexandria University

Received on: 14/11/2013 Accepted: 9/12/2013

ABSTRACT

The effects of four sesquiterpenes, artemisinin, dihydroartemisinin, artemether and artesunate on seed germination and seedling growth of three common weeds, namely Phalaris minor, Panicum repens and Silybum marianum were investigated. The tested sesquiterpenes showed promising herbicidal activity against these weeds. Artemether was the most effective compound with complete inhibition of seed germination of P. minor at concentrations of 50 and 100 µM, whereas artesunate was the less effective compound at all tested concentrations. The tested compounds were more potent germination inhibitors against P. minor than P. repens and S. marianum. Dihydroartemisinin revealed the highest inhibitory effect on seed germination of *P. repens* and *S. marianum*. Furthermore, the tested compounds revealed a strong inhibition of root growth of the three weeds. Artemether showed the highest root growth inhibition against P. minor (EC₅₀ = 1.20 μ M), while artesunate was the most potent compound against *P. repens* (EC₅₀ = 0.39 μ M) and *S. marianum* (EC₅₀ = 10.0 µM). In general, the tested compounds were more effective against P. minor than P. repens and S. marianum. On the other hand, artemether, dihydroartemisinin and artesunate caused the highest shoot growth inhibition against P. minor, P. repens and S. marianum, respectively. Although the four sesquiterpenes strongly inhibited root and shoot growth of the three weeds, the inhibition of root growth by all compounds was greater than that of shoot growth. The results of the present study indicated that artemisinin derivatives, dihydroartemisinin, artemether and artesunate, were more effective than artemisinin. This finding assured the importance of chemical modification of this class of natural compounds for obtaining new compounds with promising herbicidal activity.

Key words: sesquiterpenes, artemisinin derivatives, herbicidal activity, *Phalaris minor*, *Panicum repens*, *Silybum marianum*.

INTRODUCTION

Weeds cause more crop yield loss and add more crop production costs than other plant pests and pathogens. They reduce crop quality and quantity. Synthetic herbicides are the most widely method used for controlling of weeds; however, the intensive use of herbicides increased weed resistance. It is estimated that over 307 resistant strains of dicots and 73 resistant strains of monocots have been identified over the world (Heap, 2006).

Plant-derived secondary compounds have great potential in the development of environmentally safe herbicides with novel molecular sites of action (Duke *et al.*, 2000). Recently, the use of medicinal and allelopathic plants has been suggested as an alternative weed management under sustainable agriculture (Fujii, 2001; Hong *et al.* 2003; Singh *et al.* 2003).

Artemisinin is a naturally occurring antimalarial sesquiterpene endoperoxide lactone isolated from the shoots of *Artemisia annua* (Klayman, 1985). Its poor solubility in water and organic phases has led to the development of derivatives to increase solubility, metabolic and chemical stability and bioavailability (Ploypradith, 2004). Several research groups have developed a

series of synthetic artemisinin analogues in order to address solubility and persistence problems associated with the use of these compounds in malaria treatment. Dihydroartemisinin and other derivatives including ethers and esters (artemether and artesunate, respectively) are more potent drugs than artemisinin and are available as commercial drugs in China and other countries (Dayan *et al.* 1999). Artemisinin and several of its structural analogues are also potent plant growth inhibitors (Duke *et al.*, 1987 and 1988; Chen and Leather, 1990; Ditomaso and Duke, 1991). It has been reported that artemisinin was a selective phytotoxin with herbicidal activity similar to cinmethylin (Bhowmik and Inderjit 2003).

Phalaris minor Retz. (littleseed canarygrass, family Poaceae) is an annual invasive troublesome weed of wheat fields. It interferes with growth and development of wheat affecting the crop quality and yield. The intensive use of synthetic herbicides over the world to manage it has led to development of resistant weed (Batish et al. 2007). Panicum repens L. (torpedograss, family Poaceae) is a rhizomatous graminaceous weed of 17 crops in 27 countries (Holm et al. 1977a; Murphy et al. 1992). Torpedograss is one of the most invasive, perennial grass species of terrestrial, wetland and aquatic

natural areas in tropical and subtropical regions worldwide (Sutton 1996). *Silybum marianum* (L.) Gaertn. (milk thistle, family Asteraceae) is a serious weed in many areas of North and South America, Africa, Australia, and the Middle East. Milk thistle is grown commercially as a medicinal plant in Europe, Egypt, China, and Argentina (Holm *et al.* 1997b).

