



# Alternative properties of *Artemisia* (Asteraceae) phyto-extracts to anti-malarian ones: preliminary bibliografic review on nemato-toxic effects.

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### ABSTRACT

Phyto-extracts of *Artemisia* species (Asteraceae) are employed as natural biocides (anti-insects, anti-helminthes, and anti-biotics) from many centuries. The main aim of this review is to summarize the toxic effects of chemical extracts from *Artemisia* on Nematoda worms.

Toxic effects were reported for the following Nematoda genera of bio-medical interest: *Ascaris* (*A. galli*, *A. leonina*, *A. lumbricoides*, *A. suum*), *Bunostomum* (*B. trigonocephalum*), *Caenorhabditis* (*C. elegans*), *Chabertia* (*C. ovina*), *Dictyocaulus* (*D. filaria*), *Dirofilaria* (*D. immitis*), *Enterobius* (*E. vermicularis*), *Haemonchus* (*H. contortus*), *Heligmosomoides* (*H. polygyrus*), *Necator* (*N. americanus*), *Nematodirus*, *Oesophagostomum* (*O. columbianus*), *Protostrongylus*, *Strongyloides*, *Trichinella* (*T. spiralis*), *Trichostrongylus* (*T. colubriformis*); *Trichuris* (*T. ovis*); on *Gnathostoma spinigerum* no toxic effects are shown.

Similarly effects were reported for the following Nematoda genera of agro-ecological interest: *Ditylenchus* (*D. dipsaci*), *Helicotylenchus* (*H. dihystera*), *Meloidogyne* (*M. incognita*, *M. javanica*, *M. megadora*), *Pratylenchus* (*P. vulnus*), *Rotylenchulus* (*R. reniformis*).

The species of *Artemisia* used against Nematoda and divided by worm taxa, were the followings:

*A. absinthium*, *A. annua*, *A. cina*, *A. herba-alba*, *A. maritime*, *A. monosperma*, *A. moorcroftiana*, *A. pallens*, *A. santonica*, *A. vulgaris* (Ascaridida);

*A. afra*, *A. marittima*, *A. vulgaris* (Rhabditida);

*A. annua*, *A. nilagirica* (Spirurida);

*A. absinthium*, *A. annua*, *A. brevifolia*, *A. herba-alba*, *A. marittima*, *A. sieversiana*, *A. vulgaris* (Strongylida);

*A. absinthium*, *A. nilagirica*, *A. vulgaris* (Trichocephalida);

*A. absinthium* (Trichurida);

*A. abrotanum*, *A. absinthium*, *A. annua*, *A. apiacea*, *A. arborescens*, *A. argyi*, *A. capillaris*, *A. cina*, *A. dracuncululus*, *A. judaica*, *A. maritima*, *A. nilagirica*, *A. pallens*, *A. sieversiana*, *A. vulgaris* (Tylenchida).

Data on biological functions of *Artemisia* extracts are very interesting for a potential widespread use in bio-medicine and agro-ecology. Artemisinin is the new molecular platform for the development of a complete molecular library with potential applications also in the treatment of Nematoda helminths.

### KEY WORDS

*Artemisia*, Asteraceae, Phyto-extracts, Artemisinin, Natural Products, Biological Control, Nematoda, anti-helminthes, Agro-ecology, Co.Al.Ta. project.

### INTRODUCTION

Phyto-extracts of *Artemisia* (Asteraceae) have many interesting properties which make them a very broad front of potential applications in agro-ecological and bio-medical fields; moreover these phyto-extracts are employed as natural bio-cides (anti-insects, anti-helminthes, and anti-biotics) from many centuries (Vicidomini, 2008).

Foremost, exactly from a species of *Artemisia* (*A. annua*), has been obtained the main active principle for the treatments of the forms multi-resistant of malaria (artemisinin), one of economically and socially more expensive pathologies of the planet (Bhakuni et al., 2001; Haynes, 2006; Hsu, 2006a, 2006b; Kuhn & Wang, 2008). In the second place an always increasing research about phyto-extracts and molecules obtained from *Artemisia* has revealed effectiveness them in varied fields, as antivirals (both to DNA and RNA taxa), antibacterials, antimycotics, antiprotistas (*Acanthamoeba*, *Babesia*, *Balantidium*, *Cryptosporidium*, *Eimeria*, *Encephalitozoon*, *Entamoeba*, *Giardia*, *Haemoproteus*, *Leishmania*, *Naegleria*, *Neospora*, *Plasmodium*, *Theileria*, *Toxoplasma*, *Trichomonas*, *Trypanosoma*), allelopatics, anti molluscs and anti arthropods (Vicidomini, 2008).

Finally, various cellular cancer lines (Efferth, 2005, 2006a, 2006b) and different pathologies and disorders of the immune system (Vicidomini, 2008) are susceptible of treatment with phyto-extracts of *Artemisia*. *Artemisia* phyto-extracts are proposed as one of the fields of more profiqua and promising pharmacological survey.

Besides the powerful properties anti-malarial of artemisinin and derivatives, the phyto-extracts of *Artemisia* have showed some important curative activities as anthelmintic; infact quickly after the fight to the *Plasmodium* resistant to the conventional therapies, artemisinin and derivatives have been used with success (both

singularly and in combined therapies) against *Schistosoma* (Strigeatida), a genus of Platyzoa which is the greater socio-economic damages in the world.

Currently have been established and published also very precise protocols on doses and combinations of artemisinin and its derivatives for chemical-therapy of various schistosomiasis (*S. haematobium*, *S. japonicum*, *S. mansoni*, *S. mekongi*). Infact anthelmintic action of the *Artemisia* phyto-extracts has been demonstrated against numerous Platyzoa taxa (Opistorchida: *Clonorchis*, *Opisthorchis*; Cyclophillidea: *Dipylidium*, *Hymenolepis*, *Moniezia*, *Taenia*; Echinostomida: *Echinostoma*, *Fasciola*) and for the Annelids *Pheretima postuma* (Clitellata: Megascolecidae) (Keiser et al., 2008; Utzinger et al., 2003, 2007; Vicidomini, 2007).

Target of this review is to introduce the data available in literature on the toxic properties of the *Artemisia* phyto-extracts against the Nematoda taxon, the helminths group of greater socio-economic importance on the planet, both for agro-ecological aspects that bio-sanitary.

In the agro-ecological field the phytoparasitic nematodes are among the most difficult crop pests to control. Their control has been carried out by use of nemato-toxic chemicals, resistant crop variety, crop rotation, nematicide crops. The development of new nematicides is very difficult, and a very high numbers of substances derived from plant have nematicidal properties. The phyto-extracts have drawn the attention of researchers and agro-chemical companies, and they have some advantages over synthetic nematicidal chemicals, like: a) they are new compounds that nematodes are not able to inactivate; b) they are usually less concentrate compared to synthetic chemicals; c) they have multiple action modes; d) they derived from renewable sources (Akhtar & Mahmood, 1994; Chitwood, 2002; Ferraz et al., 2004; Sukul, 1992; see also Deschiens, 1944, as one of first report on this topic).

