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## Ascaridole: A phytochemical of modern medicinal perspective

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### ABSTRACT

American wormseed oil, also known as *Chenopodium ambrosioides* oil, is obtained from the herbs of the genus *Chenopodium* which comprises more than 200 species and belongs to the geographical region of Asia, Europe, China, India, America and other countries. *Chenopodium* has been traditionally used for digestive, respiratory, diabetes, uro-genital, nervous and vascular disorders and has anthelmintic, vermifuge, emmenagogue sedative, antipyretic, antirheumatic and abortifacient activities. Ascaridole is a bicyclic monoterpene commonly known as ascarisin or 1,4-epidioxy-p-menth-2-ene which have sedative, antifungal and pain-relieving properties. It is a potent inhibitor of *Trypanosoma cruzi*, *Plasmodium falciparum*, and *Leishmania amazonensis* and is well known for its worm-expelling potential. Ascaridole was firstly isolated by a German pharmacist in the 1900's and at that time it was one of the best anthelmintics for the treatment of ascarids and hookworms in humans and other species like cats, dogs, horses and pigs. Ascaridole could be extracted by using a non-polar solvent hexane due to its very poor solubility in water. From the literature support, it has been proved that ascaridole have very high potential in the modern and other system of medicine for the treatment of various disorders. So on the basic of its uses, here we have collected and compiled all the data regarding its medicinal uses, pharmacological activities and analytical techniques of the ascaridole in the present review and expected that this review will be beneficial for the researcher in the field of medicine and other allied science.

## 1. Introduction

*Chenopodium ambrosioides* L. (*C. ambrosioides*) is a weedy herb of the genus *Chenopodium* which comprises more than 200 species and commonly known as *Chenopodium* oil, goosefoot and American wormseed oil. *C. ambrosioides* is a natural derived drugs of Europe, Asia, India, China and America and several parts of *Chenopodium* are mainly used for different types of disorders. Seed and fruit of *C. ambrosioides* are rich sources of essential oils mainly containing ascaridole as an active phytochemical. Literature search revealed the pharmacological importance of *C. ambrosioides* which included anthelmintic, vermifuge, emmenagogue sedative, antipyretic, antirheumatic and abortifacient properties. It is used

in the respiratory, diabetes, digestive, uro-genital, nervous and vascular disorders[1]. *Chenopodium* oil is known for its anthelmintic property which is mainly because of the presence of ascaridole. Further presence of endoperoxide is essential for its anthelmintic properties. *Chenopodium* oil contains numerous phytoconstituents, i.e. ascaridole, hydrocarbons, p-cymene, terpinene, limonene, iso-ascaridole, trans-diol and cis-diol. Ascaridole produces hypothermia and decreases locomotory activity in mice but at high dose level it is lethal for animals. Effect of ascaridole against malaria was also investigated and was found to inhibit the growth of *Plasmodium falciparum* (*P. falciparum*)[2]. Ascaridole is also known as ascarisin or 1,4-epidioxy-p-menth-2-ene which is a bicyclic monoterpene. Ascaridole has sedative, antifungal and pain-relieving properties and it is also a potent inhibitor of *Trypanosoma cruzi* (*T. cruzi*), *P. falciparum*, and *Leishmania amazonensis* (*L. amazonensis*). Ascaridole is found to be active on various types of tumor cell lines, i.e. HL60 (human promyelocytic leukemia cells), CCRF-CEM (human leukemia cell lines), MDA-MB-231 (breast cancer cell line). *Melaleuca alternifolia* oil which is also known as tea tree oil showed contact allergy due to the presence of the significant amount of ascaridole[1,3].

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## 2. Biological activities of *C. ambrosioides*

*C. ambrosioides* is an herbaceous plant mainly used in traditional medicine as a condiment by different people of the world. *C. ambrosioides* belongs to Chenopodiaceae family and grows in South and Central America. *C. ambrosioides* are mainly used as a kind of anti-tumoral, anti-inflammatory, anthelmintic, vermifuge, emmenagogue, abortifacient and anti-leishmanial drug. Ascaridole is one of the most important constituents of *C. ambrosioides* which is maximum in the seeds as compared to other parts. Some other phytoconstituents are also present in *C. ambrosioides* and those are ascaridole-glycol,  $\alpha$ -pinene, myrcene, limonene, trans-pinocarveol,  $\alpha$ -terpineol aritasone and phellandrene[2,4]. Different species of *Leishmania* cause cutaneous ulcers which affect a large number of populations in the world and native people are using *Chenopodium* oil for the treatment of some disorders. *Chenopodium* oil, a potent anthelmintic, was steam distilled from *C. ambrosioides*. Ascaridole which constitutes more than 50% of the weight of the oil is mainly responsible for its anthelmintic property[2]. In another study, it has been proven that infusions of *C. ambrosioides* are safer as a vermifuge as compared to the essential oil[2]. The fruit and seed parts of *Chenopodium* contain essential oils and ascaridole is main active constituent, and further ascaridole has been attributed to its vermifuge potential[4].