In our continuous efforts to find new natural compounds with potential use for weed control (Abdelgaleil *et al.* 2009; Abdelgaleil 2010; Saad *et al.* 2012), the herbicidal activity of four endoperoxide sesquiterpenes namely, artemisinin, dihydroartemisinin, artemether, and artesunate was evaluated against three common weeds *P. minor*, *P. repens*, and *S. marianum* to explore their potential as natural herbicides.

MATERIALS AND METHODS

1. Tested seeds

Phalaris minor Retz. (littleseed canarygrass), Panicum repens L. (torpedograss), and Silybum marianum (L.) Gaertn. (milkthistle) field biotype were collected from Alexandria Desert Research Station Farm, Alexandria, Egypt. All undersized or damaged seeds were discarded, and the seeds of uniform size were selected. Germination tests were carried out before experiments and the germination percent were 60% for littleseed canarygrass, 95% for torpedograss and 90% and for milkthistle.

2. Tested chemicals

Four endoperoxide sesquiterpenes artemisinin 99% (1), dihydroartemisinin 99% (2), artemether 99% (3) and artesunate 99% (4) (Fig.1) were purchased from Shaanxi Scipharmni-Tech Industry Co. Ltd, Xiam, Shaanxi, China.

3. Phytotoxicity of endoperoxide sesquiterpenes

The effects of the endoperoxide sesquiterpenes (artemisinin, dihydroartemisinin, artemether and

artesunate) were evaluated on the germination of P. minor, P. repens and S. marianum and subsequent seedling growth. The tested sesquiterpenes were dissolved in dimethyl sulfoxide (DMSO) followed by dilution with distilled water to obtain a stock solution of 100 µM. The concentration of DMSO in this solution was 0.5% v/v. Then a series of concentrations (1, 5, 10 and 50 µM) were prepared by dilution with distilled water. An aqueous solution of DMSO (0.5% v/v) was used as control treatment. Three replicates, each of 20 seeds, were used for each treatment using Petri dishes (9 cm) lined with Whatman No. 2 filter paper. Six milliliters of each test solution were added to each Petri dish. Petri dishes were placed in the bottom of 0.1 mm thick polyethylene bags (15×30 cm) that were expanded to contain air and then closed at the top with rubber bands to prevent the loss of moisture. The Petri dishes were kept on a germination cabinet at 20±1°C with 12 h photoperiod. Germination percentages and root and shoot lengths were recorded after 11 days of sowing for P. minor and P. repens, and after 7 days of sowing for S. marianum. The growth inhibition percentages (I %) of root and shoot lengths were calculated from the following equation: I (%) = $[1-T/C] \times 100$; where T is the length of shoot or root in treatment (cm) and C is the length of shoot or root in control (cm). The concentrations causing 50% inhibition (EC₅₀) of root or shoot growth were calculated from probit analysis (Finney 1971).

4. Statistical analysis

Germination percentages, root lengths and shoot lengths were subjected to one-way analysis of variance followed by Student–Newman–Keuls test (Cohort software Inc. 1985) to determine significant differences among mean values at the probability level of 0.05.

H₃C
$$CH_3$$
 CH_3 C

Figure 1. Chemical structure of artemisinin and artemisinin derivatives.

RESULTS AND DISCUSSION

1. Effect of sesquiterpenes on seed germination

The effect of the four tested sesquiterpenes artemisinin (1), dihydroartemisinin (2), artemether (3), and artesunate (4) on the germination percentages of the three weeds P. minor, P. repens, and S. marianum is shown in Table 1. The results showed that all of the tested compounds caused significant inhibition of P. minor germination at all of the tested concentrations except the lowest concentration of 1 µM. Artemether (3) was the most effective compound with complete inhibition of seed germination at concentrations 50 and 100 µM. Artesunate (4) was the less effective compound at all of tested concentrations. Artemisinin (1) and dihydroartemisinin (2) exhibited similar inhibitory effect on seed germination of this weed. In the case of P. repens, the tested compounds showed no significant inhibition of seed germination at the concentrations of 1. 5 and 10 µM. At 50 µM, the tested compounds exhibited significant reduction of germination with compounds 2 and 3 being more effective than compounds 1 and 4. Complete inhibition of seed germination was observed when seed treated with compounds 2 and 3 at the concentration of 100 μ M. When tested against S. marianum, the sesquiterpenes showed weak inhibitory effect on germination. There were no significant reduction of seed germination at the tested concentrations of compounds 3 and 4.

