J Parasit Dis (Oct-Dec 2016) 40(4):1307–1310
DOI 10.1007/s12639-015-0676-y

ORIGINAL ARTICLE

In vitro and in vivo anthelmintic activity of seed extract of *Coriandrum sativum* compared to Niclosamid against *Hymenolepis nana* infection

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Received: 3 February 2015 / Accepted: 7 March 2015 / Published online: 21 March 2015

Abstract Phytotherapy can be an alternative for the control of gastrointestinal parasites in human and animals. Coriander (*Coriandrum sativum* L.) is a medicinal plant which grown as a spice crop all over the world. The seeds of this plant have been used to treat parasitic disease, indigestion, diabetes, rheumatism and pain in the joints. This study was carried out to compare the efficacy of Niclosamid and alcoholic seed extract of *C. sativum* on *Hymenolepis nana* infection, in vivo and vitro. For in vivo study, Balb/c mice were used, to compare the efficacy of 50 mg/kg body weight (B.W) of Niclosamid with different doses of alcoholic extracts of *C. sativum* (250, 500, and 750 mg/kg B.W). It was found that the efficacy of Niclosamid had reached 100 % after 11 days post treatment, while the efficacy of 500 and 750 mg/kg B.W of *C. sativum* reached to 100 % after 15 days after treatment. For in vitro study, special nutrient broth media was used. It was found that the addition of 1000 mg/ml of Niclosamid had paralyzed and killed worms within 5 min, while *C. sativum* killed them within 30 min. Our results showed that extract of *C. sativum* has good effect against *H. nana* and could be use in traditional medicine for treatment of parasitic disease.

Keywords *Coriandrum sativum* · Niclosamid · Anthelmintic activity · *Hymenolepis nana*

Introduction

Intestinal helminths are one of the most common causes of infections in humans, especially in tropical and subtropical countries. Current estimates suggest that over half's of the world population is infected with intestinal helminths and that most of these infected people live in remote rural areas in the developing countries (Hotez and Ehrenberg 2010). These diseases which are currently referred to as *Neglected Diseases of Neglected Populations*, cause enormous hazards to the health of people, particularly of children, by contributing to malnutrition, anaemia and retarded growth (Hotez and Kamath 2009).

Hymenolepiasis is a disease caused by *Hymenolepis diminuta* (rat tapeworm) and *Hymenolepis nana* (dwarf tapeworm) (Leder et al. 2013). Hymenolepiasis has a high prevalence in populations in tropical and subtropical climates characterized by poor hygiene and poverty (Alvarez-Fernandez et al. 2012; Kline et al. 2013). *H. nana*, is a cosmopolitan intestinal cestode helminthes of the warmer climates, whose entire life-cycle is completed in the bowel, so infection can persist for years if left untreated (Parvathi and Karemungikar 2011). *H. nana* is the most common cause of all cestode infections and is found globally. In temperate zones, its incidence is high in children and institutionalized groups. *H. nana* infections are typically asymptomatic, but heavy infections can cause headaches, weakness, anorexia, abdominal pain, and diarrhea (Sadaf

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et al. 2013). This worm is the only cestode capable of completing its cycle without an intermediate host. Infection is most commonly acquired from eggs in the feces of another infected individual, which are transferred by contamination in food (Malheiros et al. 2014).

Since ancient times, plants and herbal preparations have been used as medicine. Traditional system of medicine and folklore claiming that medicinal plants as a whole or their parts are being used in all types of diseases successfully including antibacterial, anthelmintic, and anti-inflammatory (Patel et al. 2011).

Coriandrum sativum L. (Apiaceae) is an erect annual herb 20–70 cm tall with strong smell and it is widespread throughout the world as a result of cultivation for its aromatic seeds. It's an annual herb in the family Apiaceae. Coriander is native to regions spanning from southern Europe and North Africa to southwestern Asia. The leaves are variable in shape, broadly lobed at the base of the plant, and slender and feathery higher on the flowering stems. The flowers are borne in small umbels, white or very pale pink, asymmetrical, with the petals pointing away from the center of the umbel longer (5–6 mm or 0.20–0.24 in long) than those pointing toward it (only 1–3 mm or 0.039–0.118 in long). The fruit is a globular, dry schizocarp 3–5 mm in diameter (Maroufi et al. 2010). Although sometimes eaten alone, the seeds are often used as a spice or an added ingredient in other foods. It is also used against stomachache. Extracts from seeds of *C. sativum* have several pharmacological effects such as anti-fertility, anti-diabetic, anti hyperlipidemic, antioxidant, and hypotensive activities (Asgarpanah and Kazemivash 2012; Sahib et al. 2013). In some countries, it is traditionally used for treatment of ascariasis and hepatitis in human (Eguale et al. 2007). Phytochemical screening indicated the presence of chemicals such as quercetin 3-glucoronide, linalool, camphor, geranyl acetate, geraniol and coumarins. The major fatty acid was petroselinic acid (65.7 % of the total fatty acid methyl esters) followed by linoleic acid (Matasyoh et al. 2009). Taniguchi et al. (1996) isolated three isocoumarins, coriandrones C–E, from whole plants of *C. sativum*. Two types of 2-C-methyl d-erythritol glycosides were also recently isolated from the seed of *C. sativum* (Sahib et al. 2013). The objective of the current study was therefore to assess the in vitro and in vivo anthelmintic potential of the seeds of *C. sativum* on *H. nana*.

