Annals of Parasitology 2023, 69(3/4), 91–102
doi: 10.17420/ap6903/4.513

Review article

The use of phytotherapy in the fight against parasitic diseases

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ABSTRACT. In recent years, there has been more and more new research on the therapeutic effects of plants and their positive impact on the fight against parasitic diseases. It is of great importance, as it gives the opportunity to use this knowledge for phytotherapy, which is cheaper than pharmacological treatment, and as numerous studies have shown, it can be equally effective. Scientists are still looking for newer and newer chemicals that can be isolated from plants around us, and the current medicine is more and more willing to use natural medicines. In the following work, we present an overview of the most common parasitic diseases caused by protozoa, flatworms, roundworms, as well as by arachnids and fleas. We also presented alternative methods of treating these diseases using phytotherapy, which uses extracts of, among others, mint, tea tree, garlic, ginger, pumpkin seeds, annual mugwort, musk cosmos, walnuts, cocoa, grapes or black cumin.

Keywords: phytotherapy, medicinal plants, plant extracts, parasitic diseases

Introduction

Our world is overgrown with over 500,000 species of plants, of which only per mille has been tested for pharmacology. Therefore, many unexplored plants may be a source of valuable substances in the context of disease control in the future. Scientists are still looking for new plant species, the properties of which could contribute to the treatment of, among others, parasitic diseases, which, despite increasing living standards, are still a real threat, mainly due to the progressive resistance to antibiotics. Medicines of natural origin are cheaper to produce than those obtained synthetically, so this is another argument for scientists to work on this issue. The presented work presents an overview of the possibilities presented by plants and their extracts, in selected parasitic diseases.

Protozoans

Parasitic protozoa constitute a large group of various species with a cosmopolitan range of occurrence. With drug resistance progressing all over the world and the poverty and poverty of drugs and vaccines in some regions of the world, diseases caused by protozoa are becoming a real threat [1]. They can be transmitted in various ways, e.g. through the transfer of invasive stages by arthropods. Protozoa are also transmitted through the process of blood transfusion, organ transplantation, or can be passed on by the mother to the fetus. The infections they cause affect not only humans but also animals, which entails huge costs in terms of health protection. Modern medicine cannot cope with the progressive drug resistance of pathogenic protozoa. Therefore, more and more often, alternative methods of treatment are sought among the flora around us. Scientists are increasingly conducting research aimed at extracting and identifying substances of plant

origin that could be an effective weapon in the fight against diseases caused by parasitic protozoa.

Malaria

The biggest problem is the protozoa living in the erythrocytes. These are the parasites of the genus *Plasmodium* that cause malaria in humans. Parasites that live in the plasma of mononuclear phagocytic cells (macrophages, monocytes, Langerhans cells), neuroglial cells and muscles (heart, skeletal muscles, smooth muscles) pose a lower threat. These types of parasites include those of the genus *Trypanosoma* and *Leishmania*, which cause African coma and leishmaniosis in humans. The aforementioned malaria, despite the continuous development of medicine, remains a significant health problem throughout the entire chemistry, it was the cause of 429,000 deaths in 2015. This problem affects the most sub-Saharan Africa (70% of deaths), most often affects children under 5 years of age [2]. Every year, malaria causes 300–500 million cases of disease, killing 1.5–2.7 million people worldwide.

Malaria is a parasitic disease caused in humans by 5 species of spores: *Plasmodium falciparum*, *P. vivax*, *P. ovale*, *P. malariae*, *P. knowlesi*. Most deaths were caused by *Plasmodium falciparum*, it is the most pathogenic human parasite, it is resistant to most of the currently available antimalarial drugs. As a consequence of malaria parasites becoming resistant to drugs, research has progressed to find an alternative treatment. This way was, among others, phytotherapy, which we focus on in this article. Artemisinin therapy is recommended for the treatment of *Plasmodium falciparum* malaria, which is at least as effective as other agents used in other types of malaria. Artemisinin is obtained from the annual mugwort (*Artemisia annua* L.). It is an annual plant, blooms from June to July and can grow up to 3 meters in height. It can be classified as a ruderal plant because it occurs mainly on rubble, wastelands and roadsides. Artemisinin therapy is more effective than chloroquine therapy, which has been the main ingredient in previous anti-malaria therapies. Artemisinin eliminates parasites and fever faster, moreover, a recurrence of infection is less likely after the therapy performed with it. It has a higher recovery rate on day 28 (84.2%) than that of chloroquine, for which this rate did not exceed (60%). A better outcome in the treatment of parasitemia than in the treatment with artemisinin was reported only in the case of treatment with quinine (92%) [3]. Artemisinin therapy works well in the disease caused by *Plasmodium falciparum* and *P. vivax*, moreover, it does not cause side effects [3]. However, the effect of this therapy on diseases caused, among others, by *P. malariae*, *P. ovale*, and *P. knowlesi* are unconfirmed.