Compound 2 caused significant reduction of seed germination at concentrations of 50 and 100 μ M, while compound 1 showed significant reduction of seed germination at the concentration of 100 μ M.

The results of germination bioassay on the three weeds indicated that P. minor, an annual narrowleaf weed, was more sensitive to the tested compounds than P. repens, a perennial narrow-leaf weed, whereas S. marianum, an annual or biannual broad-leaf weed, was the less sensitive one to all tested compounds. Compounds 1, 2 and 3 were reported to possess inhibitory effect on seed germination of Lactuca and Arabidopsis (Dayan et 1999). Artemisinin (1) inhibited seed al. germination of redroot pigweed (Lydon et al. 1997) and several monocot and dicot vegetables and weeds (Chen and Leather 1990; Duke et al. 1987). Other sesquiterpenes and sesquiterpene lactones have been shown to inhibit seed germination (Baruah et al. 1994; Batish et al. 2002; Barbosa et al. 2004; Abdelgaleil et al. 2009; Saad et al. 2012).

2. Effect of sesquiterpenes on root growth

The inhibitory effects of the four sesquiterpenes on root growth of *P. minor*, *P. repens* and *S. marianum* in terms of root length and percentages of root growth inhibition relative to control are shown in Table 2. The tested compounds revealed a strong inhibition of root growth of *P. minor* in a concentration-dependent manner.

Table 1: Effect of artemisinin and its analogues on seed germination of *Phalaris minor*, *Panicum repens*, Silybum marianum^a

Conc	M) Phalaris minor							
(μ M)								
	Artemisinin (1)	Dihydroartemisinin (2)	Artemether (3)	Artesunate (4)				
0	$60.0 \pm 0.0a^{b}$	$60.0 \pm 0.0a$	$60.0 \pm 0.0a$	$60.0 \pm 0.0a$				
1	$43.3 \pm 3.34b$	$53.3 \pm 3.34a$	50 ± 5.78 b	$56.7 \pm 3.34a$				
5	33.3 ± 3.34 bc	$36.7 \pm 3.34b$	$33.3 \pm 3.34c$	43.3 ± 6.67 bc				
10	30 ± 5.78 bc	26.7 ± 6.67 b	$23.3 \pm 3.34d$	40 ± 6.67 bc				
50	$23.3 \pm 3.34c$	$13.3 \pm 3.34c$	$0.0 \pm 0.0e$	26.7 ± 8.83 bc				
100	$3.3 \pm 3.34d$	$10.0 \pm 0.0c$	$0.0 \pm 0.0e$	$13.3 \pm 6.67c$				
	Panicum repens							
0	$97.0 \pm 3.34a$	$97.0 \pm 3.34a$	$97.0 \pm 3.34a$	$97.0 \pm 3.34a$				
1	$97.0 \pm 3.34a$	$93.0 \pm 6.67a$	$90.0 \pm 5.78a$	$97.0 \pm 3.34a$				
5	$90.0 \pm 5.78a$	$90.0 \pm 0.0a$	$83.0 \pm 6.67a$	$93.0 \pm 3.34a$				
10	$83.0 \pm 8.83a$	$77.0 \pm 8.83a$	$80.0 \pm 5.78a$	$87.0 \pm 3.34a$				
50	60.0 ± 5.78 b	53.0 ± 6.67 b	$53.0 \pm 3.34b$	70.0 ± 5.78 b				
100	53.0 ± 3.34 b	$0.0 \pm 0.0c$	$0.0 \pm 0.0c$	$43.0 \pm 3.34c$				
Silybum marianum								
0	$86.7 \pm 3.33a^{b}$	$86.7 \pm 3.33a$	$86.7 \pm 3.33a$	$86.7 \pm 3.33a$				
1	$83.3 \pm 3.33ab$	83.3 ± 3.33 ab	$86.7 \pm 3.33a$	$86.7 \pm 3.33a$				
5	$83.3 \pm 3.33ab$	80.0 ± 0.0 ab	$76.7 \pm 3.33a$	$86.7 \pm 3.33a$				
10	76.7 ± 3.33 ab	73.3 ± 3.33 abc	$76.7 \pm 3.33a$	$80.0 \pm 0.0a$				
50	$70.0 \pm 5.78ab$	70.0 ± 5.78 bc	$73.3 \pm 3.33a$	$76.7 \pm 3.33a$				
100	66.7 ± 3.33 b	$63.3 \pm 3.33c$	$70.0 \pm 5.78a$	$73.3 \pm 3.33a$				

^a Data are expressed as means \pm SE from experiments with three replicates of 20 seeds each.

