

Scientific justification of anthelmintic medicines based on medicinal plant material

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Abstract

Introduction: The problem of helminthiasis is particularly relevant in the recent years as this group of diseases is met in all countries of the world. Ukraine also faces the increasing number of digestive system helminthiasis, especially in children aged under 12 years. However, the existing range of anthelmintic medicines in Ukrainian pharmaceutical market is represented with derivatives of praziquantel, mebendazole, albendazole, piperazine, pyrantel, levamisole, and one herbal medicine - tansy flowers. Medicines of synthetic origin have diverse side effects (nausea, vomiting, pain in epigastria, diarrhea, allergy, dizziness, headache, etc.) and, therefore, can cause a low compliance of the patient. A good alternative to the use of synthetic medicines is phytotherapy, which is based on the centuries-old experience of folk medicine. **Materials and Methods:** As the objects of research, there were analyzed the most common prescriptions of helminthiasis phytotherapy in adults and children which are used in Ukraine, including folk anthelmintic remedies. Analysis of the possible pharmacological activity was performed with the use of power analysis and sample size (PASS)-analysis (<http://www.way2drug.com>). **Results:** Research of the existing range of phytomedicines with anthelmintic activity and the most commonly used remedies of folk medicine allowed to identify medicinal plants with high potential anthelmintic activity. **Conclusion:** The further study of their main biologically active substance with the use of PASS-analysis showed that tansy flowers, wormwood herb, wormseed flowers, elecampane rhizomes and roots, pumpkin seeds, buckthorn bark, valerian rhizomes and roots, and chamomile flowers should be considered promising medicinal plant material for development new anthelmintic medicines with narrow and broad spectrum of action with minimal toxicity.

Key words: Helminthiasis, medicinal plant material, phytotherapy, power analysis and sample size-analysis

HELMINTHIASIS IS THE WORLDWIDE HEALTHCARE PROBLEM

INTRODUCTION

It is known that the incidence of helminth infection grows worldwide and has significantly increased in Europe and the USA. Children aged from 2 to 10 years are especially vulnerable. Overall, the share of children helminthiasis of digestive system accounts for 92.3% of enterobiasis cases, 71.1% of ascariasis cases, 61.5% of trichocephalosis cases, and 66.2% of toxocariasis cases.^[1-3]

Today, the Ukrainian pharmaceutical market of anthelmintic medicines is represented with drugs based on praziquantel, mebendazole, albendazole, piperazine, pyrantel, levamisole, and one herbal remedy in the form of herbal tea - tansy flowers.

The dietary supplements, which are noteworthy, are Vormil phyto (Mili Healthcare Limited, the UK) and "Antihist" (Farmakom, Ukraine). Both supplements are of natural origin. Vormil phyto contains *Mallotus philippensis*, *Embelia ribes*, *Butea frondosa*, *Cassia fistula*, *Cyperus rotundus*, *Psoralea corylifolia*, *Apium graveolens*, *Gardenia gummifera*, *Carum carvi*, *Holarrhena antidysenterica*, *Punica granatum*, *Curcuma longa*, and *Emblia officinalis* and was designed to reduce intoxication caused by helminth invasion, general strengthening of the body, and as a source of biologically active substances of plant origin with antioxidant properties

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to support the work of the digestive organs including the intestines, bile ducts, and gallbladder. Antihist contains extracts of pumpkin seeds, garlic bulbs, sage leaves, valerian root, tansy flowers, mistletoe and is recommended for application in the complex therapy of helminthiases, allowing reduction the likelihood of complications and providing not only anthelmintic activity but also normalization of the patient's general condition.^[4,5]

PHYTOTHERAPY AS THE BASIS OF HELMINTHIASES TREATMENT

In recent years, phytotherapy, as a separate part of allopathic medicine, is actively used in the treatment of various diseases, not only as an additional method of therapy and prevention but also as an independent method of the treatment. Furthermore, medicines based on medicinal plant material provide a comprehensive effect on the body systems, act "softly" and are suitable for long-term treatment, which is especially important in the therapy of chronic diseases and those requiring long-term administration of drugs.^[6] Furthermore, phytotherapy is a priority direction of therapy in pediatrics.

The aim of our research is to find and scientifically ground the composition of anthelmintic medicines based on medicinal plant material.

The use of medicinal plants is the fundamental basis of folk medicine that covers the experience of many generations and is the basis for the creation of many medicines. Helminthiases treatment is not an exception.