## 3. Chemical components of *C. ambrosioides*

An phytochemical analysis revealed that *C. ambrosioides* contained various types of pure phytochemicals such as limonene, d-camphor, ascaridole,  $\alpha$ -pinene, p-cymene, iso-ascaridole,  $\alpha$ -terpinene, artiasone, butyric acid, ferulic-acid, geraniol, saponins and stigmasterol, etc. Among all the reported phytochemicals, the most active and effective one responsible for the pharmacological activities is ascaridole[5]. Some other active chemicals which are also present in *C. ambrosioides* are aritasone, l-pinocarvone, p-cymol, spinasterol, tartaric-acid, hydroperoxides, terpinene, hydrocarbons, vanillic-acid, menthadiene, menthadiene methylsalicylate, terpinyl-salicylate, myrcene, iso-ascaridole, trimethylamine, urease,  $\alpha$ -pinene, ascaridole, malic-acid, safrole, terpinyl-acetate, triacetyl-alcohol, trans-diol and cis-diol are derived from ascaridole[2,4].

## 4. An overview of ascaridole

Ascaridole was known for its vermifuge (worm-expelling) potential and firstly it was isolated by a German pharmacist living in Brazil in 1895. It was one of the main antihelmintics used for the treatment of ascarids and hookworms in humans, dogs, pigs, horses and cats in the early 1900's. Plants belonging to the Chenopodiaceae are distributed widely in the East Mediterranean and they are often used as drugs and spice agents because of the various useful metabolites. Plants and marine organisms are the main sources of natural peroxides and various peroxides show antimalarial, antitumor, antiviral and antibacterial activities[1]. The growth of *P.*

*falciparum* was inhibited by ascaridole *in vitro*, and cineol was found to be inactive due to the lack of internal 1,4-peroxide and artemisinin was active against *P. falciparum* due to its 1,4-endoperoxide signifying that endoperoxide was essential for its anthelmintic in ascaridole. Ascaridole decreases phasic contractions, reduces basal tone and contractions of rat gastrointestinal tissue *in vitro* induced by carbachol. Ascaridole is having unpleasant flavor and further it is shock sensitive and could be explosive[2,3]. Ascaridole have sedative, pain-relieving properties and antifungal activity because of the presence of various types of monoterpenes. In guinea pigs, topical application of the oil was found to be effective against ringworm. In some other *in vitro* studies, ascaridole was found to be active against the tropical parasite, i.e. *T. cruzi*, and showed strong antimalarial and insecticidal activities[4]. Ascaridole is a bicyclic monoterpene which is present in essential oils of different species of *Chenopodium* collected from Spain and Slovakia. Ascaridole has anthelmintic, sedative and pain-relieving properties. Ascaridole also show potent inhibitory activity against various organisms such as *P. falciparum*, *T. cruzi*, and *L. amazonensis* and active against different cancer cell lines. Ascaridole, extracted from wormseed oil, exhibited cytotoxic activity against HL60 and CCRF-CEM and MDA-MB-231. Ascaridole is also cytotoxic to human cell lines for colon cancer and leukemia, and inhibites connective tissue cancer in mice[6]. A traditional medicine known as Paico from Peru mainly contains ascaridole as a active principle and shows anthelmintic and antirheumatic potential[7]. Ascaridole is a main active constituent of boldo leaves essential oil and data show that central and northern species have higher percentages of ascaridole as compared to the southern species. Further ascaridole content was found to be less in the wild plants' leaves as compared to the cultivated plants' leaves, which revealed that the amount of ascaridole in the plant was not dependent on the genetic factors but the environmental factor[8]. Ascaridole separated from *C. ambrosioides* was found to be active against *P. falciparum*[9]. From the study, it was concluded that ascaridole is a delicate molecule and it is also sensitive to chemical attack and thermal shock[10]. Bicyclic endoperoxides such as ascaridole and dihydroascaridole have been reported to exhibit moderate antimalarial properties. A number of diaryl substituted endoperoxides was synthesized and was found to have higher activity as compared to dihydroascaridole and ascaridole[11]. Ascaridole is poor water-soluble compound and could be extracted from aqueous phase to the hexane. Ascaridole synthesised from  $\alpha$ -terpinene showed nematocidal activity and was found to be 95% pure mainly confirmed by the nuclear magnetic resonance spectroscopy[12].

## 5. Pharmacological activities of ascaridole

### 5.1. Antinociceptive and anti-inflammatory activities of ascaridole

To evaluate the compatibility of ascaridole obtained from *C. ambrosioides* molecular docking was done with the N-methyl-D-aspartate (NMDA) receptor and the results showed NMDA receptor

binding affinity. In another study, the hydro-alcoholic extract of *C. ambrosioides* was tested for osteoarthritis and it was found to be effective due to behavioral changes and reduced synovial inflammation in the pain. Furthermore, this study also revealed that this was because of the antagonistic action of ascaridole on the NMDA receptor[13]. Supercritical fluid extraction and hydrodistillation method were used for the separation of volatile oil from *Ledum palustre* (*L. palustre*) aerial parts. Then, the anti-inflammatory activities of these extracts were tested by subcutaneous carrageenan induced hind paw oedema model using ketoprofen or piroxicam as a standard drug. The results showed that different fractions of *L. palustre* essential oil significantly inhibited oedema and the results were almost similar to the standard drugs, piroxicam and ketoprofen[14].