^b Means within a column sharing the same letter for each weed are not significantly different at the 0.05 probability level.

Artemether (3) was the most active compound followed by artesunate (4), artemisinin (1) and dihydroartemisinin (2) with EC₅₀ values of 1.20, 1.72, 2.21 and 2.95 μ M, respectively. Compounds 2, 3 and 4 caused complete inhibition of root growth at concentrations of 50 and 100 μ M.

The tested compounds showed strong inhibition of root growth of P. repens with compound 4 (EC₅₀) = $0.39 \mu M$) being the most effective one. At the lowest concentrations of 1, 5 and 10 µM, compound 4 exhibited the highest reduction of root growth with growth inhibition percent of 68.3, 90.2 and 95.1%, respectively. At the highest concentrations of 50 and 100 μM , all of the tested compounds caused strong growth reduction as the root growth inhibition ranged from 92.7% to 100%. On the other hand, the tested compounds caused significant inhibition of root growth of S. marianum at all of the tested concentrations compared with control. Compound 4 was the most potent while compound 1 was the less effective one. In general, the tested compounds were more effective against P. minor

than *P. repens* and *S. marianum* except compound 4 which was more effective against *P. repens* than *P. minor*

The results of this study are consistent with previous studies on artemisinin and its derivatives. For example, artemisinin strongly reduced the root growth of Lemna minor at concentrations of 5 and 10 μM (Stiles *et al.* 1994). Chen and Leather (1990) reported that artemisinin inhibited root formation in bush bean (Phasoleus vulgaris) seedlings at levels as low as 10.0 µM. Duke et al. (1987) also reported that artemisinin inhibited roots and shoots of lettuce (Lactuca sativa), redroot pigweed (Amaranthus retroflexus), pitted morning glory (Lpomoea lacunosa), and common purslane (Portulaca oleracea) at 33.0 µM. Dayan et al. (1999) stated that artemisinin (1), dihydroartemisinin (2) and artemether (3) inhibited root growth of Lactuca and Lolium at concentrations of 35 and 350 μM.

Table 2: Effect of artemisinin and its analogues on root growth of *Phalaris minor*, *Panicum repens* and *Silybum marianum*^a

