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The comparative effect of ginseng and artemisia powder extract and Ivermection injection on treatment of *Spirocerca lupi* in dog

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ABSTRACT: Aims: Spirocercosis is caused by the nematode *Spirocerca lupi* in dogs. Because of side effects of Ivermectin injection, daily as most routine cheical treatment of *spirocerca lupi* in dogs such as shock like reaction and digestive signs such as stomach pain and vomting, so our aim is to replace artemisia and ginseng as herbal medicines of Iran.
Research method: 16 dogs which infected with *Spirocerca lupi* used in this experiment. They were divided in four groups of 4 members. In one group (control group), they were treated by surgical treatment and ivermectin injection, daily as 0.5 ml upto 90 days. In second group after surgical treatment they were fed diets containing 15 mg/kg body weight/day ginseng autoclaved powdered extract to assess its effect on immunological activity for 90 consecutive days. In third group after surgical treatment they were fed diets containing 15 mg/kg body weight/day artemisia autoclaved poweder extract to assess its effect on immunological activity for 90 consecutive days. In fourth group 3 drug administred.
Discussion and Conclusion: In current report, all results proved that none of dogs which treated with ginseng or artemisia had Relapses of disease and fecal examination didn't show any eggs.

***Keywords*:** *Ivermectin, Artemisia, Ginseng, Spirocercosis, dog*

INTRODUCTION

Spirocercosis caused by *Spirocerca lupi* is a disease with a variety of clinical presentations (Dvir et.al. 2001, Mazaki-Tovi et.al. 2002). It is a nematode parasite of Dogs and numerous wild *carnivores* (Fox et.al., 1998). Clinical findings are vomition, weight loss, coughing or regurgitation (Lobetti, 2000). Spirocercosis can cause death when the oesophageal nodules become malignant sarcoma, with metastasis to other places (van der Merwe et.al., 2008). And when it causes rupture of the aorta during larval migration, Spirocercosis can also cause death (Dvir et.al. 2010).
Schematic life-cycle of *Spirocercal lupi* **.** Eggs containing L1 larvae are found in the feces of the infected canid host (Feces: L1). The intermediate host, a dung beetle, consumes the feces and ingest the eggs (**A**). The eggs hatch and the larvae develop into L3 (Intermediate host: L1-L3). The intermediate host can either be consumed by paratenic hosts such as birds or small mammals (**B**), in which L3 arrest their development (paratenic host: L3), or by the definitive host (**C**) where the L3 larvae are released in the stomach, penetrate the gastric mucosa and

migrate within blood vessel walls to the caudal thoracic aortic wall, where they develop to L4. From there, larvae migrate to the caudal esophagus, where they mature and sexually reproduce (**E**, Definitive host: L3-L5). Alternatively, the definitive host preys on L3 infected paratenic hosts (**D**). Adult worms are found in the esophageal wall, surrounded by a nodule. The female worms pass their eggs to the gastrointestinal tract, and into the feces (**F**, Definitive host: L5-eggs) (figure1). The diagnosis of Spirocercosis are basis on fecal flotation, thoracic radiographs, clinical pathology information, Serology such as IFA, Imaging such as radiography and CT (Liesel et.al., 2008).