The profitability of artemisinin therapy in relation to other agents and its effectiveness against the disease caused by the above-mentioned protozoa are still open questions and hypotheses of scientists [4]. Malaria treatment is also done in a more traditional way, including with the help of extracts from plants growing, for example, in Ethiopia, 200 species belonging to 71 families were examined. The form of administration varied, the most common being oral. Tossing, eating leaves or consuming broths. Despite the promising prospects, the side effects and antimalarial potential have not been sufficiently described, and more comprehensive research is still needed to understand the full potential of these plants [2]. Plants from which extracts with antimalarial properties can be obtained should also be sought in Vietnam. From the *Rhaphidophora decursiva* grapevines growing there, an extract of leaves and stems was obtained, which showed antimalarial properties. Unfortunately, in the course of further research on the obtained compound, its cytotoxicity was discovered [5]. *Dicoma anomala* is very popular among plants with medicinal properties. It is used in many African countries to treat at least 66 diseases. In Zimbabwe, the roots of this plant are used in the treatment of syphilis and malaria, and in South Africa in respiratory diseases and diabetes. Its leaves are wide gray. They are used to treat breast cancer in Lesotho. Bioactive compounds extracted from the plant activate apoptotic pathways, the immune response and inhibit various phases of cell development, thus presenting anti-malarial and anti-cancer properties [6].

African coma

African trypanosomosis, also called African coma, is an infection caused by the parasitic protozoa of the genus *Trypanosoma* [7,8]. It is the cause of about 30,000 infections, and in 2010 caused 9,000 deaths (WHO). It is the most lethal disease in all of Sub-Saharan Africa [7]. The parasite is transmitted by the tsetse flies, which feed on the blood of mammals and are thus transmitted. They are oviparous, the female lays the developed larva and then buries it in the ground. There are about 30

species of these flies, these species are divided according to three criteria: the preferred habitat and the transmission of one of the two subspecies of the parasite *Trypanosoma brucei gambiense* or *T. b. rhodesiense* [8]. The first subspecies occurs in West and Central Africa and has a chronic course of the disease that may last for years before reaching its final stages [7]. It accounts for 95% of all cases [9]. The second subspecies, on the other hand, occurs in eastern and southern Africa, the course of the disease is much more severe, with a shorter course that can last from several weeks to several months [7]. After infection, the disease develops in two stages, the first called hemolymphatic, which irreversibly transforms into a second meningoencephalic disease, followed by death. In the first stage, we can observe headaches and joint pains, fever attacks and itching. Trypomastigota enter the host's lymphatic network and bloodstream, then multiply and attack peripheral organs. When parasites cross the blood-brain barrier, the meningoencephalic stage begins [9]. Few drugs are available to treat this disease. Drug resistance, limited effectiveness and many undesirable side effects also do not have a positive effect on the treatment process. That is why scientists turned to phytotherapy when creating new drugs. In a study carried out on mice, the effectiveness of an extract from the aerial part of the plant called *Artemisia abyssinica* L. against coma was confirmed. The extract was isolated by maceration with dichloromethane and 80% methanol at doses of 100, 200, 400 mg/kg for 7 days. The study showed that doses above 200 mg/kg of the body reduced parasites, relieved anemia, prevented weight loss, contributed to an increase in neutrophil levels and a decrease in lymphocytes [10]. *Buchholza coriacea* seeds are also effective in fighting diseases caused by trypomastigota. It is an evergreen tree with a height of 0.9 m to 1.8 m. Its ripe fruit is yellowish in color and has a spicy flavor [11]. The anti-trypomastigotic effect was also demonstrated by the water extract of eugenol basil leaves (*Ocimum gratissimum* L.) [12]. This has been confirmed in *in vitro* and *in vivo* tests. During the *in vitro* study, the life time and the mobility of parasites were inhibited, the time in which this happened differed depending on the concentration – it was longer in the lower and shorter in the higher. In contrast, during the *in vivo* study, infected rats were treated with the extract. Treated rats had less dramatic clinical signs and lived longer than untreated rats [13].

