



(REVIEW ARTICLE)



## Medicinal plants with scolicidal activity against *Echinococcus granulosus* protoscolices: A review

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### Abstract

The surgery is the standard treatment for hydatid cyst caused by *Echinococcus granulosus*. One of the bad sequelae of the surgery of hydatid disease is the spillage of the contents of the cyst containing protoscolices. Many scolicidal chemicals such as cetrimide, povidone iodine, hypertonic saline and silver nitrate were injected into the cyst to kill the protoscolices before cyst removal. As a result of development of resistance and side effects of chemical scolicidals, alternative drugs with minimal adverse effects are still required. Our review focused on plants with scolicidal effects, to encourage the clinical trials to determine their in vivo and clinical effectiveness, the active ingredients, the mode of action, and toxicity.

**Keywords:** Scolicidal; Protoscolices; *E. granulosus*; Hydatid disease; Plants

### 1. Introduction

*Hydatid disease caused by Echinococcus granulosus*, was the most common parasitic diseases, in animals and humans. Hydatid cysts can be occurred in different host organs which may lead to death. The benefit of protoscolicidal chemicals that they are injected into hydatid cysts prior to surgical removal of the cyst, to kill protoscolices and thus eliminating the spillage of viable protoscolices and development of secondary hydatid cysts <sup>(1)</sup>.

Different scolicidal chemicals such as cetrimide, povidone iodine, hypertonic saline and silver nitrate were used for hydatid cysts sterilization. However, the scolicidal required long exposure time to kill the protoscolices is not suitable for PAIR technique of hydatid cyst (puncture, aspiration, injection of scolicidal, reaspiration) during surgery. As a result of development of resistance and side effects of chemical scolicidals, alternative drugs with minimal adverse effects are still required <sup>(2-3)</sup>.

In this review, Scopus, Google scholar, Pub Med, Web of Science, Science Direct and EBSCO, were searched for medicinal plants with protoscolicidal effects. The current review focused on the plants with scolicidal activity, to encourage the clinical trials to determine their in vivo and clinical effectiveness, the active ingredients, the mode of action, and toxicity.

### 2. Plants with scolicidal activity

#### 2.1. *Allium sativum*

The *Allium sativum* chloroformic extract at 200 mg/ml concentration, exerted 100% protoscolicidal effect within short (2 and 5 min) exposure times <sup>(4-5)</sup>.

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The protoscolicidal activity of *Allium sativum* metanolic extract at 50 mg/ml concentration was 100% after exposure for 10 min<sup>(6-7)</sup>.

### **2.2. *Artemisia sieberi***

The protoscolicidal activity of the aqueous extract of *Artemisia sieberi* at 25 mg/ml concentration was 76 ± 1.4% (2 min exposure), 76.8 ± 1.41% (5 min exposure) and 85.7 ± 3.29% (10 min exposure) <sup>(8-9)</sup>.

### **2.3. *Atriplex halimus***

The aqueous extract from *Atriplex halimus* leaves (60 and 100 mg/ml) possessed 99.36 and 100%, scolical effect respectively<sup>(10)</sup>.

### **2.4. *Capparis spinosa***

The extract of *Capparis spinosa* at concentration of 300 and 600 mg/ml, possessed potent in vitro protoscolicidal effects, it kill all the protoscolices within 10 and 5 min, respectively<sup>(11-12)</sup>.

### **2.5. *Cinnamomum zeylanicum***

The essential oil of *Cinnamomum zeylanicum* killed 100% of protoscolices after 5 min of exposure at a concentrations of 50-100 µl/ml <sup>(13)</sup>.

### **2.6. *Citrus medica***

The aqueous extract of the *Citrus medica* fruits (90 mg/ml) killed all the protoscolices after 4 days of incubation<sup>(14-15)</sup>.

### **2.7. *Curcuma longa***

The curcumin nanoemulsion possessed 94 and 73.33% scolical activity at 1250 and 625 µg/ml concentrations after 60 min, respectively <sup>(16)</sup>.

### **2.8. *Eucalyptus globulus***

The essential oil of *Eucalyptus globulus* (0.5%) showed 100% and *Citrus medica* scolical effect within 1 and 3 min respectively<sup>(17)</sup>.

### **2.9. *Eucalyptus microtheca***

The hydroalcoholic extract (10 and 12.5 mg/ml) of *Eucalyptus microtheca* possessed 100% protoscolicidal effect. The extract also killed 99% of the protoscolices after 20 min<sup>(18-19)</sup>.

### **2.10. *Ferula asafetida***

Essential oils (0.06 mg/ml) of *Ferula asafetida* exerted 100% scolical effect within 10 min of exposure<sup>(20)</sup>.

### **2.11. *Myrtus communis***

The methanolic extract (100 and 50 mg/ml) of *Myrtus communis* showed 100% scolical effect. LC<sub>50</sub> were 11.64, 7.62, and 6.47 mg/ml, after exposure for 10, 20 and 30 min, respectively<sup>(21)</sup>.

The *Myrtus communis* extract (100 and 50 mg/ml) elevated the activity of caspases 3 and 9 and enhanced programmed cell death of protoscolices<sup>(22-23)</sup>.

### **2.12. *Nectaroscordum tripedale***

The extract of the leaves of *Nectaroscordum tripedale* at 100 mg/ml concentration killed all the protoscolices after exposure for 5 min <sup>(24)</sup>.