In the bio-medical field the nematodes of gastro-intestinal are recognized (with other taxa parasites) as a major constraint to livestock production (low productivity; low growth-reproductive rates; diseases; death), particularly in poor nations where small ruminants can play an important economic role. Modern nematicidal can be very effective if correctly used, but their cost and health consequences are a major disadvantage, two big problems in poor nations. Also in this field the phyto-extracts have drawn the attention of researchers for some advantages over synthetic nematicidal chemicals (see also previous a-d points): the local production of botanic nematicidal is cheaper than importation of chemicals; b) nematicidal inadequate use (low/high dosage; inappropriate drugs; high treatment numbers; wrong diagnosis; etc.) encourage the resistance development in gastro-intestinal worms (Dano & Bogh, 2007; Iqbal et al., 2005; Turner & Ferreira, 2005).

For these reasons several researcher groups are attempting to develop strategies based on the use of phyto-chemicals against economic relevant nematodes, both in agro-ecological field and in bio-medical one. Much of anti-parasite drugs derive from the ethno-botanic use of important plants and their phyto-extracts, as *Cinchona* and *Artemisia* against malaria (quinine and artemisinin), *Cephaelis* against amoebic (emetine) and *Artemisia* and *Digenea* against helminthes (santonin and kainicate) (Croft, 1994; Farnsworth et al., 1985).

## METHODS

This bibliographical research (updated until 2009) aims to provide a complete picture of all the possible applications of *Artemisia* phyto-extracts as nematicides and/or nemato-repellents. It is obviously impossible to mention the entire bibliography in this field, and certainly various papers will not be listed and commented, but it provides a full picture of potential applications so far known.

Results are divided by taxonomy and by publication date.

The bibliographical research was carried out with more used on-line search engines and with the following database on-line.

Institutional databases:

- Università Federico II di Napoli (<http://www.unina.it/>), Napoli and Portici town;
- Consiglio Nazionale delle Ricerche (<http://www.cnr.it/>), Portici town;
- Stazione Zoologica Internazionale A. Dohrn, Napoli (<http://www.szn.it/>);
- Consiglio Nazionale per la Ricerca e la Sperimentazione in Agricoltura (<http://www.entecra.it/>), Scafati town.

Web data bases:

- <http://trophort.com/index.html>
- <http://www.biomedcentral.com/>
- <http://www.doaj.org/>
- <http://www.efloras.org/>
- <http://www.e-journals.org/>
- <http://www.herbmed.org/>
- <http://www.medscape.com/>
- <http://www.ncbi.nlm.nih.gov/>
- <http://www.newcrops.uq.edu.au/>
- <http://www.niscair.res.in/>
- <http://www.sciencedirect.com/>

## RESULTS

### Ascaridida

Narayana et al. (1976), Farnsworth et al. (1985), Mcleod (1997) and Lans et al. (2007) they pointed out that santonin, extracted from *A. maritima* or *A. herba-alba*, was toxic for *Ascaris* (Ascaridiidae). Singh (1994) pointed out that the extract of fresh or dried leaves of *A. absinthium*, *A. maritima*, *A. moorcroftiana* was used by Kashmir human population against round worms (*Ascaris*). Lans et al. (2007) reports use of deworming-infusion for pets and pigs of *A. absinthium*, *A. annua*, *A. cina*, *A. vulgaris* against *Ascaris* and *A. absinthium*, *A. annua*, *A. cina* against *Enterobius* (Oxyuridae) in British Columbia.

Rachkovskaia (1978) describes morphological damages on *Ascaris galli* musculocutaneous sac caused by santonin, this confirmed previous reports of nemato-toxic effects caused by santonin on *Ascaris* in humans (Aksenova, 1950; Faiguenbaum, 1952; Fanta-Nunez, 1953; Guseinov, 1954, 1955; Krotov, 1957; Matsusaki et al., 1964; Sekera & Rahm, 1952; Smirnov, 1932; Ueda & Tsuji, 1954).

Sharaf et al. (1959) tests *A. monosperma* phyto-extracts obtained with water and alcoholic extractions, against *A. leonina* *in vitro* at 38°C. Results were as follows: inhibition of intestine wall motility; stimulation of worms motility; watery extracts more potent than the alcoholic extracts; effects were dose dependent; no-lethality was recorded.

Morishita (1964), Lee et al. (1972) and Rim et al. (1974) already in 1960-1970 decades proposed the combined use of santonin / kainic acid complex for mass control of *A. lumbricoides* in Japan and Korea human populations. In these papers are recorded a percentage of humans cured respectively 82.0%-82.9% (16.5 mg of santonin-kainicate), 80.5% (105 mg). Lee et al. (1972) records also the reduction of egg numbers per patient (97.7%).

Nakhare & Garc (1991) have used *A. pallens* essential oil extracted from whole plants in order to evaluate the toxic effects (paralysis and death) on *A. lumbricoides* adults *in vitro* and obtained from pigs intestine. Main results were the following (P-piperazine = reference drug):

Treatment concentration	Percentage of rapidity of paralysis, in minutes from treatment, compared to P-piperazine	Percentage of rapidity of death in minutes from treatment, compared to P-piperazine
0.1 % <i>A. pallens</i> essential oil and P-piperazine	300%	343%
0.2 % <i>A. pallens</i> essential oil and P-piperazine	250%	267%
0.4 % <i>A. pallens</i> essential oil and P-piperazine	222%	190%

ElGarhy & Nahmoud (2002) have evaluated *in vitro* *A. santonica* watery phyto-extracts (obtained from shoots) against *A. lumbricoides* eggs and larvae collected from human. The control was water, concentrations of phyto-extracts were 1% and 5%, and worm % death was assessed at 10-40 days. All the control group survived for 40 days of test; for the treated group (both at 1% that at 5%) after 10 days from treatment were all survived, at 20 days, less than 50% were living and from 30 days all were death.

Githiori (2004) and Githiori et al. (2006) reports that in the British Veterinary Codex (1953, 1965) *Artemisia* were used against *A. suum* and *Neoascaris* (Toxocaridae) in ruminants

Urban et al. (2007) carried out *in vitro* bio-essays with *A. absinthium* and *A. vulgaris* ethanol phyto-extracts against *A. suum* eggs. *A. absinthium* were very effective at all

concentrations (62.5-2000 micro-g/ml; reference drug: albendazole); *A. vulgaris* showed weak activity.