### 5.2. Anti-leishmanial effects of ascaridole

The anti-leishmanial activity of volatile oil of *C. ambrosioides* and carvacrol, caryophyllene oxide and ascaridole were evaluated *in vivo* in BALB/c mice which were infected with *L. amazonensis*. The essential oil prevented lesion development, whereas it was found to be negative in case of pure components[15]. The anti-leishmanial activity and cytotoxicity of the volatile oil of *C. ambrosioides* and major compounds including ascaridole was evaluated. Further its effect against bacteria, fungi and protozoa were also evaluated in this study. All the tested components were found to be active against *Leishmania* with reference to amastigote and promastigote forms. Ascaridole was found to have better activity and the essential oil was found to have the highest selectivity index[16]. Effect of ascaridole with caryophyllene oxide and carvacrol isolated from *C. ambrosioides* was evaluated in BALB/c mice against *L. amazonensis*. Combination of ascaridole and carvacrol was found to be effective against promastigotes mainly due to its synergistic effect, while some activities were also observed in case of ascaridole-caryophyllene oxide but it was found to be unsympathetic. Further, mice treated with the ascaridole-carvacrol showed significant differences in lesion size and parasite burden as compared to the control group[17].

### 5.3. Anti-trypanosomal, larvicidal and nematocidal activities of ascaridole

Amebiasis is a parasitic disease in developing countries. Antiamoebic activity of the volatile oil of *Dysphania ambrosioides* (L.) was evaluated by both *In vitro* and *in vivo* method and was found to be active. Further, oral treatment of infected hamster with essential oil was also cured up to significant level. Chemical analysis signified the presence of ascaridole as a main active component[18]. Four monoterpene hydroperoxides along with ascaridole were isolated from the aerial parts of *C. ambrosioides*. Ascaridole and these monoterpene hydroperoxides were tested against epimastigotes of *T. cruzi* and were found to be effective[19]. Essential oils and isolated products of leaves of *Croton regelianus* (*C. regelianus*) growing in two different regions at Ceará State were tested against

*Meloidogyne incognita*, *Aedes aegypti* and *Artemia* sp. From the bioassay it was found that the pure component ascaridole and essential oil were found to be active against *Meloidogyne incognita*, but the effectiveness were found to be the most against both *Aedes aegypti* and *Artemia* sp. larvae[20].

### 5.4. Anticancer activity of ascaridole

Antitumor effects of ascaridole and essential oil obtained from leaves of *C. regelianus* were evaluated and were found to be active in terms of the cytotoxicity. Ascaridole showed antitumor activity in sarcoma 180 murine model which signified the ethnopharmacological use of this plant for the treatment of cancer[21]. Fifty three phytochemicals isolated from plants were tested for their differential cytotoxic effects in the cell lines which were having defect in the nucleotide excision repair genes ERCC6 or XPC, and from the result it was found that ascaridol was the most effective[22]. Effects of ascaridol isolated from a commercial preparation of *Chenopodium* oil against tumor cell lines, *i.e.* HL60, CCRF-CEM, MDA-MB-231, were investigated *in vitro*, and from the result it was found that ascaridol had an antineoplastic activity[23].

### 5.5. Effect of ascaridole on eczema

Three hundred and nineteen patients with eczema were selected for the determination of the effect of ascaridole through optimal patch test and relationship between a positive reaction to ascaridole and a positive reaction to oxidized tea tree oil were also investigated. Results showed that as concentration increases the frequency of positive reactions also increased[24].

### 5.6. Antimalarial activity of ascaridole

Effects of ascaridole on *P. falciparum* were investigated and it was found that ascaridole inhibited the growth of plasmodium after 3 days. From the result, it was also found that lower concentrations mainly affected trophozoite stage whereas the ring stage was marginally affected. Further, cineol having epoxide group instead of the peroxide group found in ascaridole was found to be inactive, which revealed that peroxide group is essential for the antimalarial activity[9].

### 5.7. Effect of ascaridole on skin sensitivity

Penetration enhancers effect of cyclic terpenes and their oxides ascaridole towards 5-fluorouracil by the use of excised human epidermal membranes was investigated. Skin data showed that terpenes had various types of activities and *Chenopodium* which contained more than 70% of ascaridole was found to be less effective as compared to the isolated terpenes[25]. Effectiveness of cell line THP-1 as compared to monocyte-derived dendritic cells was evaluated using a known potent sensitizer 2,4-dinitrochlorobenzene and the terpenoid ascaridol[26]. In another study, effects of ascaridole

on protein reactivity and dendritic cell activation were studied. From the result, it was found that maturation was accompanied by the release of proinflammatory cytokines, tumor necrosis factor- $\alpha$ , interleukin (IL)-6, IL-1 $\beta$ , and IL-8. Further radical formation may be involved in the skin sensitization[27].

### 5.8. Toxicity study of ascaridole

To investigate the mechanistic study of the toxicity of the essential oil and their pure ingredients ascaridole, carvacrol, caryophyllene oxide mammalian cells and mitochondria were used. Without Fe<sup>2+</sup>, ascaridole was found to be less toxic to mammalian mitochondria as compared to other components. Further, Fe<sup>2+</sup> potentiated the toxicity of ascaridole on oxidative phosphorylation of rat liver mitochondria and ascaridole in peritoneal macrophages from BALB/c mice exhibited more significant results in terms of toxicity as compared to the isolated mitochondria[28].