Leishmaniosis

Leishmaniosis is a tropical parasitic disease caused by protozoa of the genus *Leishmania* sp., which is the second most deadly after malaria [14]. Every year, there are approximately 300–500 million cases of malaria, which causes the death of 1.5–2.7 million people worldwide. About 12 million people suffer from leishmaniosis, and about 2 million new infections are recorded each year, and about 20–40,000 people die from the infection. Despite this, it is rarely the center of attention and therefore remains a neglected disease [15]. Leishmaniosis is endemic in over 98 countries around the world. Mainly in southern Europe, North Africa, the Middle East, Central and South America, and the Indian subcontinent. More than 90% of new infections occur in 13 countries: Afghanistan, Algeria, Bangladesh, Bolivia, Brazil, Colombia, Ethiopia, India, Iran, Peru, South Sudan, and Syria [16]. It is rather unusual in eastern Asia and Australia with Oceania [15]. It is estimated that at least 2 million people are infected with this disease annually, and over 350 million people live in endangered areas [17]. It is also responsible for approximately 20–40,000 deaths per year [18]. There are three types of leishmaniosis: cutaneous, visceral, and mucocutaneous [19,20]. The same protozoan development cycle occurs in all clinical types of leishmaniosis. Animals are the reservoir of disease [15]. The vector is female sand flies that suck the host's infected blood. In the middle intestine of the vector, amastigotes transform into promastogites, these travel to the insect's mouth apparatus, from where they are transferred to other organisms, including humans [17]. Currently, there is no pharmacotherapy that brings satisfactory results. Moreover, the availability and choice of drugs is limited by high price (most cases of the disease occur in poor areas), toxicity and side effects. In addition, it has been proven that the use of drugs and the resulting drug resistance is the cause of recurrent infections in treated patients [14]. Chemotherapy is currently the fastest and most effective treatment for leishmaniosis, but unfortunately it has many side effects and is expensive. Hence, phytotherapy offers great prospects. It is known that natural products are an important source of new drugs and structures for synthetic modification of bioactivity [21]. An example is a mixture of iridoid glycosides prepared from an alcoholic extract of the rhizome and roots of *Picrorhiza kurroa* [22]. This plant is found in the

Himalayan region from Kashmir to Sikkim at an altitude of 2,700–4,800 meters above sea level. This plant is on the verge of extinction. The extract itself is not active against leishmaniosis. However, it has a hepatoprotective effect, so when used with second-line drugs, it alleviates their side effects. Another medicinal preparation is alcoholic extracts of *Yucca filamentosa*, which showed strong anti-leishmaniosis activity. Already at a concentration of 5 mg/ml, it shows greater activity than meglumine antimonate (a first-line drug) at the same concentration. From the roots of one of the snail species (*Annona haematantha*), α, β-unsaturated d-lactone was isolated and identified as argentilactone, which shows activity against various *Leishmania* strains. In clinical trials, agentilactone was as effective as the reference medicines, reducing protozoan infection by 96%. There were also no side effects of using hexane extract of soursop [18,21]. It is estimated that over 100 plants may contain substances that could be used to fight leishmaniosis. 239 plant-derived chemicals have been identified that inhibit the development and spread of leishmaniosis. These compounds mostly belong to the classes of alkaloids, triterpenes, lactones, flavonoids or steroids [21,22].

Acanthamoebosis

Species of the genus *Acanthamoeba* spp. are the etiological factors of granulomatous encephalitis, keratitis, lung or skin infections. These amoebae are widely distributed in the free environment. Infections with this protozoan are not only a problem of developing countries, and cases of infection can be found in all latitudes. *Acanthamoeba* spp. trophozoites are resistant to most chemotherapeutic agents, such as: antibiotics, antiseptics, antifungal agents, antiprotozoals, including metronidazole. So far, cysts are most effective, but their number is small. Therefore, research continues to discover compounds (preferably natural) that could be used to fight *Acanthamoeba* spp. The greatest hopes are placed on three species of free-living plants: *Passiflora incarnata*, *Passiflora caerulea* and *Passiflora alata*. These plants are found in the areas of South America, the Netherlands, Spain, Italy and Poland. Research shows that in the leaf extract of each of the 3 species of the above-mentioned plants, over 36 substances exhibiting amoebicidal properties are present. These are mainly flavonoids (including apigenin, isovitexin, vitexin, luteolin). Studies have shown that the highest concentration of apigenin is found in *Passiflora alata* leaf extract. Concentrations of these plant extracts from 4 to 12 mg/ml show amoebostatic or amoebicidal activity. Higher concentrations, above 12 mg/ml, have an amoebicidal effect or convert trophozoites into cysts. Lower concentrations reduce the rate of amoeba multiplication [23].