### **2.13. *Nicotiana tabacum***

At 100 mg/ml, the the ethanolic extract of *Nicotiana tabacum* (leaves, stems, and branches) killed 91.19 % of protoscolices after exposure for 10 min <sup>(25-26)</sup>.

#### **2.14. *Nigella sativa***

The essential oil (0.01-10 mg/ml) of *Nigella sativa* and (0.125-1.0 mg/ml) thymoquinone were tested for scolicidal effect for 5 to 60 min. 10 mg/ml essential oil and 1 mg/ml thymoquinone possessed high protoscolicidal effects after exposure for 10 min<sup>(27-28)</sup>.

The aqueous extract of *Nigella sativa* seeds (50 mg/ml, after exposure for 30 min) and the methanolic extract (50 mg/ml, after exposure for 10 min), showed 100% scolicidal effect<sup>(29)</sup>.

#### **2.15. *Olea europaea***

The leaves extract of *Olea europaea* at 300 mg/ml concentration killed all the scoleces after exposure for 10 min, and at 150 mg/ml concentration, it killed all the scoleces after exposure for 20 min. When the leaves extract of *Olea europaea* at 150 and 300 mg/ml concentrations, injected directly into the cyst, it killed all the scoleces after incubation for 12 and 25 min, respectively<sup>(30-31)</sup>.

The aqueous leave extract of *Olea europaea* at the concentration of 0.1% and 0.01% exerted high protoscolicidal activities within 120 min of exposure<sup>(32)</sup>.

#### **2.16. *Pistacia atlantica***

The hydroalcoholic extract of *Pistacia atlantica* fresh fruit extract, 0.1% mg/ml caused 99.09 ± 1.27% mortality of protoscolices, and the hydroalcoholic extract of the leaves 89.25 ± 18.42% mortality in 360 min of exposure<sup>(33)</sup>.

#### **2.17. *Prosopis farcta***

The crude alkaloids and crude ethanolic extracts of the leaves of *Prosopis farcta* showed potent scolicidal activity at 37°C<sup>0</sup>, more potency was recorded for the crude alkaloids extract in comparison with the ethanolic extract, the crude alkaloid extract showed a potent scolicidal effect with lower concentrations and shorter exposure time<sup>(34)</sup>.

#### **2.18. *Quercus infectoria***

The extract of *Quercus infectoria* caused 100% scolicidal effect after 5 min of exposure at 1000 mg/ml concentration, the mortality rate of protoscolices at 500 mg/ml concentration was 100% after 10 min incubation<sup>(35)</sup>.

#### **2.19. *Rheum ribes***

*Rheum ribes* extract possessed strong protoscolicidal effect, the mortality rate of the protoscolices reached 56.3 and 100% at the concentration of 450 and 900 mg/ml, after 10 min exposure, respectively<sup>(36)</sup>.

#### **2.20. *Rhus coriaria***

The methanolic extract of *Rhus coriaria* at 10 mg/ml concentration killed 100, 97.67 and 94.13% of protoscolices after exposure for 30, 20 and 10 min, respectively. The mortality rate reached 100 and 98.89%, after 20 and 10 min, respectively, at 30 mg/ml concentration<sup>(37)</sup>.

#### **2.21. *Sambucus ebulus***

The methanolic extract of the fruits of *Sambucus ebulus* (100, 50, 10 and 1 mg/ml) showed a high *in vitro* scolicidal effect against protoscolices aspirated from sheep hepatic hydatid cysts (P < 0.0001)<sup>(38)</sup>.

#### **2.22. *Satureja khuzestanica***

*Satureja khuzestanica* hydroalcoholic leaves extract (0.1%) possessed very high scolicidal effects in 30 min of exposure<sup>(39)</sup>.

#### **2.23. *Sideritis perfoliata***

*Sideritis perfoliata* aerial part methanol extract possessed 43.6, 32.5 and 29.6% scolicidal effects at the concentration of 50, 37.8 and 0.1% within 30 min of exposure<sup>(40)</sup>.

### 2.24. *Silybum marianum*

*Silybum marianum* alcoholic extract alone possessed 77%, while scolicidal effect, albendazole killed 69% of the protoscolices, at a concentration of 500 µg/ml for 60 min. However, the more potent scolicidal activity was obtained when the alcoholic extract of *Silybum marianum* was combined with albendazole (79%)<sup>(41)</sup>.

### 2.25. *Thymus fontanesii*

*Thymus fontanesii* essential oils (9.25 and 13.875 mg/ml) killed all the protoscolices after exposure for 5 min<sup>(42)</sup>.

### 2.26. *Xanthium strumarium*

*Xanthium strumarium* oil showed a significant scolicidal activity (79.22% mortality) at 20 mg/ml concentration, after 60 min<sup>(43)</sup>.

### 2.27. *Zataria multiflora*

*Zataria multiflora* oils exerted 100% scolicidal activity at a concentration of 0.02 mg/ml after 10 min exposure<sup>(20)</sup>.

### 2.28. *Ziziphora tenuior*

The ethanolic extract of *Ziziphora tenuior* killed all protoscolices after 20 min at 10 mg/ml concentration. However, the extract take shorter time (10 min) to kill all the protoscolices at 25 mg/ml concentration<sup>(44-45)</sup>.

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## 3. Conclusion

The current study reviewed the plant extract or chemicals with scolicidal activity, especially these characterized by high protoscolicidal effect in a short exposure time. These natural remedies can be used as alternatives to the chemical scolicidals for their efficacy and suitability for hydatid cyst PAIR technique during surgery, and because of rapid development of resistance and side effects to the chemical scolicidals.

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## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

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