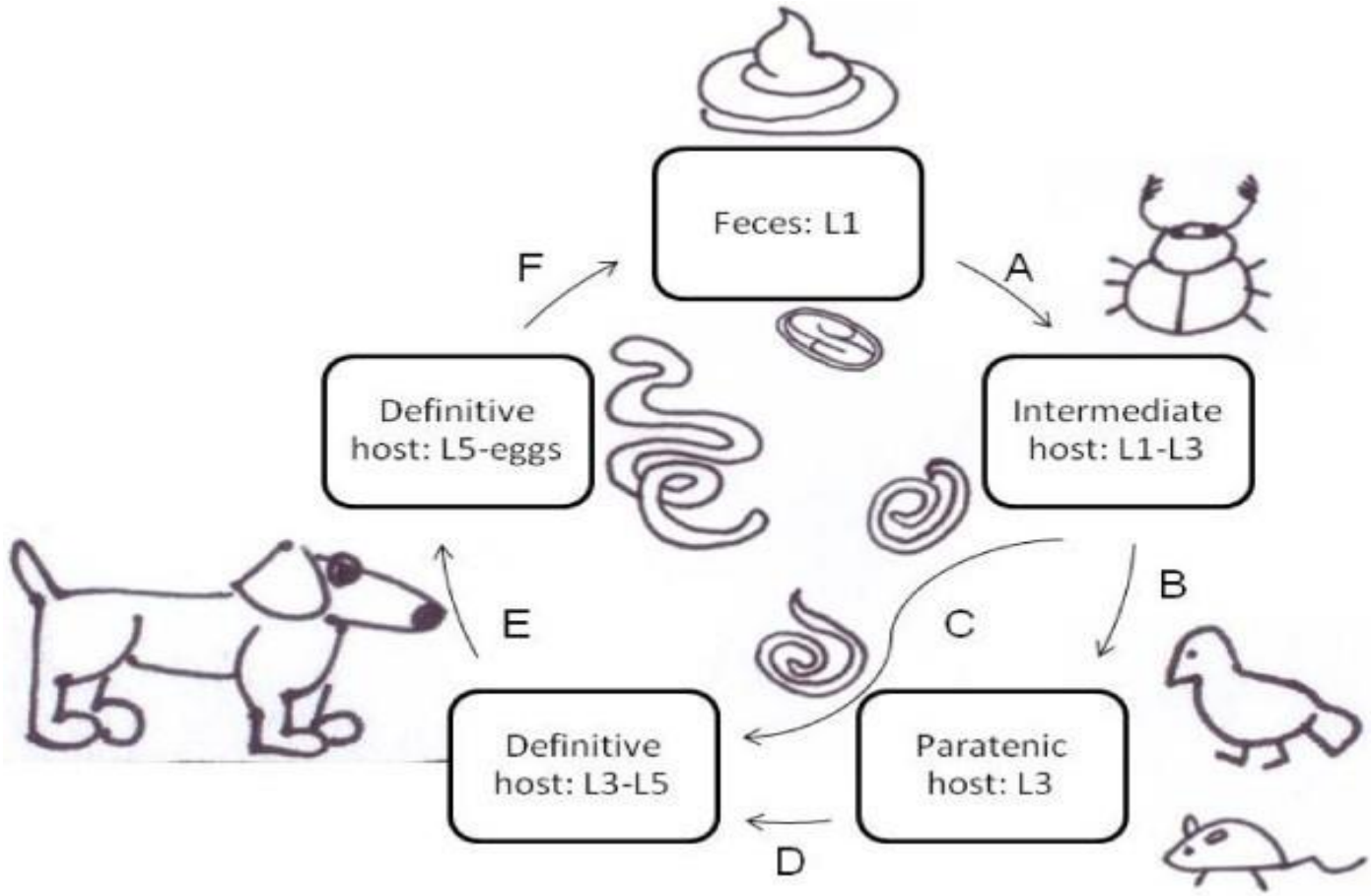

Figure 1: *Spirocerca lupi* life cycle in dogs.

Ivermectin is a commonly used anti-parasitic in animals, which is in macrolid drug group and it's also used in people to treat some parasitic diseases. Ivermectin is a semisynthetic, anthelminitic agent. It is an avermectin which a group of pentacyclic sixteen-membered lactone (i.e. a macrocyclic lactone disaccharide) derived from the soil bacterium Streptomyces avermitilis. Avermectins are potent anti-parasitic agents. Ivermectin is the most common avermectin. It is a broad spectrum antiparasitic drug for oral administration. It is sometimes used to treat human onchocerciasis (river blindness). It is the mixture of 22, 23-dihydro-avermectin B1a (at least 90%) and 22, 23-dihydro-avermectin B1b (less than 10%). Ivermectin binds selectively and with high affinity to glutamate-gated chloride ion channels in invertebrate muscle and nerve cells of the microfilaria. This binding causes an increase in the permeability of the cell membrane to chloride ions and results in hyperpolarization of the cell, leading to paralysis and death of the parasite. Ivermectin also is believed to act as an agonist of the neurotransmitter gamma-aminobutyric acid (GABA), thereby disrupting GABA-mediated central nervous system (CNS) neurosynaptic

transmission. Ivermectin may also impair normal intrauterine development of O. volvulus microfilariae and may inhibit their release from the uteri of gravid female worms. Ivermectin is metabolized in the liver, and ivermectin and/or its metabolites are excreted almost exclusively in the feces over an estimated 12 days, with less than 1% of the administered dose excreted in the urine. Its side effects in dogs are digestive signs such as: vomting, diarrhea and stomach pain (Karlgren et.al., 2012).