Foreign experience of helminthiases treatment does not recommend using herbal remedies at any stage of therapeutic scheme, including complementary therapy. However, research on the anthelmintic action of plant extracts is carried out. For example, in the EU and the UK elfwort is recommended as anthelmintic remedy.^[7]

In Asian countries, herbal remedies, including those for helminth infestations treatment, are extensively used and studied. Chinese traditional medicine uses hundreds of different medicinal plants. Pumpkin seeds (*Cucurbita moschata* Duch) and daylily (*Hemerocallis thunbergii*) deserves special attention in helminthiases treatment, as their anthelmintic activity has been clinically proven.^[8,9] The active study of anthelmintic activity of plants takes place in India. The greatest attention is given to such plants extract as *Swietenia mahagoni*, *Acalypha indica* L., *Euphorbia hirta*, *Piliostigma thonningii*, *Butea monosperma*, *Cucurbita maxima*, *P. granatum*, *Capparis decidua*, *Capparis spinosa*, *Anacardium occidentale*, *Mimusops elengi* Bark, *Cleome icosandra*, *Zingiber officinale*, *Piper longum*, *Trachyspermum ammi*, *Acorus calamus*, *Glycyrrhiza glabra*, *Cuminum cyminum*, and *Saussurea lappa*.^[10-14]

MATERIALS AND METHODS

As the objects of research, there were analyzed the most common prescriptions of helminthiases phytotherapy in adults and children which are used in Ukraine, including folk anthelmintic remedies.^[15-19,6]

Data processing was performed using the methods of economic and statistical analysis and the results processing - with the help of computer programs. Prediction of activity of the main biologically active substances was performed with power analysis and sample size (PASS)-analysis.^[20]

RESULTS

The frequency of application of medicinal plants the most commonly used in the composition of mono- and multi-component anthelmintic medicines in Ukraine is represented in Figure 1.

As seen from Figure 1, the most frequently met medicinal plants in anthelmintic species are tansy flowers (21), wormwood herb (18), buckthorn bark (12), valerian rhizomes with roots (8), chamomile flowers (7), and pumpkin seeds (6).

Based on the results of analysis there were chosen medicinal plants that are perspective for the further creation of phytomedicines with complex anthelmintic activity [Table 1].^[7,6,19,21-24]

Results of the further PASS-analysis of the main biologically active substances (BAS) of the chosen medicinal plants are given in Table 2.^[1,6,20]

Mechanism of anthelmintic action of the main BAS^[6,7,23,25] is given in Table 3.

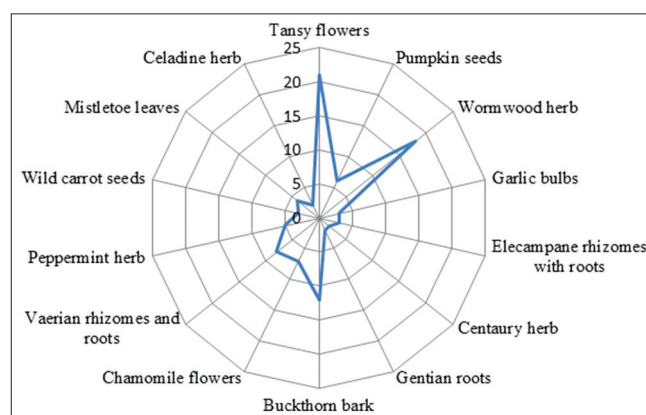


Figure 1: Medicinal plants in the composition of mono- and multi-component anthelmintic medicines in Ukraine. Medicinal plants, which occur in rare species, are not reflected in Figure 1