AlWaili (1988) used *A. herba-alba* leaves and shoots in order to obtain watery phyto-extracts for treats *Enterobius vermicularis in vivo* in humans. Two treatment groups were 25 and 50 ml of phyto-extract per 3 days per human (10 patients). Both with 25 and 50 ml the worms and its eggs disappeared totally from 10 patients for 6 months.

Akhtar et al. (1982) evaluates the efficacy of santonin (single dose: 5.0, 10.0, 15.0 mg/kg) and piperazine (single dose: 88 mg/kg) in buffalo calves infected with *Neoscaris vitulorum*. The percentage reduction of egg/g of with 15 mg/kg of santonin in calves highly and moderately infected, were respectively 92.3%, 95.8% after 3 days of treatment (piperazine: 82.0%, 92.2%) and 100.0%, 100.0% after 7 days of treatment (piperazine: 88.0%; 97.0%). Santonin efficacy was recorded also at 5 and 10 mg/kg but not comparable to piperazine 88 mg/kg.

### Rhabditida

Wat et al. (1981) have evaluated that *A. vulgaris* polyacetylenes (see: Drake & Lam, 1974) are activated with 400nm-UV for 1 h, against *in vitro* culture of *Caenorhabditis elegans* (Rhabditidae). The polyacetylene **3-OH-2-nona-1-en-3,5,7-trino-tetrahydropyran** was lethal for at least 67% of worms at 0.5 mg/l.

McGaw et al. (2000) tests phyto-extracts of *A. afra* leaves against *C. elegans* cultured on agar. Three phyto-extract were used (hexane, ethanol, water) at two concentrations (1 and 2 mg/ml of culture) for two hours at 25°C; Levamisole at 5 micro-g/ml was the reference drug. Hexane phyto-extracts were without differences compared to Levamisole; for the other two the results were the following:

Phyto-extract and concentration	% of death compared to levamisole at 2 h from treatment	% of death compared to levamisole at 168 h from treatment
Ethanol: 1 mg	+50%	+20%
Ethanol: 2 mg	+50%	+20%
Water: 1 mg	+50%	+20%
Water: 2 mg	+20%	+0%

The movement of Nematodes was also affected by phyto-extract types (ethanol < water) with a dose-dependent trend.

Githiori et al. (2003) have pointed out that santonin was effective against *Heligmosomoides polygyrus* (Heligmosomatidae) adult instar but not against its eggs.

Sharma (1993) has used *Jantana* mixture, containing several herbal powder (as *A. maritima*), to test toxic effects on *Strongyloides* (Strongyloididae) eggs in cattle calves. The control group at 7 days showed an eggs population ranged from 300 to 1100 eggs/g of faeces; the treated calves no egg was detected.

ElGarhy & Nahmoud (2002) pointed out that *Artemisia* seed were active against *Strongyloides*.

### Spirurida

Sukul et al. (1999) have tested *in vivo* some homoeopathic drugs obtained from *A. nilagirica* flowering meristems against *Dirofilaria immitis* (Filaridae) microfilaria, collected from pariah dogs. Drugs were obtained from ethanol extract and via ultra-dilutions progressive process, they have obtained the homoeopathic solution named *Cina-teta*, *Cina-200*, *Cina-1000*. Treatment with *Cina-teta* was 10 mg of solution per kg/day/15 days and 20 mg/kg/day/15 days; treatment with *Cina-200* and *Cina-1000* was

0.1 ml of solution in 4 ml of cow milk per 30 days. The results are summarized in the following scheme:

Treatment	Reduction of microfilariae at 30 days from treatment start	Reduction of microfilariae at 75 days from treatment start
<i>Cina-teta</i>	78.4%	57.1%
<i>Cina-200</i>	63.1%	42.4%
<i>Cina-1000</i>	71.4%	64.2%

Sukontason et al. (2000) have evaluated, *in vitro* at 37°C, anti-malarial drugs against larvae-III of *Gnathostoma spinigerum* (Gnathostomatidae) collected from freshwater eels (*Fluta*). The worms were maintained in treatment medium for 21 days. Main results were the followings:

Groups, treatment, concentration	Total death n.	Total ipomotility n.	Worm histological damage
Control (= culture medium; see paper)	0	0	NO
Quinine-dihydro-chloride, 20 <i>micro</i> -l/ml	0	0	NO
Artemether, 0.5 <i>micro</i> -l/ml	0	0	NO

### Strongylida

DeBairaclı (1973) has reported that the infusion of *A. vulgaris* dry flower is toxic for *Bunostomum* (Ancylostomatidae), *Dictyocaulus* (Dictyocaulidae) and *Protostrongylus* (Protostrongylidae).

Sadykhov & Ryabinin (1979) have evaluated the toxic properties of *A. absinthium* against *Dictyocaulus filaria* (Dictyocaulidae) larvae and adults obtained from sheep and cultured *in vitro*. *A. absinthium* leaves and stems (100-150 g) were placed in infusion in water (350-400 ml at 80-100°C for 12-15 h). The infusion was lethal for larval and adult instars of the worm after 7 h.

Prakash et al. (1980) used an alcoholic extract of *A. siversiana* against *Haemonchus contortus* (Trichostrongylidae) eggs in sheep. The alcoholic extract was added in eggs suspension at 27°C for 7 days and at 750 *micro*-g/g 80% of eggs were inhibited.

Idris et al. (1982) used *A. herba-alba* root dry powder against *H. contortus in vivo* in Nubian goats, with the following results:

Treatment	Worm decrease post/pre-treatment (days from treatment)	Reduction of eggs in faeces at 5 week post-treatment compared with data at treatment (from table.2 in Idris et al., 1982, p.140)
No	75.5% (22)	100,0%
2 g in 1 day	100.0% (41)	100,0%
30 g divided in 3 day	97.2% (11)	100,0%
10 g divided in 2 day	96.5% (41)	96,5%

The histo-anatomical damages induced by worms in Nubian goats were partially suppressed/recovered in the treated-group respect to control-group.

Iqbal et al. (2004) have carried out both *in vivo* and *in vitro* tests of *A. brevifolia* (whole aerial part) phyto-extracts obtained with water, methanol and dry powder against *H. contortus* in sheep. Concentrations used for *in vivo* tests were 1, 2, 3 g/kg of three phyto-extract types and 25 mg/ml for *in vitro* tests but only water and methanol types; a

single dose was used with Levamisole (0.55 mg/ml) and PBS (P-buffer saline solution) as controls; temperature of tests was 25-30°C. The main results were the followings:

<i>In Vitro</i>				
Hour from treatment	Percentage of paralysis of <i>H. contortus</i>			
	0 h	3 h	6 h	6 h post treatment + 30 min in PBS
<i>A. brevifolia</i> water extr.	0%	20%	30%	4%
<i>A. brevifolia</i> methanol extr.	0%	57%	80%	80%
Levamisole	0%	40%	80%	80%
PBS	0%	0%	4%	4%

  

<i>In Vivo</i>	
Treatment	Eggs/g of faeces reductions after 14 days post-treatment; data in % compared to untreated
<i>A. brevifolia</i> powder (3 g/kg)	62%
<i>A. brevifolia</i> water extr. (3 g/kg)	67%
<i>A. brevifolia</i> methanol extr. (3 g/kg)	0%
Levamisole	99%

Turner & Ferreira (2005) have evaluated the efficacy of artemisinin from *A. annua* against *H. contortus* eggs with 300 mg/day/meat goat for 7 days (control = no artemisinin administered). At 1 day after treatment the eggs/g of faeces was about 2500 (control = 900/1000), and at 7 days was 2000 (control = 1200/1300); not significant differences was showed for treated group at 1 and 7 days but significant was the difference between control and treated groups.