Panax ginseng is one of the tonic remedies of oriental medicine (Chen et.al., 1998) and it had a variety of beneficial effects (Jin et.al., 1999). It can improve immune function, psychologic function, exercise performance and modulate cardiovascular function, metabolic processes, neuro-endocrine system activities (Gillis et.al., 1997, Kiefer et.al., 2003, Liu and Xiao, 1992). For a long time, it was well known that Panax ginseng had a vasorelaxing effect in several vessels (Kim et.al., 1994, Chang et.al., 1994). Its pharmacological activity showed that it can reduce stress (Farnsworth and Bederka, 1973, Siegel, 1979). *T*here are a mixture of glycosides in the active chemical constituents of ginseng (Leung, 1980).

Artemisia is a plant of the genus Plantae of the order Asterales of the family Asteraceae under the family Asteroideae of the genus Anthemideae and the genus artemisia. In Persian, this plant is called artemisia, wormwood and rice bran. Artemisia grows in temperate climates from both hemispheres, but is more common in arid and semi-arid habitats (Watson, 2002).There are several species of artemisia, with between 200-400 worldwide and 33 species in Iran. Most of them have bitter and fragrant leaves caused by trinoids and lactone and also have more or less similar medicinal properties. So far, extensive studies have been conducted on the chemical composition of different species of artemisia. Among the species of this genus that are cultivated in different countries and have medicinal importance can be A.pontica, A. maritima, A.kurramensis, A.dracunculus, A.ciniformis, A.absinthium, A.abrotanum, A. vulgaris (Kordali, 2005), A.kulbadica (Rahimi, 2014), A.santolina, A. annua, A. turanica (Emami, 2008), A. aucheri boiss (Rostami, 2009), A. seiberi (Dalimi, 2013), A.roxburghiana (Karabegović, 2011) And A.scoparia (Afshar, 1990).

The result of these studies is the discovery of new and unique compounds in plants of this genus. In general, the chemical compounds in artemisia can be classified into monoterpenes, sesquiterpenes and especially sesquiterpene-lactones, flavonoids, phenylpropanoids, polystylenes and coumarins (Schwabe, 2005).

The present study was conducted to evaluate the effects of ginseng and artemisia on treatment of *S.Lupi* in dogs in comparison to Sc (Subcutaneou**)** injectional ivermectin.

Research method

In this research,16 dogs weighing approximately 7 kg and 2 *years old*, which infected with *Spirocerca lupi* used in this experiment. They were examined at the start of the experiment. Dogs selected after endoscopic identification of *S. lupi* .They were all have esophageal nodules or granulomas caused by *S. lupi* that were identified by endoscopic method. They were divided in four groups of 4 members. In one group (control group), they were treated by surgical treatment and ivermectin injection, daily as 0.5 ml upto 90 days. In second group after surgical treatment they were fed diets containing 15 mg/kg body weight/day ginseng autoclaved powdered extract to assess its effect on immunological activity for 90 consecutive days. In third group after surgical treatment they were fed orally diets containing 15 mg/kg body weight/day artemisia autoclaved powder extract to assess its effect on immunological activity for 90 consecutive days. In fourth group 3 drug administered, in the same time with 3 other groups. Endoscopic examinations were performed after 3 mouths. Both herbal drug powders was autoclaved in oven at 240 centigrade degree for 5 minutes before usage. Group's number 2, 3 and 4 was treatment groups in our study.