Table 1: Medicinal plant material with anthelmintic activity

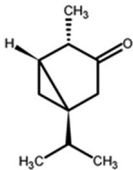
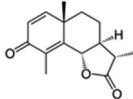
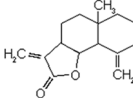
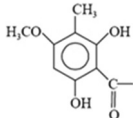
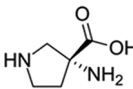
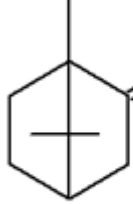
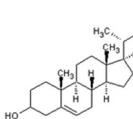
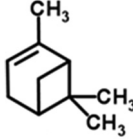
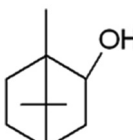
Medicinal plant material	Main biologically active substances
Tansy flowers (Flores <i>Tanacetum vulgare</i> , <i>Tanacetum vulgare</i> L., Asteraceae)	Steroids (β -sitosterol, kampesterol, cholesterol), terpenoids (α -amiryn, β -amiryn, sesquiterpene lactones), essential oils (β -thujone, camphor, α -pinene, borneol)
Wormseed flowers (Flores <i>Artemisinin</i> , <i>Artemisia cina</i> L., Asteraceae)	Santonin, essential oil (cineol, d, 1- α -pinene, terpinen, terpineol, etc.), sesquiterpene, betaine, choline
Wormwood herb (Herba <i>Artemisiae absinthii</i> , <i>Artemisia absinthium</i> L., Asteraceae)	Absynt, anabsyntyntyn, flavonoids, essential oil (β -thujone, α -pinene, etc.), volatile alkaloids, organic acids, saponins
Pumpkin seeds (Semen <i>Cucurbitae</i> , <i>Cucurbita pepo</i> L., Cucurbitaceae)	Fatty oil, kukurbityn, phytosterols (β -sitosterol, kampesterol), fatty acids (linoleic, oleic)
Garlic bulbs (Bulbus <i>Allii sativi</i> , <i>Allium sativum</i> L., Alliaceae)	Sulfur-containing substances thiosulfate (allitsyn, vinylidithiin, sulphides), essential oil
Fern rhizomes (Rhizomatis <i>Dryopteris Filicis maris</i> , <i>Dryopteris filix-mas</i> L., Dryopteridaceae (Aspidiaceae))	Floroglucides (aspidinol, baspidin) filix acid derivatives, tannins, terpenoids, higher aliphatic alcohols, higher fatty acids and their esters (recommended on liny preparations for adults and children over 12 years)
Aspen bark (Cortex <i>Populi tremulae</i> , <i>Populus tremula</i> L., Salicaceae)	Simple phenols, phenolic glycosides, benzoic acid derivatives, coumarin, derivatives of cinnamic acid and quinine, flavonoids, catechins
Elecampane rhizomes and roots (Rhizomatis <i>Cum radibus Inula helenium</i> , <i>Inula helenium</i> L., Asteraceae)	Inulin, mucus, terpenoids (β -sitosterol, stigmasterol), essential oil (alantolakton, azulene)
Ginseng rhizomes (Rhizome <i>Zingiber officinale</i> , <i>Zingiber officinale</i> , Zingiberaceae)	Tsingiberen, starch, camphene, linalool, gingerine, phellandrene, bisabolene, essential oil
Centaury herb (Herba <i>Centaurii</i> , <i>Centaurium erythraea</i> Rafn., Gentianaceae)	Xanthonen, bitter glycosides (erythaurin, eritrocentaurine), alkaloids (mainly gencian), flavonoids, triterpenoids (oleanolacid), phytosterols, essential oil
Gentian roots (<i>Radix gentianae</i> , <i>Gentiana lutea</i> L., Gentianaceae)	Alkaloids (gencyanine), bitter glycosides, secoiridoides (geniciopirin and others), flavonoids, catechins, pectin, gum, and up to 6% of fatty oil
Birch buds (<i>Gemmae betulae</i> , <i>Betula pendula</i> Roth., Betulaceae)	Essential oil, saponins, flavonoids (apigenin, izoramnetyn), tannins, resins, nicotinic acid and ascorbic acid, carotene, hyperoside
Carnation buds (<i>Gemmae Eugenii</i> , <i>Eugenia caryophyllata</i> , Myrtaceae)	Essential oil, mono- and sesquiterpenoids, flavonoids, tannins, steroids
Buckthorn bark (Cortex <i>frangulae</i> , <i>Frangula alnus</i> Mill., Rhamnaceae)	Anthraglycosides, genin (emodine, isoemodin, chrysofanol), triterpene glycosides, resinous substance
Chamomile flowers (Flores <i>Chamomillae</i> , <i>Chamomilla recutita</i> (L.) Rausch., Asteraceae)	Essential oil (chamazulene, prohamazulen and other terpenes and sesquiterpenes), flavonoids, coumarin, polysaccharides, mineral salts, carotene, ascorbic acid, sitosterol, choline, organic acids
Valerian rhizomes and roots (Rhizomata <i>Cum radibus valerianae</i> , <i>Valeriana officinalis</i> L., Valerianaceae)	Essential oil, isovaleric acid, borneol, borneol esters with acids, terpenoids (camphene, limonene, myrtenol, pinene), alkaloid aktinidin, glycoside valeryde, tannins, sugars, valepotriates

DISCUSSION

The composition of the stated medicinal plant material (tansy flowers, wormwood herb, wormseed flowers, elecampane rhizomes and roots, pumpkin seeds, buckthorn bark, valerian