### 5.9. Effect of ascaridole as potential fumigant

For the development of the better and potential natural insecticides against cockroaches, volatile oil of Chinese *C. ambrosioides* and their main active ingredients were evaluated. From the result, it was found that the essential oil and pure components isoascaridole, (Z)-ascaridole, and  $\rho$ -cymene have fumigant toxicity against the tested cockroaches. Further, topical application bioassay also showed that these components were toxic against cockroaches and (Z)-ascaridole was found to have the strongest potential among all the tested samples[29]. In another study, crude volatile oils and active phytoconstituents (Z)-ascaridole from *C. ambrosioides* were tested against the maize weevil *Sitophilus zeamais* to get the better natural fumigant. From the result, it was found that the essential oil of *C. ambrosioides* and their main active constituent (Z)-ascaridole could be used as a natural potential fumigant[30].

## 6. Analytical aspect of ascaridole

In the present day, quality control and standardization of essential oils and its based product are demanding task in the world because of the increased trend and the improper product availability in the market. Chromatography and extraction methods including chiral chromatography were used in this study because of the stereospecificity. During the storage, there is the chance of some alteration in the chemical profile of this oil and formation of endoperoxides, peroxides, 1,2,4-trihydroxymethane, ascaridole and alterations of other components due to oxidative reactions if proper attentions have not been paid[31]. For simultaneous determination of ascaridole and other phytochemicals in rat plasma, gas chromatography-mass spectrometer (GC-MS) technique was developed and validated. By this accurate and precise method, naphthalene was used as internal standard. Ethyl acetate was used as a solvent for extraction process, whereas HP-5MS capillary analytical column and quadrupole mass spectrometer detector were used in

the adopted chromatographic method[32]. *Conyza linifolia* and *C. ambrosioides* were subjected to hydrodistillation for the separation of volatile oil and further GC-MS technique was performed for their analysis. From the results, it was concluded that essential oil of *Conyza linifolia* mainly contained sesquiterpenes ascaridole whereas *C. ambrosioides* was found to contain significant amount of monoterpenes[33]. Supercritical fluid extraction and hydrodistillation method were used for the separation of essential oil from *L. palustre* aerial parts. Further, both the samples were analysed by GC-MS technique and results showed that ascaridole and ledol were found to be present in the extracts as a chief components[14].

Phytochemical analysis of the volatile oil of *Dysphania ambrosioides* (L.) was performed to know the chemical profile and from the result it was found that it contained ascaridole as a main component[18]. Hydrodistillation process was used for the separation of volatile oils of *Cymbopogon citrates*, *Cymbopogon schoenanthus*, *Securidaca longepedunculata*, *C. ambrosioides*, *Cochlospermum tinctorium*, *Cochlospermum planchonii* and *Cymbopogon giganteus*, and further their chemical characteristics were checked by GC-MS technique. Ascaridole was found to be the major active constituent in *C. ambrosioides*[34]. Hydrodistillation method was used for the separation of essential oil from the leaves of *Curcuma longa* L. and further it was subjected to GC-MS technique to know their chemical constituents. The GC-MS analysis of oil showed the presence of 25 constituents and out of them eucalyptol was found to be the chief constituent. Ascaridole epoxide and some other phytoconstituents were also present in considerable amount[35]. Hydrodistillation method was used for the separation of the essential oils of the leaves of *Artemisia vulgaris*, *Artemisia indica* and *Artemisia dubia* and GC-MS method was used for their analysis. *Artemisia indica* oil was found to contain trans-p-mentha-2,8-dien-1-ol, ascaridole, iso-ascaridole and trans-verbenol[36]. GC-MS technique was used for the determination of the chemical composition of volatile oil of *C. ambrosioides*. Twenty-two components were found to be present in the essential oil whereas  $\rho$ -cymene, (Z)-ascaridole, iso-ascaridole and piperitone were found to be present in the significant level[29]. Hyphenated GC-MS method were used to know the chemical constituents of dichloroethane, *n*-hexane, ethyl acetate, chloroform, methanol, and 60% ethanol root extracts of *Rhodiola imbricata* Edgew. Chemical analysis of the root extracts revealed the presence of 63 phytochemicals including ascaridole as a major component[37]. GC-MS method was used for the determination of the chemical profile of the volatile oils of *C. ambrosioides*. The chemical profile showed that the major components presented in the *C. ambrosioides* were  $\rho$ -cymene,  $\alpha$ -terpinene and ascaridole[38]. Capillary gas chromatography-flame ionization detector and GC-MS techniques were used for the determination of the phytochemicals of the essential oil of *Drimys winterii* and *Peumus boldus*.  $\rho$ -Cymene, ascaridole and 1,8-cineole were found to be present in the major portion and even though more than 96%[39].