Giardiosis and Entamoebosis

Giardia intestinalis and *Entamoeba histolytica* are one of the most common protozoa in humans. The disease caused by *G. intestinalis* – gardiosis, can be found all over the world, but most often in poor countries with poor sanitary conditions. In Poland, the infection rate does not exceed 4%. On the other hand, *E. histolytica* causes 50 million cases of disease a year. Control of diseases caused by protozoa is expensive and time consuming due to recontamination. Therefore, readily available plants with parasiticidal applications are sought. The research carried out on the plant *Zanthoxylum liebmannianum*, growing in Central America, showed that extracts from the leaves of this plant inhibit the multiplication of trophozoites. Chloroform extracts obtained from plants such as *Boesenbergia pandurata*, *Eclipta prostrata*, *Piper betle*, *P. chaba*, *Zingiber zerumbet* or methanol extracts from *B. pandurata* and *E. prostrata* are also suitable for the control of *G. intestinalis* and *E. histolytica*. We will meet these plants in the tropical zone. They inhibit the growth of protozoa in vitro, while in vivo they reduce the effects in HIV-infected patients.

In the *in vitro* control of *E. histolytica* and *G. intestinalis* are used water, methanol, acetone and hexane extracts from mature leaves of *Artemisia ludoviciana*, by the people inhabited North America, among others, in Mexico [24]. The introduction of chemotherapy helped to deal with a huge number of diseases, unfortunately, to this day, there are diseases that modern pharmacology is unable to deal with. Especially in developing countries, phytotherapy is becoming more and more popular due to its lower costs than traditional pharmacology. Plants are a valuable source of substances used in phytotherapy. Thanks to them, modern medicine is better and better at fighting diseases caused by drug-resistant protozoa. Plant extracts are used more and more often in pharmaceutical products, which has a positive effect on the effectiveness in combating diseases, but also reduces the price and increased availability.

Helminths

Flukes

Fasciolosis is a parasitic disease caused by flukes *Fasciola hepatica* and *F. gigantica*. In humans, infection most often occurs through the consumption of infected plants, such as cress, or with water, in which metacercariae that previously develop in the snail's body are present.

Myrrh from *Commiphora myrrha* is a substance used to treat fasciolosis. It has been tested for its antiparasitic activity against flatworms of the species *Fasciola gigantica*. It has been shown to damage the shell, making it easier to kill [25]. Another study, where myrrh was also used showed that apart from damage to the shell, displacement of the spines on the body of the parasite and disruption of the basal lamina were observed [26].

Schistosomosis is a parasitic disease caused by flukes of the genus *Schistosoma*. It is the second most common parasitosis globally, after malaria. According to statistics, it is responsible for around 280,000 deaths annually among 78 different countries in the world [27]. Symptoms may vary depending on the species of flukes causing the disease in humans. Schistosomosis mainly spreads in poor countries with a tropical climate, such as Malaysia or the countries of equatorial Africa. Its prevalence in these places is primarily due to neglect and lack of basic personal hygiene. People who settle near water reservoirs, in the absence of access to cleaning products, are most likely to become infected with this parasite, because people most often become infected when they come into contact with water in which cercariae developed previously.