Conc	Artemisini	in (1)	Dihydroartem	isinin (2)	Artemether	r (3)	Artesunate	(4)	
(µM)	Phalaris minor								
	Root length	I (%) ^b	Root length	I (%)	Root length	I (%)	Root length	I (%)	
	(cm)		(cm)		(cm)		(cm)		
0	$3.27 \pm 0.18a^{c}$	0.0	$3.27 \pm 0.18a$	0.0	$3.27 \pm 0.18a$	0.0	$3.27 \pm 0.18a$	0.0	
1	$2.03 \pm 0.09b$	37.9	$2.67 \pm 0.18b$	18.2	1.6 ± 0.06 b	49.2	2.3 ± 0.35 b	28.7	
5	$1.53 \pm 0.09c$	53.0	$1.3 \pm 0.09c$	57.7	$0.97 \pm 0.12c$	70.3	$0.33 \pm 0.03c$	89.9	
10	$0.4 \pm 0.06 d$	87.8	$0.17 \pm 0.03d$	94.8	$0.03 \pm 0.03 d$	99	$0.27 \pm 0.03c$	91.7	
50	$0.2 \pm 0.06 d$	93.9	0.0 ± 0.0 d	100	$0.0 \pm 0.0 d$	100	$0 \pm 0c$	100	
100	$0.07 \pm 0.07 d$	97.9	0.0 ± 0.0 d	100	$0.0 \pm 0.0 d$	100	$0 \pm 0c$	100	
EC_{50}^{d}	2.21		2.95		1.20		1.72		
			F	Panicum rep	ens				
0	$4.1 \pm 0.12a^{c}$	0.0	$4.1 \pm 0.12a$	0.0	$4.1 \pm 0.12a$	0.0	$4.1 \pm 0.12a$	0.0	
1	$3.9 \pm 0.03a$	4.9	$3.2 \pm 0.17b$	22.0	3.2 ± 0.09 b	22.0	1.3 ± 0.15 b	68.3	
5	$2.4 \pm 0.19b$	41.5	$1.3 \pm 0.12c$	68.3	$2.9 \pm 0.06b$	29.3	$0.4 \pm 0.06c$	90.2	
10	$0.6 \pm 0.1c$	85.4	$1.0 \pm 0.03c$	75.6	$2.5 \pm 0.17c$	39.0	$0.2\pm0.0c$	95.1	
50	0.3 ± 0.03 cd	92.7	$0.1 \pm 0.03d$	97.6	$0.2 \pm 0.03d$	95.0	$0.16 \pm 0.03c$	96.1	
100	$0.1 \pm 0.03d$	97.6	$0.0 \pm 0.0 d$	100	$0.0 \pm 0.0 d$	100	$0.1 \pm 0c$	97.6	
EC_{50}	5.40		2.98		10.63	10.63		0.39	
Silybum marianum									
0	$5.67 \pm 0.09a^{c}$	0.0	$5.67 \pm 0.09a$	0.0	$5.67 \pm 0.09a$	0.0	$5.67 \pm 0.09a$	0.0	
1	$4.10\pm0.0b$	27.7	$4.13 \pm 0.06b$	27.2	4.20 ± 0.06 b	25.9	4.10 ± 0.06 b	27.7	
5	$3.67 \pm 0.03c$	35.3	$3.77 \pm 0.03c$	33.5	$3.77 \pm 0.03c$	33.5	$3.63 \pm 0.03c$	36.0	
10	$2.87 \pm 0.03d$	49.4	$2.87 \pm 0.03 d$	49.4	2.93±0.03d	48.3	$2.87 \pm 0.03d$	49.4	
50	$2.63 \pm 0.06e$	53.6	$2.10 \pm 0.06e$	63.0	$1.93 \pm 0.03e$	66.0	$1.10 \pm 0.0e$	80.6	
100	2.10 ± 0.06 f	63.0	$0.83 \pm 0.03 f$	85.4	1.67 ± 0.03 f	70.5	$0.83 \pm 0.03 f$	85.4	
EC_{50}	21.32		10.35		13.57		10.0		

^a Data are expressed as means \pm SE from experiments with three replicates of 20 seeds each.

^b I = inhibition.

^c Means within a column sharing the same letter are not significantly different at the 0.05 probability level.

 $^{^{\}rm d}$ EC₅₀ = concentration of compound causing 50% root growth inhibition.

3. Effect of sesquiterpenes on shoot growth

The effects of the four sesquiterpenes on the shoot growth of P. minor, P. repens and S. marianum are summarized in Table 3. Compound 3 $(EC_{50} = 8.05 \mu M)$ showed the highest shoot growth reduction of P. minor, followed by compound 1 $(EC_{50} = 13.17 \mu M)$, whereas compound 4 $(EC_{50} =$ 21.06 µM) was the less effective one. On the other hand, compound 2 caused the highest shoot growth inhibition of P. repens, followed by compound 1 and 4 with EC₅₀ values of 20.78, 22.74 and 28.79 μM, respectively. In the case of S. marianum, compound 4 showed the strongest shoot growth inhibition, whereas compound 1 revealed the lowest growth inhibition. The inhibitory effects of the tested compounds on root and shoot growth of P. were more potent than those of sesquiterpenes isolated from Eupatorium adenophorum (Kundu et al. 2013). As was observed in the effect of compounds on root growth, the tested compounds exhibited the strongest shoot growth inhibition on P. minor, followed by P. repens and S. marianum.

The results revealed that the inhibitory effects of the tested compounds on root growth were

greater than on shoot growth. These results are consistent with those reported elsewhere for other sesquiterpenes and some plant extracts (Chung and Miller 1995; Turk and Tawaha 2002; Abdelgaleil *et al.* 2009; Saad *et al.* 2012). This finding might be expected, because it is likely that roots are the first to absorb the allelochemical compounds from the media (Turk and Tawaha, 2002). It was also observed that the inhibitory effect of tested sesquiterpenes on root and shoot growth was greater than that on germination. Similarly, Leather and Einhellig (1985) demonstrated that bioassays determining seedling growth are usually more sensitive than those measuring germination.

The modes of action of artemisinin and its analogues on the seedling growth remain unknown. However, several studies were conducted to illustrate the mechanisms of action of these compounds and other sesquiterpene lactones. For examples, Dayan *et al.* (1999) stated that artemisinin and its analogues inhibited cell division and reduced chlorophyll contents of lettuce and rye. Picman (1986) reported that sesquiterpene lactones react with the -SH group of amino acids, proteins, and enzymes.