For the detection of ascaridole in the Australian tea tree oil (*Melaleuca alternifolia*), multi heart-cut multidimensional gas chromatographic system coupled with mass spectrometer and by

conventional enantio-GC were used and further method validation was also carried out for monitoring the repeatability of the traditional one-dimensional peak detection, routine application, two-dimensional peak detection, limit of detection and limit of quantification[31]. GC and GC-MS chemical profiling of the hydrodistilled volatile oil from *Tanacetum macrophyllum* and *Achillea grandifolia* Friv through Clevenger-type apparatus revealed the identification of more than 215 components. and ascaridole,  $\alpha$ -thujone, camphor, borneol and (Z)-jasmone were found to be the chief active constituents whereas borneol, 1,8-cineole, camphor, copaborneol, isobornyl acetate and  $\gamma$ -eudesmol were found to be in the *Tanacetum macrophyllum* oil[40]. Hydrodistilled volatile oil of the *C. ambrosioides* has been subjected to isolation process and analyzed by GC-MS method. Ascaridole, p-cymene and  $\alpha$ -terpinene were found to be present as chief components in the sample[41]. GC-MS technique was used for the determination of the ascaridole in leaves of medicinal plants of the genus *Chenopodium* and ascaridole was found to be present as the chief active constituent in the form of peroxy monoterpene. Further, three minor isomers cis-isoascaridole, trans-isoascaridole and trans-ascaridole were also detected[42]. GC-MS method was used for the determination of ascaridole in rat plasma using naphthalene as an internal standard. Ethyl acetate was used for the separation of the samples from plasma and further separated by GC method using HP-5MS capillary analytical column and quadrupole mass spectrometer operated in ion monitoring mode[43]. Variation of total alkaloid concentration and essential oil components of Boldo tree of southern, northern and central parts were studied. Ascaridole content of the volatile oil was found to be the highest in the north population and p-cymene was found to be the most in cases of south population[44]. GC, GC-MS and carbon-13 nuclear magnetic resonance techniques were used for the determination of the components of the commercial sample of *C. ambrosioides* of Madagascar. p-Cymene, ascaridole,  $\alpha$ -terpinene, iso-ascaridole and limonene were found to be present in significant levels in the tested samples[45].

GC and GC-MS method were used for the determination of the chemical components of the *Artemisia molinieri* aerial parts and among the 69 compounds the major components were 1,8-cineole,  $\alpha$ -terpinene, ascaridole, p-cymene and germacrene D[46]. Isolation of the main component of "Paico", another name of *C. ambrosioides*, and "Aritasou", the Japanese name of *C. ambrosioides*, was performed and ascaridole was found to be the main active principle in both samples[7]. Optical activity and chromatographic resolution of naturally occurring ascaridole and several synthetic derivatives were evaluated and the results showed that *C. ambrosioides* and *Peumus boldus* produce have ascaridole in racemic form[47]. GC-MS method was used for the determination of the essential oil composition of the *C. ambrosioides* prepared through hydrodistillation process and five active components p-cymene, 2-carene, (Z)-ascaridole, iso-ascaridole and  $\alpha$ -terpinene were found to be present in the *C. ambrosioides*[30]. In another study, ascaridole and other monoterpene hydroperoxides were isolated from *C. ambrosioides* and further the structures of these monoterpenes were determined through

spectroscopic methods and chemical correlations[19]. GC-MS and gas chromatography-flame ionization detector methods were used for the determination of the chemical composition of the leaf essential oil of *C. regelianus* collected in Brazil. Twenty monoterpenoids including p-cymene, ascaridole and camphor were identified and quantified as major active constituents[20]. Gastro-floating tablets of ascaridole were prepared and developed for prolong the gastric residence time and therapeutic efficacy. Direct compression techniques were used for the preparation of the tablets whereas content uniformity, friability, weight variation and hardness parameter were taken for their evaluation. Further, drug release behaviors, total floating time, floating lag time were also evaluated during the study[48].

## 7. Conclusion

Human being and other species need natural products for their better growth, development and reproduction. Before these era, people mainly depend on the herbal medicines for the treatment of disorders on their own believes that these herbal drugs have less side effects and more economic values. A huge number of people of different countries used traditional products for their primary health care since very long time ago. Many synthetic components which are used as medicines have been derived from plants, minerals and organic matter. The World Health Organization has listed various types of plant products and their materials as drugs due to their beneficial medicinal properties. Plants contain huge number of phytochemicals categorized into primary and secondary metabolites are mainly responsible for various pharmacological activities[49-53].

For the treatments of intestinal worm infections, *C. ambrosioides* has been used in America for long time ago and volatile portion of this drug contains significant amount of ascaridole, which has already been proven as one of the best and potent anthelmintic. Ascaridole is one of the major components of *C. ambrosioides* which is responsible for its nematocidal activity[2]. Various forms of preparation such as decoctions and infusions of various parts of the plants like inflorescences, leaves, roots of *C. ambrosioides* and related species have been used for centuries as a traditional anthelmintics and dietary condiments by native peoples against intestinal worms. Ascaridol and commercial preparations of oil of chenopodium were mainly used for the treatment of intestinal worms[54].

Due to the presence of diverse phytoconstituents, many medicinal plants have different pharmacological activities and could be used as starting materials for developing better and safer drugs of new classes. Various types of currently used drugs are derived from natural sources and people use plants as dietary supplements even without knowing their mode of action. Hence, there is a need of more investigative reports and evidence-based support along with laboratory support for their pharmacological activity and safety issue[55,56]. From all the compiled data, we can conclude that ascaridole has a huge number of potential in the field of medicine, pharmaceutical, agriculture and many more, so it could be used as a remedy for the treatment of various complications of human being

and other species in the future. The present review summarizes all the needed information regarding its general properties, the sources of this unique phytoconstituent, ancient uses, medicinal uses, pharmacological activities, analytical aspects and other scientific data. So, from all these discussions we can finally conclude that the overall compiled information written in this review paper will be beneficial to the communities of the modern medicine and related areas.