The three main causative species are: *S. mansoni*, *S. haematobium*, and *S. japonicum* [28]. The drugs used in the treatment of schistosomosis have many harmful side effects or are not effective enough. For this reason, in Egypt, a study was conducted on people infected with flukes of the genus *S. mansoni* and *S. haematobium*, experimentally giving them a preparation based on an extract of myrrh oil, a fragrant resin from the tree of the species *C. myrrha*. After three months of therapy, the effectiveness of the experiment was checked on a research group of over a thousand people. The effectiveness of *S. haematobium* turned out to be slightly higher than that of *S. mansoni* carriers, but still almost 100%. The treatment did not produce any life-threatening side effects, and myrrh from *C. myrrha* has been found to be an effective and safe antiparasitic drug against the above-mentioned species of flukes [29]. In addition to the use of myrrh oil, extracts of marjoram (*Origanum majorana*), Christ's thorns (*Ziziphus spina-christi*) and shrub sage (*Salvia fructiosa*) [30] have also found their pharmacological purpose. Studies have shown that the administration of medicinal products from these plants kills all parasites after their incubation. Another study showed that aqueous extracts of the plants listed, varying in concentrations, have a degenerative effect on *S. haematobium* (i.e., reduction/lack of mobility, lifetime, degeneration of integuments), where the higher the concentration, the greater the changes. Therefore, it is safe to say that O. *majorana*, *Z. spina-christi* and *S. fruticosa* extracts have an antiparasitic effect and may someday be used in the treatment of schistosomosis [30]. Other experiments [31] on the action of black cumin oil (*Nigella sativa*) and cyanosis extract (*Chroococcus turgidus*) against flukes (*S. mansoni*). showed that these substances caused deformation of the suction cups or loss of spines, especially in male worms. This led to the fact that they could not stay on the blood vessel wall in any way, so they ended up in the bloodstream, and there they could be easily killed by the host's immune system. *Nigella sativa* oil has been shown to increase its effect when administered with an antiparasitic drug, as the percentage of dead eggs/parasites is even greater than without the drug [31]. It was also found that the *Chroococcus turgidus* extract decreased female fertility, and thus the lack of additional eggs [31]. Nobel Prize-winning substances may also be promising compounds against schistosomosis [32]. These are avermectin and artemisinin. It is true that they require many other experiments, but the preliminary analysis gives hope for the use of these compounds in the future. Studies of peppermint oil (*Mentha piperita* L.), which contains menthol and menthone, also indicate that it may be an effective substance in the treatment of schistosomosis. This is demonstrated by studies in which mice infected with the parasite were used. It was shown that the number of eggs in faeces was reduced, as was the number of adult worms. Liver histopathology showed a decrease in the number of eggs in this organ and a decrease in the number of cocci. It was emphasized that many other studies should be carried out on peppermint oil, but it is possible that in the future it could be used in the treatment of schistosomosis [33].

Tapeworms

Cestodoses are caused, among others, by *Taenia saginata*, *Taenia saginata*, *Diphyllobothrium latum* and other species. Their prevalence depends on factors such as: culinary habits in a given culture, meat storage, hygienic behavior. The most common way of spreading the parasite is contact with the infected or consumption of meat contaminated with tapeworm eggs [34]. In addition, in recent times, capsules with these eggs have become a new way to lose weight, so the dominion of this parasite is quite common.

Currently, praziquantel and nicklosamide are the most commonly used antiparasitic drugs to combat this disease [35]. Before the use of these two substances was discovered, however, people had to resort to folk medicine. To combat tapeworms, the extract from the rhizome of *Dryopteris filix-mas*, a representative of forest ferns, was used [36]. However, it is a highly poisonous plant, and the aforementioned pharmaceuticals have their disadvantages in the form of price or undesirable side effects [35]. For this reason, it was decided to look for an alternative way of treating tapeworms. Home methods of getting rid of this flatworm from the gastrointestinal tract include, among others, infusions of oregano, wormwood, black cumin seeds or buckthorn bark. In addition, scientists from Asia and Europe conducted studies on the effectiveness of treating tapeworm caused by *Taenia* spp. with pumpkin seed and areca nut extract. Their goal was to create an alternative, plant-based treatment method that would overcome the problems associated with the use of the synthetic substances mentioned above. The research showed an enormously high efficiency of the complete elimination of the parasite from the body, reaching almost 80%. This had a decisive impact on the traditional medicine routinely used in China [35].

Other plants have also found use in the treatment of tapeworm caused by other species of tapeworm. A novel method of controlling rat tapeworm *Hymenolepis diminuta* was papaya extract [36], and in the case of *Echinococcus granulosus* – an aqueous extract from an endemic plant found in Iran, i.e. *Artemisia sieberi* [37].