Table 3: Effect of artemisinin and its analogues on shoot growth of *Phalaris minor*, *Panicum repens* and Silvbum marianum^a

Conc	Artemisinin	(1)	Dihydroartemis	inin (2)	Artemether	(3)	Artesunate	e (4)	
(μ M)	Phalaris minor								
	Shoot length	I (%) ^b	Shoot length	I (%)	Shoot length	I (%)	Shoot length	I (%)	
	(cm)		(cm)		(cm)		(cm)		
0	$4.8 \pm 0.12a^{c}$	0.0	$4.8 \pm 0.12a$	0.0	$4.8 \pm 0.12a$	0.0	$4.8 \pm 0.12a$	0.0	
1	$4.43 \pm 0.15a$	7.7	$4.77 \pm 0.15a$	0.6	$4.53 \pm 0.26a$	5.6	$4.53 \pm 0.29a$	5.6	
5	$3.37 \pm 0.27b$	29.8	4.0 ± 0.29 b	16.3	$4.1 \pm 0.31a$	14.6	$4.17 \pm 0.17a$	13.1	
10	$2.6 \pm 0.21c$	45.8	1.93 ± 0.23 bc	59.8	1.7 ± 0.21 b	64.6	$3.13 \pm 0.24b$	34.8	
50	$1.63 \pm 0.17d$	66.0	$1.53 \pm 0.18c$	68.1	$0.0 \pm 0.0c$	100	$1.8 \pm 0.12c$	62.5	
100	$0.23 \pm 0.4e$	95.2	0.7 ± 0.06 d	85.4	$0.0 \pm 0.0c$	100	$0.47 \pm 0.24d$	90.2	
EC_{50}^{d}	13.17		16.35		8.05		21.06		
			Par	nicum repe	ens				
0	$2.1 \pm 0.09a^{c}$	0.0	$2.1 \pm 0.09a$	0.0	2.1± 0.09a	0.0	$2.1 \pm 0.09a$	0.0	
1	$1.9 \pm 0.09ab$	9.5	$2.1 \pm 0.03a$	0.0	$2.0 \pm 0.03a$	4.7	$2.2 \pm 0.1a$	-4.7	
5	$1.8 \pm 0.09 b$	14.3	1.8 ± 0.06 b	14.3	$1.9 \pm 0.06ab$	9.5	$2.1 \pm 0.07a$	0.0	
10	1.7 ± 0.06 b	19.0	1.7 ± 0.03 b	19.0	$1.8 \pm 0.0.09$ b	14.3	$2.0 \pm 0.03a$	4.7	
50	$0.6 \pm 0.07c$	71.0	0.6 ± 0.09	71.0	$1.1 \pm 0.09c$	47.6	$0.8 \pm 0.0 b$	61.9	
100	$0.3 \pm 0.06d$	85.7	0.0 ± 0.0 d	100	0.0 ± 0.0 d	100	$0.2 \pm 0.03c$	90.5	
EC ₅₀	22.74		20.78		28.79		37.99		
	Silybum marianum								
0	$2.23 \pm 0.07a^{c}$	0.0	$2.23 \pm 0.07a$	0.0	$2.23 \pm 0.07a$	0.0	$2.23 \pm 0.07a$	0.0	
1	1.83 ± 0.03 b	17.9	1.93 ± 0.03 b	13.5	$1.77 \pm 0.03b$	20.6	1.90 ± 0.06 b	14.8	
5	$1.50 \pm 0.0c$	32.7	$1.70 \pm 0.06c$	23.8	$1.70 \pm 0.0b$	23.8	1.80 ± 0.06 b	19.3	
10	$1.37 \pm 0.03c$	38.6	1.50 ± 0.06 d	32.7	$1.50 \pm 0.06c$	32.7	$1.60 \pm 0.0c$	28.3	
50	1.17 ± 0.07 d	47.5	$1.13 \pm 0.03e$	49.3	$1.07 \pm 0.03d$	52.0	1.07 ± 0.03 d	52.0	
100	$1.17 \pm 0.03d$	47.5	$0.93 \pm 0.03f$	58.3	$1.03 \pm 0.03d$	53.8	$0.80 \pm 0.06e$	64.1	
EC ₅₀	> 100		50.86	50.86 60.63			43.27		

^a Data are expressed as means \pm SE from experiments with three replicates of 20 seeds each.