Data analysis method

In order to compare the means in different groups used to one-way analysis of variances (ANOVA) and independent t-test and to examine the relationship the variables were Spearman correlation coefficient was used. Data analyzed using SPSS 14 software and GraphPad Prism 5 used to draw graphs. In all cases, p≤0 / 05 was

considered as a significant level, but because in this research, our most aim was to show the effect of herbal drugs (ginseng and artemisia) in prevention of digestive side effects, so in findings we alone, reported the digestive signs of these 16 dogs, as a table not spss results.

Findings (Results and Discussion)

Endoscopic examinations were performed after 3 mouths. 4 dogs from control groups had relapses and the size of nodules were smaller than before, but none of dogs which treated with ginseng or artemisia alone or both of them with each other, had relapses of disease and fecal examination didn't show any eggs. It confirmed that ginseng and artemisia powdered extract can enhance immune system and prevent relapses of disease that both of them can be useful as herbal treatment. There are many investigation about using drugs as treatment of *S.lupi*. In some studies, treatment with Doramectin can resolve the eosophagal nodules (Wayne, 2000, Lavy et.al., 2002). In a study on effects of feeding Ginseng extract in Beagle dogs proved that there is no treatment-related effects seen in body-weight gain. food consumption, haematology, clinical chemistry, ophthalmology or gross and histopathological findings (Hess et.al., 2013).

In another study on effect of Korea red ginseng (KRG) on the blood pressure in conscious hypertensive rats revealed that that KRG has a hypotensive effect because of its saponin fraction of KRG in the conscious rats (Jeon et.al., 2000) and in another similar study on effect of Panax Ginseng Alcohol Extract on Cardiovascular System showed hypotensive effect of ginseng From these results it is speculated that the hypotensive effect of ginseng which inhibited myocardial contractility (Jong et.al., 1978).

In a study on effect of Ginseng Saponin in Cardiac Sarcolemma in dogs indicated that phosphorylation sites and the concentration of ouabain binding sites (Bmax) were decreased by low dose of ginseng saponin (Shin et.al., 1986).

In a survey, Panax Ginseng in combination with brewers' yeast was useful as a stimulant for geriatric dogs (Helim-Bjorkman, 2007). Despite of many studies about Ginseng extract, there is no information about its effect on improving immune system in S. lupi, so the present study was done for first time in Iran.

About artemisia treatment role in spirocercosis in dog, our research maybe is the first herbal research in the world because I can't find any article in this media to compare with our work, so I think it must be done more works about this herbal drug (artemisia) because its best results in *spirocercal lupi* as one nematode in our research in dog.

This is the first research work in this comparative herbal drugs as powder so don't have any same results but before some research has done in the world as uroupe as alone in labratory not comparative on ginseng so most research must be done for comparison. All digestive signs came as the table 1 as below.

Table 1- Comparative study of changes in digestive signs during 90 days of daily use of drugs (4 dog in each group) (In all 4 groups Spirocercosis had been treated)) (every18day, we check digestive signs)

Group 1 (Sc injectional Ivermectin)	Group 2 (Ginseng)	Group 3 (Artemisia)	Group 4 (3 drugs)
Day 1upto18 no sign	Day 1upto18 no sign	Day 1upto18 no sign	Day 1upto18 mild stomach pain
Day 19 upto 36 severe diarrhea	Day 19 upto 36 no sign	Day 19 upto 36 no sign	Day 19 upto 36 no sign
Day 37 upto 54 stomach pain	Day 37 upto 54 no sign	Day 37 upto 54 no sign	Day 37 upto 54 moderate stomach pain
Day 55 upto 72 stomach pain and diarrhea	Day 55 upto 72 no sign	Day 55 upto 72 no sign	Day 55 upto 72 mild diarrhea
Day 72 upto 90 moderate diarrhea	Day 72 upto 90 no sign	Day 72 upto 90 no sign	Day 72 upto 90 moderate diarrhea

Conclusions

In current report, both ginseng and artemisia as herbal medicines had no side effects in comparison to Sc injectional ivermectin as chemical drug, so we suggested after applying the same our research in different conditions, animals and countries, replace them in dogs and then with more researches in more species as herbal anti- spirocercosis drug because there are safe, potent and available herbal drugs.

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