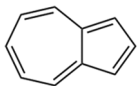
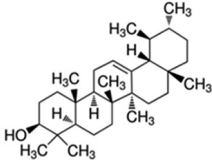
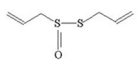
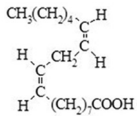
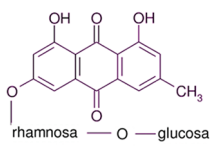
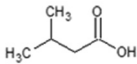
rhizomes and roots, and chamomile flowers) provides anthelmintic, antiparasitic, anti-inflammatory, antibacterial, antiseptic, hepatoprotective, nephroprotective, laxative, anti-allergic, spasmolytic, anesthetic, and sedative activity. The appropriate articles for the chosen medicinal plant material

Table 2: Prediction of BAS pharmacological activity

BAS	Structural formula	Pharmacological activity	Activity index PASS	Medicinal plant material
β -thujone		Anthelmintic, antiparasitic	0,470	Tansy flowers, wormwood herb
		Anti-inflammatory	0,902	
		Hepatoprotective	0,503	
		Nephroprotective	0,606	
Santonin		Anthelmintic, antiparasitic	0,803	Wormseed flowers
		Anti-inflammatory	0,782	
Alantolaktone		Anthelminthic, antiparasitic	0,808	Elecampane rhizomes and roots
		Anti-inflammatory	0,708	
		Antibacterial, antiseptic	0,813	
Aspidynol		Anthelminthic, antiparasitic	0,558	Fern rhizomes
		Anti-allergic	0,806	
Cucurbitin		Anthelminthic, antiparasitic	0,354	Pumpkin seeds
Camphor		Antibacterial, antiseptic	+*	Tansy flowers
		Anti-inflammatory	+	
		Spasmolytic	0,612	
β -Sitosterol		Antibacterial, antiseptic	+	Tansy flowers, pumpkin seeds, elecampane rhizomes and roots, chamomile flowers
		Hepatoprotective	0,770	
		Anti-allergic	0,774	
		Anesthetic	0,859	
α -Pinen		Spasmolytic	0,646	Tansy flowers, wormseed flowers, wormwood herb, valerian rhizomes and roots
Borneol		Antibacterial, antiseptic	+	Tansy flowers, valerian rhizomes and roots

(Contd...)

Table 2: (Continued)

BAS	Structural formula	Pharmacological activity	Activity index PASS	Medicinal plant material
Azulene		Anti-inflammatory	0,571	Elecampane rhizomes and roots
α -Amyrin		Anti-inflammatory Hepatoprotective	0,843 0,926	Tansy flowers
Allicin		Anti-inflammatory Anthelmintic, antiparasitic	0,998 +	Garlic bulbs
Linoleic acid		Anti-inflammatory	0,738	Pumpkin seeds
Anthraglycosides	 Frangulin A	Laxative	+	Buckthorn bark
Fatty oil	-	Laxative	+	Pumpkin seeds
Isovaleric acid		Nephroprotective	0,725	Valerian rhizomes and roots

BAS: Bile acid sequestrants, PASS: Power analysis and sample

Table 3: Mechanism of anthelmintic action of the main BAS

BAS	Mechanism of anthelmintic action
β -thujone	Causes paralysis of the helminths central nervous system, leading to its death (worm motility is associated with important neurotransmitter or neuromodulator). Furthermore, it causes morphological changes in tegument of parasites
Santonin	Causes changes in muscular bag (cuticle, hypodermis, and muscle cells) of helminth through the direct action on its muscle cells, which leads to a complete relaxation of muscles and loss of ability to be fixed on the walls of the intestine and then worms are evacuated with the feces masses
Alantolactone	Clear mechanism of anthelmintic action is unknown, but it is suggested that the substance adversely affects the tubular polymerization of worms, which results in the loss of cytoplasmic microtubules in parasites cells
Aspidynol	Muscle poison. It is specifically toxic to the cell protoplasm of cold-blooded muscular system, including helminths (in warm-blooded it adversely affects the central nervous system)
Cucurbitin	Changes helminth motor activity, causing first the relaxation and then contracture of muscles, followed by worms evacuation with the feces masses
Allicin	Capable to modify the thiol groups of proteins, which leads to activation or inactivation of different regulatory proteins that are responsible for the transmission of intracellular signals, intercellular contacts, and cell division

BAS: Bile acid sequestrants

are represented in State Pharmacopoeia of Ukraine and European Pharmacopoeia.^[2,10] It is also possible to choose original compositions for the treatment of nematodes, trematodes, cestodes, and for their complex therapy.

CONCLUSION

On the basis of biblio-semantic research and with the use of PASS-analysis resource it can be concluded in the theoretical and scientific substantiation of the designated medicinal plants for creation of complex anthelmintic medicines for adults with a wide range of activities.

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