### Conflict of interest statement

I declare that I have no conflict of interest.

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### References

- [1] Dembitsky V, Shkrob I, Hanus LO. Ascaridole and related peroxides from the genus *Chenopodium*. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub* 2008; **152**(2): 209-15.
- [2] MacDonald D, VanCrey K, Harrison P, Rangachari PK, Rosenfeld J, Warren C, et al. Ascaridole-less infusions of *Chenopodium ambrosioides* contain a nematocide(s) that is(are) not toxic to mammalian smooth muscle. *J Ethnopharmacol* 2004; **92**(2-3): 215-21.
- [3] Bakker CV, Blömeke B, Coenraads PJ, Schuttelaar ML. Ascaridole, a sensitizing component of tea tree oil, patch tested at 1% and 5% in two series of patients. *Contact Dermatitis* 2011; **65**(4): 240-1.
- [4] Potawale SE, Luniya KP, Mantri RA, Mehta UK, Md.Sadiq MW, Vetal YD, et al. *Chenopodium ambrosioides*: an ethnopharmacological review. *Pharmacologyonline* 2008; **2**: 272-86.
- [5] Lohdip AM, Aguiyi JC. Some pharmacological activities of hexadec-12-enoic acid isolated from *Chenopodium ambrosioides* Linn. *Glob J Pure Appl Chem Res* 2013; **1**(2): 12-21.
- [6] Morteza-Semnani K. A review on *Chenopodium botrys* L.: traditional uses, chemical composition and biological activities. *Pharm Biomed Res* 2015; **1**(2): 1-9.
- [7] Okuyama E, Umeyama K, Saito Y, Yamazaki M, Satake M. Ascaridole as a pharmacologically active principle of "Paico," a medicinal Peruvian plant. *Chem Pharm Bull (Tokyo)* 1993; **41**(7): 1309-11.
- [8] Vogel H, Razmilic I, Acevedo P, González B. Alkaloid and essential oil concentration in different populations of *Peumus boldus*. Leuven: International Society for Horticultural Science. [Online] Available from: [http://www.lib.teiep.gr/images/stories/acta/Acta%20676/676\\_24.pdf](http://www.lib.teiep.gr/images/stories/acta/Acta%20676/676_24.pdf) [Accessed on 25th July, 2016]
- [9] Pollack Y, Segal R, Golenser J. The effect of ascaridole on the *in vitro* development of *Plasmodium falciparum*. *Parasitol Res* 1990; **76**(7): 570-2.
- [10] Alitonou GA, Sessou P, Tchobo FP, Noudogbessi J, Avlessi F, Yehouenou B, et al. Chemical composition and biological activities of essential oils of *Chenopodium ambrosioides* L. collected in two areas of Benin. *Int J Biosci* 2012; **2**(8): 58-66.
- [11] Hatzakis E, Opsenica I, Solaja BA, Stratakis M. Synthesis of novel polar derivatives of the antimalarial endoperoxides ascaridole and dihydroascaridole. *ARKIVOC* 2006; **2007**(8): 124-35.
- [12] Aubry JM, Bouttemy S. Preparative oxidation of organic compounds in microemulsions with singlet oxygen generated chemically by the sodium molybdate/hydrogen peroxide system. *J Am Chem Soc* 1997; doi: 10.1021/ja9644079.
- [13] Calado GP, Lopes AJ, Costa Junior LM, Lima Fd, Silva LA, Pereira WS, et al. *Chenopodium ambrosioides* L. reduces synovial inflammation and pain in experimental osteoarthritis. *PLoS One* 2015; **10**(11): e0141886.
- [14] Baananou S, Bagdonaite E, Marongiu B, Piras A, Porcedda S, Falconieri D, et al. Supercritical CO<sub>2</sub> extract and essential oil of aerial part of *Ledum palustre* L.--chemical composition and anti-inflammatory activity. *Nat Prod Res* 2015; **29**(11): 999-1005.
- [15] Monzote L, Pastor J, Scull R, Gille L. Antileishmanial activity of essential oil from *Chenopodium ambrosioides* and its main components against experimental cutaneous leishmaniasis in BALB/c mice. *Phytomedicine* 2014; **21**(8-9): 1048-52.
- [16] Monzote L, García M, Pastor J, Gil L, Scull R, Maes L, et al. Essential oil from *Chenopodium ambrosioides* and main components: activity against *Leishmania*, their mitochondria and other microorganisms. *Exp Parasitol* 2014; **136**: 20-6.
- [17] Pastor J, García M, Steinbauer S, Setzer WN, Scull R, Gille L, et al. Combinations of ascaridole, carvacrol, and caryophyllene oxide against *Leishmania*. *Acta Trop* 2015; **145**: 31-8.
- [18] Avila-Blanco ME, Rodríguez MG, Moreno Duque JL, Muñoz-Ortega M, Ventura-Juárez J. Amoebicidal activity of essential oil of *Dysphania ambrosioides* (L.) mosyakin & clematis in an amoebic liver abscess hamster model. *Evid Based Complement Alternat Med* 2014; **2014**: 930208.
- [19] Kiuchi F, Itano Y, Uchiyama N, Honda G, Tsubouchi A, Nakajima-Shimada J, et al. Monoterpene hydroperoxides with trypanocidal activity from *Chenopodium ambrosioides*. *J Nat Prod* 2002; **65**(4): 509-12.
- [20] Torres MC, Assunção JC, Santiago GM, Andrade-Neto M, Silveira ER, Costa-Lotuf LV, et al. Larvicidal and nematocidal activities of the leaf essential oil of *Croton regelianus*. *Chem Biodivers* 2008; **5**(12): 2724-8.
- [21] Bezerra DP, Marinho Filho JD, Alves AP, Pessoa C, de Moraes MO, Pessoa OD, et al. Antitumor activity of the essential oil from the leaves of *Croton regelianus* and its component ascaridole. *Chem Biodivers* 2009; **6**(8): 1224-31.
- [22] Abbasi R, Efferth T, Kuhmann C, Opatz T, Hao X, Popanda O, et al. The endoperoxide ascaridol shows strong differential cytotoxicity in nucleotide excision repair-deficient cells. *Toxicol Appl Pharmacol* 2012; **259**(3): 302-10.
- [23] Efferth T, Olbrich A, Sauerbrey A, Ross DD, Gebhart E, Neugebauer M. Activity of ascaridol from the anthelmintic herb *Chenopodium anthelminticum* L. against sensitive and multidrug-resistant tumor cells. *Anticancer Res* 2002; **22**(6C): 4221-4.
- [24] Christoffers WA, Blömeke B, Coenraads PJ, Schuttelaar ML. The optimal patch test concentration for ascaridole as a sensitizing component of tea tree oil. *Contact Dermatitis* 2014; **71**(3): 129-37.
- [25] Williams AC, Barry BW. Terpenes and the lipid-protein-partitioning