Ascariosis

The human roundworm (*Ascaris lumbricoides*) is a parasite found in the small intestine in approximately one quarter of the world's population, and in some regions it affects 90% of the population. Females can reach a length of 40–50 cm, while males 15–35 cm. The human roundworm has a life cycle of about 2–3 months and lay up to 200,000 eggs per day. The invasive form for humans are eggs containing larvae, which enter the gastrointestinal tract through the oral route together with thoroughly washed vegetables, fruit or water [38]. It is widespread all over the world, and especially where poverty prevails and, consequently, poor sanitation.

Africa is a zone of particularly intense endemic endemic species. Intensive infections and complications of ascariosis cause about 60,000 deaths annually in the world. Parasites cause anemia in hundreds of thousands of infected people. In the context of dealing with this type of disease, a study was carried out to assess the effectiveness of musk quinoa (*Chenopodium ambrosioides*) in the fight against intestinal parasites, including human roundworm (*A. lumbricoides*) [39]. The phyto-therapeutic treatment consisted of administering „Ka'aré" oil macerated in 70% ethyl alcohol. In the treatment assessment, the prevalence of parasites in the overall population was significantly reduced [39]. Similar applications as the musk quinoa also have calamus (*Acorus calamus*), also known under folk names as ajer and tartar herb. The range of this species includes, among others Asia and North America. In Poland, this species is common throughout the area, except for the Carpathian Mountains [40].

Enterobiosis

The human pinworm (*Enterobius vermicularis*) is a parasite of the digestive system. Counted among round worms. It occurs all over the world, especially in temperate climates. They most often colonize the large intestine, less often the appendix or the end part of the small intestine. It feeds on the sucked up intestinal content and the nutrients it contains. Enterobiosis is caused by poor personal hygiene. The most common infection occurs through the oral-fecal route (often in the form of auto-infection), and it also occurs through inhalation or by retroinvasion (internal self-infection). Mainly children are sick. At a very young age, it is caused, among other things, by the sucking habit. Eggs can be carried on unwashed hands, everyday items, bedding and underwear. Along with the dust, it happens that they end up in the upper respiratory tract. The larvae hatch from the egg after reaching the duodenum. They travel further to the large intestine where they mature within 2–4 weeks.

Then the females make their way to the area of the anus to lay about 8,000–12,000 eggs in the skin folds in sticky secretions. They do it at night, which is why sick children sleep badly due to severe itching. In women, the area around the entrance to the vagina may become infected and itching of the vulva [41]. The average life cycle of pinworms is approximately 8 weeks. The symptoms of pinworms depend on the intensity and individual sensitivity of the host. It may be asymptomatic. Many patients suffer from itching around the anus, which may result in lack of sleep. There is also abdominal pain, decreased appetite and weight loss, recurrent diarrhea, as well as problems controlling urinary incontinence and teeth grinding. Nervous ailments are manifested by excessive excitability and general fatigue.

Phytotherapeutic treatment of pinworms involves the use of herbal mixtures for parasites, which are largely based on mugwort wormwood, walnut leaves, tansy, thyme, onion (containing a high concentration of natural sulfur compounds). Some of these herbs are ingredients of preparations supporting the functioning of the digestive system in the period of pinworms. The anthelmintic properties are also attributed to oregano oil. Some of these herbs cannot be used by women during pregnancy and breastfeeding. Diet with pinworms should be rich in fiber (dietary fiber), protein. Complementary, you can use herbal teas for the intestines, such as chamomile, which soothes inflammation [42]. Garlic is also used to treat against *E. vermicularis*. This antiparasitic property of garlic is particularly important from an economic point of view as parasitic diseases often affect a poor part of the population. Garlic (*Allium* L.) removes pinworms directly from the intestines and effectively destroys pinworm eggs. It can be used both internally (eat fresh raw garlic) and externally [43]. Pumpkin seeds (*Cucurbita* L.) contain cucurbitacin in a film between the seed and the shells. It damages the nervous system of pinworms. She is called the „parasite killer". It also has antibacterial and anti-cancer effects. Its bitter taste can be dismissive. Cucurbitacin is not absorbed from the gastrointestinal tract and does not irritate the intestinal mucosa. Treatment should last 2 weeks and end with the use of laxatives [42]. Unripe walnuts (still green) contain worm-fighting substances. They are made into a tincture which contains juglone. Tincture of walnuts in alcohol has an anti-haemorrhagic effect because it tightens the mucous membranes. It also has anti-inflammatory and anti-infectious properties. Areca nut extract tablets have the same therapeutic effects as pyrantel pamoate. Areca walnut contains pyridine group alkaloids such as arekadine and arecoline. Arecolin depresses the central nervous system and paralyzes the muscles of the parasite due to binding to acetylcholine receptors [44].