Sharma (1993) has used *Jantana* mixture, capsules with 10 g of several herbal species powder (as *A. maritima*), to test toxic effects on eggs of *Haemonchus*, *Trichostrongylus* (Trichostrongylidae), *Nematodirus* (Molineidae) in cattle calves. The control group at 7 days showed an eggs population ranged from 300 to 1100 eggs/g of faeces; the treated calves no egg was detected.

Tariq et al. (2008) have carried out (T = 37°C) both *in vitro* (adults) that *in vivo* (eggs) tests against *H. contortus* and other gastro-intestinal Nematoda of sheeps. They have used watery and ethanol *A. absinthium* phyto-extracts (whole plant). In *in vitro* tests were evaluated adult mortality at 1, 2, 4, 8 h (concentration used: 25 mg/ml); in *in vivo* tests were evaluated egg reductions after 5, 10, 15 gg post treatment (concentration used: 1 and 2 g/kg). Drug reference was albendazole. Main results were as follows:

<i>In vitro</i> : Percentage of paralysis of <i>H. contortus</i>		
Hour from treatment	2 h	4 h
<i>A. absinthium</i> water extr.	30.0%	40.0%
<i>A. absinthium</i> ethanol extr.	40.0%	55.0%
Albendazole (55 mg/ml)	85.0%	98.5%

  

<i>In vivo</i> : Eggs/g of faeces reductions after 15 days post-treatment (*)	
<i>A. absinthium</i> water extr. (2 g/kg)	80.5%
<i>A. absinthium</i> ethanol extr. (2 g/kg)	90.5%
Albendazole	97.4%
Untreated	6.7%

\* = specie recognized for egg counts were: *Bunostomum trigonocephalum*, *Chabertia ovina* (Strongylida: Chabertiidae), *H. contortus*, *Oesophagostomum columbianus* (Strongylida: Strongylidae), *Trichuris ovis* (Trichurida: Trichuridae)

Urban et al. (2007) have carried out *in vitro* bio-assays with *A. absinthium* and *A. vulgaris* ethanol phyto-extracts against *Trichostrongylus colubriformis* larvae-III. *A. absinthium* was very effective at all concentrations (0.063-2.000 mg/ml) more than reference drug (albendazole); *A. vulgaris* showed weak activity.

Idris et al. (1982) have reported that santonin is used against hookworms *Necator americanus* (Ancylostomatidae) in North America.

## Trichocephalida

Sukul et al. (2005) evaluate *in vivo* some homoeopathic drugs extracted by ethanol from *A. nilagirica* (flowering tops) against *Trichinella spiralis* (Trichinellidae) larvae in Swiss albino mice. The ultra-diluted drugs were *Cina-teta* and *Santonin-teta*. The group treated was 32 mice, with two controls (untreated infected; Ethanol 30 treated and infected). Treatment started 7 days post-infection, with 200 larvae/mouse, and was continued for 120 days (0.05 ml/mouse/day); at 121st day the mice were sacrificed for larval counts. Main results were the following (Mean larval n. at 121st day and % decrease compared to control): Control uninfected and untreated (8956; 0%); Ethanol 30 (7638; 14.7%); *Cina-teta* (1423; 84.1%); *Santonin-teta* (1682; 81.2%).

Caner et al. (2008) evaluate *in vivo* *A. absinthium* and *A. vulgaris* methanol phyto-extracts (from whole epigeal parts) against *T. spiralis* adults (enteral phase) and encapsulated larvae (parenteral phase) obtained from rats. Two groups were treated, for 20 days, with 300 mg of phyto-extracts per kg, diluted in 2 ml of distilled water; treatment was started 120 h after adult inoculation. Two groups were treated, for 120 h, with 600 mg of phyto-extracts per kg, diluted in 2 ml of distilled water; treatment started 45 days after encapsulated larvae inoculation. At the control group was administered distilled water only. Data recorded were: a) mean worm numbers per g of muscle (biceps-triceps; diaphragm; quadriceps; tongue) during the two phases and b) worm reduction percentages. Main results were the followings:

<i>A. absinthium</i>				
	Biceps-triceps	Diaphragm	Quadriceps	Tongue
worm reduction with 300 mg/kg	60.5%	37.7%	46.2%	63.5%
worm reduction with 600 mg/kg	46.4%	50.0%	43.7%	59.9%
<i>A. vulgaris</i>				
worm reduction with 300 mg/kg	66.7%	53.4%	67.8%	75.6%
worm reduction with 600 mg/kg	60.2%	57.4%	47.6%	66.4%

## Tylenchida

Insunza (1990) examined some Chilean plants used for nematicidal properties. Bioassays regarding also *A. abrotanum* phyto-extracts (whole plant used; fresh sap extraction) against *Ditylenchus dipsaci* (Anguinidae) *in vitro* on lucerne callus. Tests were carried out at room temperature and light, using 2 ml of phyto-extract for 100 worms; death percentages were assessed at 24-104 h post-treatment. *A. abrotanum* caused 100% of mortality after 24 h post-treatment.

Ferraz et al. (2004) pointed out that *D. dipsaci* was reduced of 90-96% by mulching soil with 2-4% of *A. dracunculus* plant matter.

Abivardi (1971) evaluates several Iranian plant against larvae-II of *Meloidogyne incognita* (Heteroderidae) as *A. absinthium* (leaves), *A. cina* (flowering tops), *A. dracunculus* (leaves). Treatments were carried out at 20-22°C in soil samples sealed for two weeks post-treatment. The main results are reported in the following table:

Extract; concentration in ppm	Reduction of larvae-II in 40 g of soil, compared to untreated	% reduction of gall per root system, compared to untreated
<i>A. absinthium</i> ; 40 / 80	31.7% / 75.9%	20.8% / 32.6%
<i>A. cina</i> ; 40 / 80	73.9% / 80.7%	55.0% / 76.5%
<i>A. dracunculus</i> ; 40 / 80	71.2% / 79.7%	10.7% / 23.7%
Acetone; 1600	13.2%	17.2%
Untreated	0.0%	0.0%

Abivardi (1971: p.305) pointed out that in a previous bioassay on *M. incognita*, *A. absinthium* phyto-extract at dose of 400 ppm was lethal for 100% of larvae-II, but in soil sample not sealed post-treatment and with chloroform as solvent.