Materials and methods

Mice, *C. sativum*, Niclosamid, and parasite collection

White Balb/c mice were obtained from Institute Pasteur, Tehran, Iran. They were offered diet obtained from general company for animal diet, after sterilization in autoclave at 120 °C at 15 lb/in^2 pressure (Pal et al. 1984). Niclosamid was obtained from Parsdarou, Tehran, Iran. *C. sativum* was obtained from local market in Tehran.

The eggs from adult worms were obtained from naturally infected mice, after dissecting their intestine. Experimental mice were infected with 2000 eggs/mouse by stomach tube. Egg counts were performed daily after 10–14 days post administration to ensure the infection. The eggs count was done by modified McMaster method (Levecke et al. 2011).

In vivo study

Twelve hundred male mice was used; they were divided into eight groups (24 mice in each group). Group 1, was as untreated (control), the second group was treated with 50 mg/kg B.W Niclosamid. The third, fourth and fifth groups were treated with 250, 500 and 750 mg/kg of alcoholic extract of *C. sativum*, respectively. The efficacy of Niclosamid and *C. sativum* were estimated using the method described previously (Hrckova and Velebny 2013).

In vitro study

To study the effect of Niclosamid, and alcoholic seed extract of *C. sativum*, 36 adult worms were collected from small intestine of mice which experimentally infected with *H. nana*. The worms were washed in petridishes containing physiological normal saline solution and 500 IU crystalline penicillin for 30 min to prevent bacterial contamination. The adult worms were divided into 13 groups (four worms in each group). Each group of worm was kept in sterile test tube containing 3 ml of nutrient broth (10 g pepton, 2.5 g yeast extract, 5.0 g NaCl, and 1000 ml distilled water) and antibiotics were added to prevent bacterial growth. The first group was as control without treatment. In groups 2, 3, 4, and 5 added 0.2 ml of 10, 100, 500, and 1000 µg/ml of Niclosamid, respectively. In groups 6, 7, 8 and 9 the same concentration of alcoholic extracts of *C. sativum* were added, respectively. The viability of worms was followed for 24 h using microscopically technique.

Results

Tables 1 and 2 shows the effect of treatments on the number of eggs passed in the faeces. It is shown that Niclosamid leads to decline the mean number of eggs to 28 per gram faeces from 458 eggs after 8 days after treatment with efficacy 94 % then reached to 100 % after 11 days after treatment.

Table 1 Average number (mean ± SD) of eggs passed by experimental mice treated with alcoholic seed extract of *Coriandrum sativum* and Niclosamid

Groups	Days before treatment	Days after treatment				
		3	8	11	15	21
Control (untreated group)	413.3 ± 20.3	712.6 ± 154.2	689.1 ± 186.5	716.3 ± 201.4	718.6 ± 181.4	732.8 ± 195.7
Niclosamid	534.8 ± 201.4	421.1 ± 150.4	32.1 ± 28.5	0	0	0
C. sativum (250 mg/kg B.W)	541.8 ± 174.5	482.3 ± 179.4	401.5 ± 184.3	327.2 ± 202.9	208.2 ± 185.2	162.8 ± 99.8
C. sativum (500 mg/kg B.W)	572.4 ± 212.3	512.5 ± 191.4	231.3 ± 141.9	28.4 ± 30.5	0	0
C. sativum (750 mg/kg B.W)	594.7 ± 234.1	248.9 ± 174.5	39.2 ± 31.2	4.8 ± 20.1	0	0

Table 2 Efficacy of alcoholic seed extract of *Coriandrum sativum* and Niclosamid on *H. nana* infection In vivo

Groups	Efficacy percentage in different days			
	8	11	15	21
Niclosamid	94	100	100	100
C. sativum (250 mg/kg B.W)	11.5	27.9	34.9	60.9
C. sativum (500 mg/kg B.W)	65.8	95	100	100
C. sativum (750 mg/kg B.W)	92.5	98	100	100

The effect of 250 mg/kg B.W of *C. sativum* leads to decrease in the number of eggs present per gram of faeces to 181 after 21 days post-treatment with efficacy of 60.9 %. Dose of 500 and 750 mg/kg B.W of *C. sativum* leads to complete disappearance of eggs in faeces after 15 days post-treatment with efficacy of 100 %.