- theory of skin penetration enhancement. *Pharm Res* 1991; **8**(1): 17-24.
- [26] Tietze C, Blomeke B. Sensitization assays: monocyte-derived dendritic cells versus a monocytic cell line (THP-1). *J Toxicol Environ Health A* 2008; **71**(13-14): 965-8.
- [27] Krutz NL, Hennen J, Korb C, Schellenberger MT, Gerberick GF, Blömeke B. Activation of the endoperoxide ascaridole modulates its sensitizing capacity. *Toxicol Sci* 2015; **147**(2): 515-23.
- [28] Monzote L, Stamberg W, Staniek K, Gille L. Toxic effects of carvacrol, caryophyllene oxide, and ascaridole from essential oil of *Chenopodium ambrosioides* on mitochondria. *Toxicol Appl Pharmacol* 2009; **240**(3): 337-47.
- [29] Zhu WX, Zhao K, Chu SS, Liu ZL. Evaluation of essential oil and its three main active ingredients of Chinese *Chenopodium ambrosioides* (family: Chenopodiaceae) against *Blattella germanica*. *J Arthropod Borne Dis* 2012; **6**(2): 90-7.
- [30] Chu SS, Feng Hu J, Liu ZL. Composition of essential oil of Chinese *Chenopodium ambrosioides* and insecticidal activity against maize weevil, *Sitophilus zeamais*. *Pest Manag Sci* 2011; **67**(6): 714-8.
- [31] Sciarrone D, Ragonese C, Carnovale C, Piperno A, Dugo P, Dugo G, et al. Evaluation of tea tree oil quality and ascaridole: a deep study by means of chiral and multi heart-cuts multidimensional gas chromatography system coupled to mass spectrometry detection. *J Chromatogr A* 2010; **1217**(41): 6422-7.
- [32] Hu X, Chu Y, Ma G, Li W, Wang X, Mo H, et al. Simultaneous determination of ascaridole, p-cymene and  $\alpha$ -terpinene in rat plasma after oral administration of *Chenopodium ambrosioides* L. by GC-MS. *Biomed Chromatogr* 2015; **29**(11): 1682-6.
- [33] Harraz FM, Hammoda HM, El Ghazouly MG, Farag MA, El-Aswad AF, Bassam SM. Chemical composition, antimicrobial and insecticidal activities of the essential oils of *Conyza linifolia* and *Chenopodium ambrosioides*. *Nat Prod Res* 2015; **29**(9): 879-82.
- [34] Bossou AD, Mangelinckx S, Yedomonhan H, Boko PM, Akogbeto MC, De Kimpe N, et al. Chemical composition and insecticidal activity of plant essential oils from Benin against *Anopheles gambiae* (Giles). *Parasit Vectors* 2013; **6**: 337.
- [35] Parveen Z, Nawaz S, Siddique S, Shahzad K. Composition and antimicrobial activity of the essential oil from leaves of *Curcuma longa* L. Kasur variety. *Indian J Pharm Sci* 2013; **75**(1): 117-22.
- [36] Satyal P, Paudel P, Kafle A, Pokharel SK, Lamichhane B, Dosoky NS, et al. Bioactivities of volatile components from Nepalese *Artemisia* species. *Nat Prod Commun* 2012; **7**(12): 1651-8.
- [37] Tayade AB, Dhar P, Kumar J, Sharma M, Chauhan RS, Chaurasia OP, et al. Chemometric profile of root extracts of *Rhodiola imbricata* Edgew. with hyphenated gas chromatography mass spectrometric technique. *PLoS One* 2013; **8**(1): e52797.
- [38] Monzote L, Nance MR, García M, Scull R, Setzer WN. Comparative chemical, cytotoxicity and antileishmanial properties of essential oils from *Chenopodium ambrosioides*. *Nat Prod Commun* 2011; **6**(2): 281-6.
- [39] Verdeguer M, García-Rellán D, Boira H, Pérez E, Gandolfo S, Blázquez MA. Herbicidal activity of *Peumus boldus* and *Drimys winterii* essential oils from Chile. *Molecules* 2011; **16**(1): 403-11.
- [40] Radulović NS, Blagojević PD, Skropeta D, Zarubica AR, Zlatković BK, Palić RM. Misidentification of tansy, *Tanacetum macrophyllum*, as yarrow, *Achillea grandifolia*: a health risk or benefit? *Nat Prod Commun* 2010; **5**(1): 121-7.