Mahmood et al. (1979) evaluate phyto-extracts from several Indian plants as *A. sieversiana* (leaves) against *M. incognita* (hatched larvae = larvae-II) and *Rotylenchulus reniformis* (Pratylenchidae). Leaves were dried at 60°C and 10 g of powder suspended in 100 ml of distilled water and filtered. The authors termed this solution as Standard (= S) and then they obtained S/2, S/10, S/100, S/1000 dilutions with distilled water additions. Post-treatment evaluations of worm mortality were carried out at 12, 24, 48 h; for control was used distilled water. Main results were the followings:

<i>Artemisia sieversiana</i> phyto-extract concentrations	<i>M. incognita</i> mortality at 24 and 48 h post-treatment	<i>R. reniformis</i> mortality at 24 and 48 h post-treatment
S	100%; 100%	100%; 100%
S/10	81%; 90%	85%; 100%
S/100	58%; 80%	68%; 87%
S/1000	34%; 60%	35%; 56%

Pandey (1990) carried out bioassays with phyto-extracts from several Indian plants as *A. annua* and *A. pallens* (shoots) against larvae-II *M. incognita*. Shoots (25 g) were placed in 75 ml of distilled water for 24 h and then filtered. The author termed this solution as Standard (= S) and then he obtained S/2, S/10, S/100 dilutions with distilled water additions. Post-treatment evaluations of worm mortality were carried out at 12-120 h; control used was distilled water. Main results were the followings:

Treatments	<i>M. incognita</i> mortality at 24, 48 and 120 h post-treatment	<i>M. incognita</i> not hatched eggs after 120 h post-treatment
<i>A. annua</i> - S	100%; 100%; 100%	99.6%
<i>A. annua</i> - S/10	41; 44; 48	71.3%
<i>A. annua</i> - S/100	3; 3; 6	41.9%
<i>A. pallens</i> - S	100%; 100%; 100%	99.0%
<i>A. pallens</i> - S/10	15%; 18%; 25%	72.7%
<i>A. pallens</i> - S/100	0%; 2%; 5%	43.8%
Control	-; -; -	4.0%

Sharma & Trivedi (1992a) evaluate, in a first round of bioassay, phyto-extracts from several Indian plants as *A. absinthium* (roots) against larvae-I (inside egg shell) of *M. incognita*. Fresh roots (2 g) were crushed in a mortar with distilled water, filtered and placed in refrigerator for 12 h. The authors termed this solution as Standard (= S) and then they obtained S/25, S/50, S/75 and S/100 dilutions with distilled water additions. Post-treatment evaluations of mortality were carried out at 24-72 h at 30°C; the control was distilled water. Main results were the followings:

Treatments	<i>M. incognita</i> not hatched at 24, 48 h post-treatment	Total <i>M. incognita</i> not hatched after treatment
<i>A. absinthium</i> S/25	94.0%; 95.4%	91.9%
<i>A. absinthium</i> S/50	93.7%; 94.4%	91.4%
<i>A. absinthium</i> S/100	89.7%; 91.4%	87.0%
Control	76.4%; 60.0%	47.7%

Sharma & Trivedi (1992b) in a second round of bioassay evaluate *A. absinthium* dry root powder (3 and 6 g/kg soil) against *M. incognita* larvae-II. Post-treatment evaluations were carried out at day 60 (temperature 30°C; control was the soil without powder; host plant was *Solanum melongena*). Main results were the followings:

Treatments	Decrease of root gall at 60 days post-treatment compared to control
<i>A. absinthium</i> 3 g/kg	12,3%
<i>A. absinthium</i> 6 g/kg	14,5%

Korayem et al. (1993) evaluate phyto-extracts from several Egyptian plants as *A. absinthium* (shoots) against *M. incognita* larvae-II and *Helicotylenchus dihystra* (Hoplolamidae) adults. Shoot powders (25 g) were mixed in 500 ml of watery distilled, then filtered and used after 72 h of recovery. The authors termed this solution as Standard (= S) and then they obtained S/2 and S/10 dilutions with distilled water additions. Motility evaluations were carried out at 1, 2, 3 days post-treatment; mortality evaluations were carried out at 3 and 30 days post-treatment; control was distilled water; temperature was 30°C. Main results were the followings:

Treatments	Not motility in <i>M. incognita</i> larvae-II at 24 and 48 h post-treatment and total mortality after 72 h	Not motility in <i>H. dihystra</i> at 24 and 48 h post-treatment and total mortality after 72 h	Not hatching in <i>M. incognita</i> at 30 days post-treatment
<i>A. absinthium</i> S	70.0%; 98.0%; 94.5%	22.5%; 35.0%; 54.5%	99%
<i>A. absinthium</i> S/2	20.0%; 60.0%; 14.5%	15.0%; 30.0%; 1.5%	98%
<i>A. absinthium</i> S/10	0.0%; 0.0%; 0.0%	12.5%; 15.0%; 0.5%	40%
Control	10.0%; 14.0%; -	10.0%; 12.5%; -	20%

Karayem et al. (1993) performed also both post-treatment (*A. absinthium*) and control (oxamyl) acetylcholine-esterase activity percentage on *M. incognita* L-II: S, 75% of reduction; S/2, 38.7%; oxamyl 7200 ppm, 53.3% of reductions; distilled water, 0% of reduction.

Sukul & Sukul (1999) evaluate *in vivo* an homoeopathic drug extracted by ethanol from *A. maritima* against *M. incognita* larvae-II. The ultra-diluted drug was Cina-1000; *Vigna unguiculata* was the host plant; temperature and RH were 29°C and 80-90%. The groups were: untreated and un-inoculated; untreated and inoculated; treated and inoculated. Treatment started 4 days post-inoculation (2100 larvae-II/plant), and was continued for 10 days (one time per day); at day 30 post-inoculation the plants were uprooted for larval/gall counts and root-protein percentage. Main results were the followings:

Treated group	Gall per root decrease compared to inoculated untreated	Larvae-II decrease per 2 g of root compared to inoculated untreated	Root protein of untreated-uninoculated, untreated-inoculated and Cina-1000
<i>Cina-1000</i>	16.1%	69.9%	12.8%, 6.2%; 13.6%

Dias et al. (2000) evaluate *in vitro* phyto-extracts from several Brazilian plants as *A. absinthium* and *A. verlotum* (whole aerial parts,) against *M. incognita* larvae-II obtained from *Lycopersicon esculentum*. Phyto-extracts were obtained both for infusion and for crushing. Treatments were carried out at 26.5°C and lasted 24 h; control was water. Post-treatment worm mortality evaluation (at 1, 6, 24 h) was carried out putting larvae-II in water for 24 h. Main results were reported in the following table:

Phyto-extract concentration	type and	Mortality at 24 h post-treatment with <i>A. absinthium</i>	Mortality at 24 h post-treatment with <i>A. verlotum</i>	Mortality at 24 h post-treatment with control
Infusion 2.5 ml/ 250 worms		47.2%	66.6%	3.8%
Crushing 2.5 ml/ 250 worms		90.0%	92.2%	-

Sukul et al. (2001) evaluate *in vivo* some homoeopathic drugs extracted by ethanol from *A. nilagirica* flowering tops against *M. incognita* larvae-II. The ultra-diluted drugs were Cina-200, Cina-1000; *Lycopersicon esculentum* was the host plant. The groups treated were: untreated and un-inoculated; untreated and inoculated; treated and inoculated. Treatment started post-inoculation and was foliar spray (10 ml of solution per plant per day per 10 days); at day 24 post-inoculation the plants were uprooted for

larval/gall counts and root-protein percentage. The control solution was ethanol 90% and sucrose. Main results were the following:

Treated group	Gall per root decrease compared to inoculated-untreated	Larvae-II decrease per 2 g of root compared to inoculated-untreated	Larvae-II decrease per 200 g of soil compared to inoculated-untreated	Root protein of untreated-uninoculated, untreated-inoculated, <i>Cina-200</i> and <i>Cina-1000</i>
<i>Cina-200</i>	74.7%	76.1%	78.9%	0.83%, 1.05%
<i>Cina-1000</i>	69.1%	69.5%	69.1%	0.86%, 0.88%

Pandey et al. (2004) carried out *in vitro* bioassays with artemisinin-derivative chemicals obtained from *A. annua* whole aerial parts with hexane extraction against *M. incognita* larvae-II obtained from *L. esculentum*. The controls were acetone (Ac) and dimethyl sulphoxide (DMSO); dose was 1000 ppm. Main results were:

Chemicals (solvent)	Larvae-II decrease at 24 h post-treatment	Decrease of larvae-II emergence from egg 120 h post-treatment compared to control
<i>Alpha</i> -artemether (Ac)	91,4%	81,6%
<i>Beta</i> -artemether (Ac)	87,8%	87,9%
Artesunate (Ac)	18,9%	66,7%
<i>Beta</i> -arte-propyl-ether (DMSO)	92,7%	91,8%
Arte-Cl-acetate (DMSO)	93,9%	86,7%
<i>Beta</i> -arte-benzyl-ether (DMSO)	74,1%	56,5%
<i>Beta</i> -arte-butyl-ether (DMSO)	77,0%	68,7%
Arte-propionate (DMSO)	11,6%	76,2%
Control: acetone	2,0%	-
Control: DMSO	3,0%	-

Shakil et al. (2004) evaluate *A. annua* essential oil (from leaves) against *M. incognita* larvae-II and *Rotylenchulus reniformis* (Pratylenchidae) adults. The mortality (compared to control) was recorded at 24 and 48 h; also the *M. incognita* larvae penetration in root host (*Vigna unguiculata*) was recorded; the temperature was 29°C. Main results were:

Concentration	<i>M. incognita</i> mortality (24h; 48h)	<i>R. reniformis</i> mortality (24h; 48h)
250 ppm	100,0%; 100,0%	100,0%; 100,0%
125 ppm	80,2%; 85,2%	81,2%; 78,3%
62,5 ppm	58,2%; 60,7%	57,1%; 48,1%
ED50	53,96 ppm; 52,22 ppm	54,83 ppm; 57,49 ppm
Control	-	-

Datta (2006) evaluates *in vivo* an homoeopathic drug extracted by ethanol from *A. nilagirica* against *M. incognita* larvae-II. The ultra-diluted drug were *Cina-200* but also *Cina-Mother Tincture* was used; *Morus alba* was the host plant. Treatment groups were (30°C; 75% rh): untreated and un-inoculated; untreated and inoculated; treated and un-inoculated; treated and inoculated. Treatment was foliar spray (10 ml of solution per plant every 3 days); the groups treated were divided in treated pre-inoculation (9 days in total) and treated post-inoculation (35 days in total); 60 days post last treatment the plants were uprooted for larval/gall counts. Main results were:

Treated group	Gall / root decrease compared to inoculated-untreated	Larvae-II decrease / 2 g of root compared to inoculated-untreated
Inoculated <i>Cina-MT</i> (pre-inoculation)	98,0%	96,4%
Inoculated <i>Cina-MT</i> (post-inoculation)	97,0%	92,6%
Inoculated <i>Cina-200</i> (pre-inoculation)	99,0%	97,5%
Inoculated <i>Cina-200</i> (post-inoculation)	98,2%	95,6%

Sukul et al. (2006) evaluate *in vivo* some homoeopathic drugs extracted by ethanol from *A. nilagirica* flowering tops against *M. incognita* larvae-II. The ultra-diluted drugs

were *Cina-30c*, *Santonin-30c*; *Hibiscus esculentum* was the host plant. Treatment groups were (temperature was 30°C): untreated and un-inoculated; untreated and inoculated; treated and inoculated. The treatment started 7 days post-inoculation and was foliar spray (5-10 ml of solution per plant per day per 10 days); at day 30 post-inoculation the plants were uprooted for larval/gall counts and root-protein percentage. Control solution was ethanol-30c. Main results were:

Treated group	Gall per root decrease compared to inoculated-untreated	Larvae-II decrease per 2 g of root compared to inoculated-untreated	Larvae-II decrease per 200 g of soil compared to inoculated-untreated	Root protein
Inoculated untreated	-	-	-	5,78%
Inoculated and treated: ethanol-30c	8,6%	103,6%	123%	4,84%
Inoculated and treated: <i>Cina-30c</i>	51,2%	20,8%	320%	2,58%
Inoculated and treated: <i>Santonin-30c</i>	50,3%	19,6%	283%	2,96%

Ferris & Zheng (1999) evaluate *in vitro* phyto-extracts from several Chinese plants as *A. apiacea* (whole aerial parts), *A. argyi* (leaves), *A. capillaris* (seedlings), against *M. javanica* larvae-II and *Pratylenchus vulnus* (Pratylenchidae) adults. Watery extracts of *A. argyi* and *A. capillaris* were lethal for *M. javanica* but not effective against *P. vulnus*; *A. apiacea* was ineffective against *M. javanica* but lethal for *P. vulnus*.