ED50 for eggs passed by experimental mice was estimated. ED50 for *C. sativum* when used for 8, 11, 15, 21 days were 520, 455, 350 and 175 µg/kg B.W. The effects of treatments on the number of adult worms are shown in Table 3. According to results Niclosamid leads to disappearance of worms from the gut on day 11 post-treatment. Treatment with 250 mg/kg B.W of *C. sativum* had no effect on the adult worms. On the other hand 500 mg/kg B.W of *C. sativum* lead to disappearance of worms after 15 days, while 750 mg/kg B.W of *C. sativum* lead to disappearance of parasite after 11 days of treatment. Addition of 10, 100, 500, and 1000 µg/ml of Niclosamid lead to death of adult worms within 21, 10, 6, and 4 min, respectively. While addition of the same concentration of *C. sativum* lead to death of worms after 240, 120, 65 and 25 min, respectively (Table 4).

Discussion

Using doses of 250, 500 and 750 mg/kg B.W of *C. sativum* in this study is due to lack of references, about using the proper doses of these plant extracts. This is the first report of effect of *C. sativum* extract on helminthes parasites in our country.

The doses of *C. sativum* were repeated for 7 days, to be sure about reaching the treatment on all stages of the parasite. The treatment started 14 days post infection, due to parasites become adults and start laying eggs after 12–14 days after infection (4). The efficacy of *C. sativum* with doses of 250, 500 and 750 mg/kg B.W reached 60.9, 100, and 100 % after 21 days, respectively. This indicates

Table 3 Average number (mean ± SD) of worms in the intestine of experimental mice treated with alcoholic seed extract of *Coriandrum sativum* and Niclosamid

Groups	Days before treatment	Days after treatment				
		3	8	11	15	21
Control (untreated group)	32.5 ± 1.8	24.1 ± 2.1	24.7 ± 2.3	29.5 ± 3.9	30.1 ± 2.8	32.5 ± 2.1
Niclosamid	19.4 ± 2.7	17.1 ± 4.1	2.1 ± 3.5	0	0	0
C. sativum (250 mg/kg B.W)	24.0 ± 1.2	22.1 ± 2.1	20.1 ± 5.5	20.0 ± 2.8	17.0 ± 5.8	15.0 ± 3.6
C. sativum (500 mg/kg B.W)	24.2 ± 2.5	24.1 ± 3.8	14.3 ± 2.5	2.0 ± 3.1	0	0
C. sativum (750 mg/kg B.W)	20.1 ± 4.2	9.0 ± 3.1	2.0 ± 2.8	0	0	0

Table 4 Viability of *H. nana* adult worms in different concentrations of *C. sativum* and Niclosamid

Concentration (mg/ml)	Type of treatment		
	Niclosamid	*C. sativum*	Control
10	21 min	240 min	Over 24 h
100	10 min	120 min	–
500	6 min	65 min	–
1000	4 min	25 min	–

that doses of 500 and 750 mg/kg B.W of *C. sativum* had significant effect on the worm. The effect of *C. sativum* as anthelmintics might be due to its content of some medical component including volatile fats (5). The efficacy of Niclosamid in this study is in agreement with that reported by other workers (6, 7, 8 and 9), who showed the efficacy of Niclosamid were 100 % on immature and adult worms. According to our results, it is possible to say that plants will remain an important source to find new materials, which have great efficacy as chemically produced drugs (10). It is recommended to encourage people to use medical plants as substitute for chemical drugs because they have neither side effects nor toxicity.

In conclusion, the plant evaluated in the current study had already been reported as anthelmintic agents. Therefore, the current finding is the first step to justify their use in folk medicine. Further investigation of isolated fractions at different dose levels should be pursued. In addition, tests with animals can be performed with *C. sativum* essential oil or extract to evaluate the toxicity and to confirm their anthelmintic activity in target species.

Acknowledgments We would like to thank all the people who cooperated in this study especial researcher and worker in Institute Pasteur, Tehran, Iran.

Conflict of interest The authors have no financial or personal relationship with other people or organizations that could inappropriately influence or bias this paper.

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