^b I = inhibition.

^c Means within a column for each weed sharing the same letter are not significantly different at the 0.05 probability level.

 $^{^{\}rm d}$ EC₅₀ = concentration of compound causing 50% shoot growth inhibition.

Moreover, parthenin caused damage to the cell membrane, reducing dehydrogenase, protease, and peroxidase activities, and reducing chlorophyll content as well as affecting protein content and respiration of water hyacinth weed and mung bean plant (Batish *et al.* 2002; Pandey 1996). Finally, parthenolide has been shown to inhibit acetolactate synthase, which is a target enzyme for several classes of commercial herbicides (Abdelgaleil *et al.* 2009).

CONCLUSION

From the present study, it could be concluded that artemisinin and its analogues have promising herbicidal activity against *P. minor*, *P. repens*, and *S. marianum*. These compounds are more effective against narrow-leaf weeds than broad-leaf weeds. Moreover, artemether(3) showed stronger herbicidal activity than artemisinin(1) indicating that derivatization and/or structure modification are an important step for obtaining new compounds with interesting herbicidal activity.

REFERENCES

- Abdelgaleil, S.A.M. **2010**. Assessment of mosquitocidal, herbicidal and molluscicidal potentials of extracts and phytochemicals isolated from three Egyptian plants. Alex. J. Agric. Res. **55**: 59–73.
- Abdelgaleil, S.A.M., N. Abdel-Razeek and S.A. Soliman **2009**. Herbicidal activity of three sesquiterpene lactones on wild oat (*Avena fatua*) and their possible mode of action. Weed Sci. **57**: 6–9.
- Barbosa, L.C.A., A.V. Costa, D. Pilo-Veloso, J.L.C. Lopes, M.G. Hernandez-Terrones and B K. Lotina-Hennsen **2004**. Phytogrowth-inhibitory lactones derivatives of glaucolide B. Z. Naturforsch. **59**c: 803–810.
- Baruah, N.C., J.C. Sarma, N.C. Barua, S. Sarma, and R.P. Sharma **1994**. Germination and growth inhibitory sesquiterpene lactones and a flavone from *Tithonia diversifolia*. Phytochemistry **36**: 29–36.
- Batish, D.R., H.P. Singh, R.K. Kohli, D.B. Xaxena and S. Kaur **2002**. Allelopathic effects of parthenin against two weedy species, *Avena fatua* and *Bidens pilosa*. Environ. Exp. Bot. **47**: 149–155.
- Batish, D.R., H.P. Singh, R.K. Kohli, S. Kaur, D.B. Saxena and S. Yadav **2007**. Assessment of parthenin against some weeds. Z. Naturforsch. **62**c: 367-372.
- Bhowmik, P.C. and Inderjit **2003**. Challenges and opportunities in implementing allelopathy for natural weed management. Crop Prot. **22**: 661-671.

- Chen, P.K. and G.R. Leather **1990**. Plant growth regulatory activities of artemisinin and its related compounds. J. Chem. Ecol. **16**: 1867-1876
- Chung, I.M. and D.A. Miller **1995**. Natural herbicide potential of alfalfa residues on selected weed species. Agron. J. **87**: 920–925.
- Cohort Software Inc. **1985**. Costat User's Manual. Version 3. Tucson, AZ: Cohort.
- Dayan F.E., A. Hernandez, S.T. Allen, R.T. Moraes, J.A. Vroman, M.A. Avery and S.O. Duke **1999**. Comparative phytotoxicity of artemisinin and several sesquiterpene analogues. Phytochemistry **50**: 607–614.
- Ditomaso, J.M. and S.O. Duke **1991**. Evaluating the effect of cinmethylin and artemesinin on polyamine biosynthesis as a possible primary site of action. Pestic. Biochem. Physiol. **39**: 158-167.
- Duke S.O., K.C. Vaughn, E.M.J Croom and H.N. Elsohly **1987**. Artemisinin, a constituent of annual wormwood (*Artemisia annua*), is a selective phytotoxin. Weed Sci. **35**: 499–505.
- Duke, S.O., J.G. Romagni and F.E. Dayan **2000**. Natural products as sources for new mechanisms of herbicidal action. Crop Prot. **19**: 583-589.
- Duke, S.O., R.N. Paul and S.M. Lee **1988**. Terpenoids from the genus *Artemisia* as potential pesticides. In *Biologically Active Natural Products: Potential Use in Agriculture;* Cutler, H. G., Ed.; American Chemical Society: Washington, DC, pp 318-334.
- Finney, D. J., **1971**. Probit Analysis, third ed. Cambridge University Press, London, 318 p.
- Fujii, Y., **2001**. Screening and future exploitation of allelopathic plants as alternative herbicides with special reference to hairy vetch. J. Crop Prod. **4**: 257-275.
- Heap, I., **2006**. The International Survey of Herbicide Resistant Weeds. [Cited 2 June **2006**.] Available from URL: http://www.weedscience.com.
- Holm, L.G., D.L. Plucknett, J.V. Pancho and J.P.Herberger, 1977b. The World's Worst Weeds:Distribution and Biology. University Press of Hawaii, Honolulu.
- Holm, L.G., J. Doll, E. Holm, J. Pancho and J. Herberger 1997a. World Weeds. Natural Histories and Distribution. Wiley, NewYork.
- Hong, N.H., T.D. Xuan, T. Eiji, T. Hiroyuki, M. Mitsuhiro and T.D. Khanhc 2003. Screening for allelopathic potential of higher plants from Southeast Asia. Crop Prot. 22: 829-836.
- Klayman, D.L., **1985**. Quinghaosu (artemisinin): an antimalarial drug from China. Sci. **228**: 1049-1055.