Oka et al. (2000) evaluate *in vitro* (25°C) essential oils from several plants (leaves) as *A. arborescens*, *A. dracuncululus*, *A. judaica*, against *M. javanica* larvae-II and eggs. Main results were:

Treatments	Larvae-II not-motility at 48 h post-treatment	Not-hatching at 7 days post-treatment
<i>A. arborescens</i> - 1 ml/l	38.9%	91.8%
<i>A. dracuncululus</i> - 1 ml/l	31.0%	81.5%
<i>A. judaica</i> - 1 ml/l	85.0%	98.8%
<i>A. judaica</i> - 0.6 ml/l	-	74.4%
Control - ethanol 1 ml/l	2.0%	67.5%

Costa et al. (2003) carried out a complex bioassays, both *in vitro* and *in vivo*, with ethanol phyto-extracts from *A. vulgaris* (powder) against *M. megadora* eggs and larvae-II obtained from coffee plants. The temperature was 25°C, the control was distilled water, host plant was *Cucumis sativus*, concentrations were from 0,5 to 100 mg/ml for all bioassays. Main results were:

mg/ml	Egg mortality (%) post-treatment compared to control			Larvae-II mortality (data from chart p.439 in Costa et al., 2003) compared to control		Larvae-II decrease	
	72 h	168 h	360 h	50% mortality	100% mortality	in roots	in roots + soil
0,0	-	-	-	-	-	43,0%	41,4%
0,5	5,1	11,1	13,0	-	-	-	-
1,0	47,6	23,1	24,1	-	-	-	-
12,5	85,7	94,2	94,3	-	-	-	-
25,0	90,9	95,7	96,3	21 h	26 h	80,8%	78,7%
50,0	100	100	100	18 h	22 h	85,2%	82,5%
100,0	-	-	-	7,5 h	9 h	95,8%	89,6%

## DISCUSSION

The main results were summarized in the table n.1.

Six Nematoda orders were listed in the present review as sensitive to *Artemisia* phyto-extracts; five orders of bio-medical interest (Ascaridida, 3 genera and 6 species; Rhabditida, 3 and 3; Spirurida, 2 and 2; Strongylida, 10 and 10; Trichocephalida, 1 and 1;) and one of agro-ecological interest (5 genera and 7 species).

*Artemisia* taxa with elevate targets versus Nematoda species were:

*Artemisia absinthium* (11 Nematoda species of bio-medical interest and 2 of agro-ecological interest)

*Artemisia vulgaris* (8 and 1)

*Artemisia maritima* (5 and 1)

*Artemisia annua* (3 and 2)

*Artemisia cina* (1 and 2)

*Artemisia nilagirica* (2 and 1)

*Artemisia sieversiana* (1 and 2).

Nevertheless the high number of *Artemisia* species that have how target Nematoda taxa, the chemicals identified were very scarce; were recognized how molecules active: artemether, artemisinin, artemisinin-derivatives, santonin, polyacetylenes, santonin-kainicate complex.

Regarding Nematoda instars we have that 35 bio-assay were carried out on larvae (9 on species of bio-medical interest and 26 on species of agro-ecological interest), 22 on eggs (18 bio-medical, 4 agro-ecological), 20 on adults (14 bio-medical, 6 agro-ecological).

An high *Artemisia* specie numbers have showed nemato-toxic effects on eggs, larvae and juveniles.

A very interesting field would be the future study on combined actions between anti-cancer and anti-helminthes effects of *Artemisia* phyto-extracts, because of cancerogenesis helminthes improved and/or started (Mayer & Fried, 2007).

**Table n.1 – Main results of mini-review for *Artemisia* species used in the bio-assay versus Nematoda taxa, with indication of instars.**

<i>Artemisia</i>	Plant part (Flowers: F; Leaves: L; Shoots: S; Roots: R; Whole plant: P; Powder mixture: Pm; Root powder: Pr; Seedlings: See). Chemicals (Eo: essential oils). Extractive solvents (Water: W; Alcohol: A; Ethanol: E; Hexane: H; Methanol: M).	Nematoda species	Nematoda instars (E = not hatched eggs; L = larva; L-II = larvae II instar; A = adults)
-	Santonin	<i>A. galli</i>	A
-	santonin/kainicate	<i>A. lumbricoides</i>	E; A
-	Artemether	<i>G. spinigerum</i>	L
-	Santonin	<i>H. polygyrus</i>	E; A
-	(artemisinin-derivatives; P; H)	<i>M. incognita</i>	L-II
-	Santonin	<i>N. americanus</i>	-
-	Santonin	<i>N. vitulorum</i>	E
<i>abrotanum</i>	(P)	<i>D. dipsaci</i>	-
<i>absinthium</i>	(L)	<i>Ascaris</i>	-
<i>absinthium</i>	(W)	<i>Ascaris</i>	-
<i>absinthium</i>	(E)	<i>A. suum</i>	E
<i>absinthium</i>	(P; E; W)	<i>B. trigonocephalum</i>	E
<i>absinthium</i>	(P; E; W)	<i>C. ovina</i>	E
<i>absinthium</i>	(L; S; W)	<i>D. filaria</i>	L; A
<i>absinthium</i>	(W)	<i>Enterobius</i>	-
<i>absinthium</i>	(P; E; W)	<i>H. contortus</i>	A; E
<i>absinthium</i>	(S; W)	<i>H. dihystrera</i>	A
<i>absinthium</i>		<i>M. incognita</i>	L-II