- [41] Owolabi MS, Lajide L, Oladimeji MO, Setzer WN, Palazzo MC, Olowu RA, et al. Volatile constituents and antibacterial screening of the essential oil of *Chenopodium ambrosioides* L. growing in Nigeria. *Nat Prod Commun* 2009; **4**(7): 989-92.
- [42] Dembitsky V, Shkrob I, Hanus LO. Ascaridole and related peroxides from the genus *Chenopodium*. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub* 2008; **152**(2): 209-15.
- [43] Chu Y, Li W, Han J, Mo H, Li X, Zhou S, et al. Determination and pharmacokinetics of ascaridole in rat plasma by gas chromatography-mass spectrometry. *J Pharm Biomed Anal* 2008; **48**(3): 997-1000.
- [44] Vogel H, Razmilic I, Muñoz M, Doll U, Martin JS. Studies of genetic variation of essential oil and alkaloid content in Boldo (*Peumus boldus*). *Planta Med* 1999; **65**(1): 90-1.
- [45] Cavalli JF, Tomi F, Bernardini AF, Casanova J. Combined analysis of the essential oil of *Chenopodium ambrosioides* by GC, GC-MS and <sup>13</sup>C-NMR spectroscopy: quantitative determination of ascaridole, a heat-sensitive compound. *Phytochem Anal* 2004; **15**(5): 275-9.
- [46] Masotti V, Juteau F, Bessière JM, Viano J. Seasonal and phenological variations of the essential oil from the narrow endemic species *Artemisia molinieri* and its biological activities. *J Agric Food Chem* 2003; **51**(24): 7115-21.
- [47] Johnson MA, Croteau R. Biosynthesis of ascaridole: iodide peroxidase-catalyzed synthesis of a monoterpene endoperoxide in soluble extracts of *Chenopodium ambrosioides* fruit. *Arch Biochem Biophys* 1984; **235**(1): 254-66.
- [48] Zhao Q, Gao B, Ma L, Lian J, Deng L, Chen J. Innovative intragastric ascaridole floating tablets: development, optimization, and *in vitro-in vivo* evaluation. *Int J Pharm* 2015; **496**(2): 432-9.
- [49] Patel DK, Laloo D, Kumar R, Hemalatha S. *Pedaliium murex* Linn.: an overview of its phytopharmacological aspects. *Asian Pac J Trop Med* 2011; **4**(9): 748-55.
- [50] Patel DK, Prasad SK, Kumar R, Hemalatha S. Cataract: a major secondary complication of diabetes, its epidemiology and an overview on major medicinal plants screened for anticataract activity. *Asian Pac J Trop Dis* 2011; **1**(4): 323-9.
- [51] Patel DK, Kumar R, Prasad SK, Hemalatha S. Pharmacologically screened aphrodisiac plant-a review of current scientific literature. *Asian Pac J Trop Biomed* 2011; **1**(Suppl 1): S131-8.
- [52] Patel DK, Prasad SK, Kumar R, Hemalatha S. An overview on antidiabetic medicinal plants having insulin mimetic property. *Asian Pac J Trop Biomed* 2012; **2**(4): 320-30.
- [53] Patel K, Patel DK. Medicinal significance, pharmacological activities, and analytical aspects of ricinine: a concise report. *J Coast Life Med* 2016; **4**(8): 663-7.
- [54] Kliks MM. Studies on the traditional herbal anthelmintic *Chenopodium ambrosioides* L.: ethnopharmacological evaluation and clinical field trials. *Soc Sci Med* 1985; **21**(8): 879-86.
- [55] Patel DK, Kumar R, Laloo D, Hemalatha S. Diabetes mellitus: an overview on its pharmacological aspects and reported medicinal plants having anti-diabetic activity. *Asian Pac J Trop Biomed* 2012; **2**(5): 411-20.
- [56] Patel K, Singh RB, Patel DK. Medicinal significance, pharmacological activities, and analytical aspects of solasodine: a concise report of current scientific literature. *J Acute Dis* 2013; **2**(2): 92-8.