- Kundu, A., S. Saha, V. Ahluwalia and S. Walia **2013**. Plant growth inhibitory terpenes from *Eupatorium adenophorum* leaves. J. Appl. Bot. Food Oual. **86**: 33–36.
- Leather, G.R. and F.A. Einhellig **1985**. Mechanisms of allelopathic action in bioassay. In: Thompson, A.C. (Ed.), The Chemistry of Allelopathy. ACS, Washington, pp. 197–205.
- Lydon, J., J.R. Teasdale and P.K. Chen **1997**. Allelopathic activity of annual wormwood (*Artemisia annua* and the role of artemisinin). Weed Sci. **45**: 807–811.
- Murphy, T.R., D.L. Colvin, R. Dickens, J.W. Everest, D. Hall and L.B. McCarty **1992**.
- Weeds of Southern Turf grasses: Golf Courses, Lawns, Roadsides, Recreational Areas, Commercial Sod. Reprinted **2002**. Cooperative Extension Service, University of Florida, Institute of Food and Agricultural Sciences SP 79. University of Florida, Gainesville.
- Pandey, D.K., **1996**. Phytotoxicity of sesquiterpene lactone parthenin on aquatic weeds. J. Chem. Ecol. **22**: 151–160.
- Picman, A. K., **1986**. Biological activities of sesquiterpenes. Biochem. Syst. Ecol. **14**: 255–281

- Ploypradith, P., **2004**. Development of artemisinin and its structurally simplified trioxane derivatives as antimalarial drugs. Acta Tropica **89**: 329-342.
- Saad, M.M.G., S.A.M. Abdelgaleil and T. Suganuma **2012**. Herbicidal potential of pseudoguaninolide sesquiterpenes on wild oat, *Avena fatua* L. Biochem. Syst. Ecol. **44**: 333-337
- Singh, H.P., D.R. Batish and R.K. Kohli **2003**. Allelopathic interactions and allelochemicals: New possibilities for sustainable weed management. Crit. Rev. Plant Sci. **22**: 239-311.
- Stiles, L.H., G.R. Leather and P.K. Chen **1994**. Effects of two sesquiterpene lactones isolated from *Artemisia annua* on physiology of *Lemna minor*. J. Chem. Ecol. **20**: 969-978.
- Sutton, D.L., **1996**. Growth of torpedograss from rhizomes planted under flooded conditions. J. Aquat. Plant Manag. **34**: 50–53.
- Turk, M.A. and A.M. Tawaha **2002**. Inhibitory effects of aqueous extracts of black mustard on germination and growth of lentil. Pak. J. Agron. **1**: 28–30.

- -

artemether dihydroartemisinin artemisinin

artesunate

artemether

artesunate

•

dihydroartemisinin

.

 $(EC_{50}=1.20~\mu\text{M}) \label{eq:ecc_50}$ artemether $(EC_{50}=10.0 \qquad (EC_{50}=0.39~\mu\text{M}) \label{ecc_50}$ artesunate

. μ M)

artesunate dihydroartemisinin artemether

·

artemether .

.artemisinin artesunate dihydroartemisinin

.