<i>absinthium</i>	(L)	<i>M. incognita</i>	L-II
<i>absinthium</i>	(R; W)	<i>M. incognita</i>	L-I
<i>absinthium</i>	(Pr)	<i>M. incognita</i>	L-II
<i>absinthium</i>	(S; W)	<i>M. incognita</i>	L-II
<i>absinthium</i>	(S; W)	<i>M. incognita</i>	L-II
<i>absinthium</i>	(P; W)	<i>M. incognita</i>	L-II
<i>absinthium</i>	(P; E; W)	<i>O. columbianus</i>	E
<i>absinthium</i>	(E)	<i>T. colubriformis</i>	L
<i>absinthium</i>	(P; E; W)	<i>T. ovis</i>	E
<i>absinthium</i>	(M; P)	<i>T. spiralis</i>	L; A
<i>afra</i>	(E, H, W)	<i>C. elegans</i>	A
<i>annua</i>	(W)	<i>Ascaris</i>	-
<i>annua</i>	(W)	<i>Enterobius</i>	-
<i>annua</i>	Artemisinina	<i>H. contortus</i>	E
<i>annua</i>	(S; W)	<i>M. incognita</i>	L-II
<i>annua</i>	(L; Eo)	<i>M. incognita</i>	L-II
<i>annua</i>	(L; Eo)	<i>R. reniformis</i>	A
<i>apiacea</i>	(P; W)	<i>M. javanica</i>	L-II
<i>apiacea</i>	(P; W)	<i>P. vulnus</i>	A
<i>arborescens</i>	(L; Eo)	<i>M. javanica</i>	E; L-II
<i>argyi</i>	(L; W)	<i>M. javanica</i>	L-II
<i>argyi</i>	(L; W)	<i>P. vulnus</i>	A
<i>brevifolia</i>	(P; W; M; Pw)	<i>H. contortus</i>	E; A
<i>capillaris</i>	(See; W)	<i>M. javanica</i>	L-II
<i>capillaris</i>	(See; W)	<i>P. vulnus</i>	A
<i>cina</i>	(W)	<i>Ascaris</i>	-
<i>cina</i>	(W)	<i>Enterobius</i>	-
<i>cina</i>	(F)	<i>M. incognita</i>	L-II
<i>dracunculus</i>	(P)	<i>D. dipsaci</i>	-
<i>dracunculus</i>	(L)	<i>M. incognita</i>	L-II
<i>dracunculus</i>	(L; Eo)	<i>M. javanica</i>	E; L-II
<i>herba-alba</i>	Santonin	<i>Ascaris</i>	-
<i>herba-alba</i>	(L, S; W)	<i>E. vermicularis</i>	-
<i>herba-alba</i>	(Pr)	<i>H. contortus</i>	E; A
<i>judaica</i>	(L; Eo)	<i>M. javanica</i>	E; L-II
<i>maritima</i>	Santonin	<i>Ascaris</i>	-
<i>maritima</i>	(L)	<i>Ascaris</i>	-
<i>maritima</i>	(P)	<i>H. contortus</i>	E
<i>maritima</i>	(E)	<i>M. incognita</i>	L-II
<i>maritima</i>	(P)	<i>Nematodirus</i>	E
<i>maritima</i>	(Pm)	<i>Strongyloides</i>	E
<i>maritima</i>	(P)	<i>Trichostrongylus</i>	E
<i>monosperma</i>	(A, W)	<i>A. leonina</i>	A
<i>moorcroftiana</i>	(L)	<i>Ascaris</i>	-
<i>nilagirica</i>	(E; F)	<i>D. immitis</i>	L
<i>nilagirica</i>	(F; E)	<i>M. incognita</i>	L-II
<i>nilagirica</i>	(E)	<i>M. incognita</i>	L-II
<i>nilagirica</i>	(F; E)	<i>M. incognita</i>	L-II
<i>nilagirica</i>	(E; F)	<i>T. spiralis</i>	L
<i>pallens</i>	(Eo; P)	<i>A. lumbricoides</i>	A
<i>pallens</i>	(S; W)	<i>M. incognita</i>	L-II
<i>santonica</i>	(W; S)	<i>A. lumbricoides</i>	L; A
<i>sieversiana</i>	(A)	<i>H. contortus</i>	E
<i>sieversiana</i>	(L; W)	<i>M. incognita</i>	L-II
<i>sieversiana</i>	(L; W)	<i>R. reniformis</i>	A
<i>verlotum</i>	(P; W)	<i>M. incognita</i>	L-II
<i>vulgaris</i>	(W)	<i>Ascaris</i>	-
<i>vulgaris</i>	(E)	<i>A. suum</i>	E
<i>vulgaris</i>	(W; P; F)	<i>Bunostomum</i>	-
<i>vulgaris</i>	Polyacetylenes	<i>C. elegans</i>	A
<i>vulgaris</i>	(W; P; F)	<i>Dictyocaulus</i>	-
<i>vulgaris</i>	(Pm; E)	<i>M. megadora</i>	E; L-II
<i>vulgaris</i>	(W; P; F)	<i>Protostrongylus</i>	-
<i>vulgaris</i>	(E)	<i>T. colubriformis</i>	L
<i>vulgaris</i>	(M; P)	<i>T. spiralis</i>	L; A

## ARTEMISININ AS THE MOLECULAR PLATFORM OF THE NEW CENTURY ?

The agro-chemicals market is in a decade of turning and junction, both in terms of Western perception of individual occidental consumers, both in terms of market demand, both in terms of regulatory and legislative revisions.

In the last decades of the last century prevailed the principle of maximizing agricultural productivity that justified intervention extensive and not always rational of the drugs synthesis.

The new century instead it has established a policy much more respectful of the environment and human and animal health, with an ever more rational and environmentally sustainable use of pesticides.

Research is dedicating a spasmodic attention, geometrically increasing, at the active ingredients of botanical origin to be used as an alternative to synthetic products, or even as feedstocks in organic-biodynamic-integrated agricultural.

In this evolving scenario fits excellently the *Artemisia* and many products of its secondary metabolism, with a range of potential applications economically significant, ranging from chemotherapeutic anti-cancers, chemotherapeutic immuno-modulators and anti-inflammatory drugs, from antibiotics against bacteria, fungi, protists, to anti-viral, until the anti-helminthic and insecticides, covering virtually all major fields of interest in agro-ecological and bio-medical applications.

Especially significant have been proved the properties of sesquiterpenes and, in particular those characterized by the endoperoxide bridge, which seem to have a potential universal use. These molecules are the object of great attention from the specialists, both for the creation of numerous classes and subclasses of synthetic variants of the structural parent artemisinin, that for the exploration of a wide range of organisms and plants, looking for alternative artemisinin forms (see bibliography in: Vicidomini, 2008).

Research infact has now produced a molecular library that consists of multiple artemisinin variants, perhaps well beyond 1000, and recently stable cycloperoxides were also isolated outside the plant kingdom (some species of sponges: Parazoa) as well as synthesized in laboratory.

Artemisinin and its derivatives are also active part of a flourishing field of research on new treatments for malaria chemotherapeutic ACT combined and / or the identification of natural remedies currently unknown, as happened with the new peroxide yingzhaosu-A, and the new antimalarial alkaloid, indolochinolin cryptolepine, isolated from *Cryptolepis* (see bibliography in: Vicidomini, 2008).

Based on the number of biological taxa successfully treatable with phyto-extracts of *Artemisia*, on the diversity of these taxa (viruses, bacteria, protists, helminths, higher animals, higher plants), on the variety and number of molecules involved and on many mechanisms of action, *Artemisia* sp. itself propose as one of the herbaceous plants not comestible of major interest and economic potentiality of the new century, well beyond the ultimate goal of the project Co.Al.Ta.

Therefore, a significant note of credit must be given to project management Co.Al.Ta. and Artemis\_projects [<http://www.ibimet.cnr.it/Staff/predieri/artemisia>] for have guessed beforehand the potential of this essence.

Similarly to the physostigmine for the carbamates, to the spinosina for the spinosoidi and quinoline-methanol derivative of quinine, the artemisinin itself propose as "molecular platform" for the coming decades, in the agro-ecological and bio-medical, also and above all by virtue of increasing activities anti-cancer exhibited by artemisinin

derivatives and the vast potential and uses as immune modulators and anti-atherosclerotic of phyto-extracts (see bibliography in: Vicidomini, 2008).

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