Trichinellosis

Trichinella spiralis is a parasite that causes trichinellosis. Infection occurs after eating infected meat, in the case of humans, most often pig or boar meat, containing invasive larvae and not subjected to appropriate heat treatment. Trichinellosis is a serious problem on a global scale. According to estimated data, there may be as many as 10 million people infected with the *Trichinella* parasite in the world. The World Health Organization is encouraging research into medicinal plants to produce new, easy-to-use anthelmintic compounds with fewer side effects in the fight against human disease in underdeveloped countries. The wider acceptance of medicinal plants as medicinal agents is due to the pharmacological effects attributed to their phytonutrients, fewer side effects and better viability than their synthetic counterparts. The most commonly used therapeutic drug in the clinical treatment of trichinosis is a synthetic drug – benzimidazole. However, it has many disadvantages. The search for alternative natural compounds to combat the above disease is the goal of many researchers. In a 2003 study, the anthelmintic properties of the water extract from the stem bark of the *Mangifera indica* species were analyzed, with particular emphasis on the effects of *Mangifera* and the polyphenol present in those extracts administered orally with the infected *T. spiralis* nematode. Treatment with mangiferin throughout the life cycle of the parasite resulted in a significant decrease in the number of parasite larvae encapsulated in the muscles; however, no treatment has been effective for adults in the gut [45]. These results suggest that mangiferin may be useful in the treatment of trichinosis.

Arachnids and Insects

Human scabies (*Sarcoptes scabiei*) belongs, inter alia, to the parasitic arachnids. It causes a rash all over the body, especially around the genitals, buttocks, back of the hand and groin. The condition

is called scabies and, if left untreated, it can lead to serious complications such as sepsis and heart disease. Human scabies spreads intensively in poor and developing countries, where the incidence in rural areas oscillates around 8%. In turn, in Africa it reaches the level of up to 50% and this is an inherent problem of the local population. Scabies is treated symptomatically with various types of creams, ointments and emollients [46]. In addition, however, the use of this parasite has been found among many plant-derived substances. One of them turned out to be 5% tea tree oil (*Melaleuca alternifolia*). A case was described in which this substance was used with emulsifiers on a woman brought to the hospital with a diagnosis of scabies. It took effect shortly after topical application. Tea tree oil is recognized as a useful remedy [46] In addition, rosemary (*Rosmarinus officinalis*), camphor cinnamon (*Cinnamomum camphor*), or *Curcuma longa* are used to treat scabies [46]. *Demodex* sp. is one of the most common external parasites inhabiting humans. It causes demodicosis, which is a disease where the parasite attacks the hair follicles and the sebaceous glands. The use of tea tree oil (TTO) was used as a substance against *Demodex*, which attacks the eyelids of ophthalmic demodicosis patients. This treatment showed that the use of tea tree oil scrub helped to reduce and even combat demodicosis in patients suffering from it [47]. In the fight against demodicosis, drops are also used, which include plant extracts containing active ingredients such as: geraniol, eugenol, limonene [48]. In turn, plants such as aloe, yarrow herb, angelica root, willow bark and even olive oil produced from European olive are ingredients of medicines used to counteract demodicosis and have anti-inflammatory effects. Essential oils that have a lethal effect on *Demodex* sp. are raw materials obtained from mint leaves, chia seeds, lavender leaves or eucalyptus leaves [49].

Human fleas (*Pulex irritans*) are ectoparasites of the order *Siphonaptera* that live on the surface of the skin. They have a laterally flattened body, chitinous armor, reach 1–4 millimeters, and do not have wings. They come in a variety of colors from light to dark brown. Thanks to their jumping legs, they can cover a distance of up to 1 meter. They avoid light by hiding in their hair, hair or feathers. They appear on clothing and bedding. They feed on the blood of mainly birds and mammals, leaving an itchy trail resembling a mosquito bite after biting them. During the day, they can drink 20 times more than they weigh themselves. The substance that causes flea allergy dermatitis (FAD) is hapten. Bubbles or pustules that are infected by bacteria may also appear. They can be infected mainly in public, humid and neglected places. Their host can also be domestic animals, which become a source of infection for their owners. The dog flea (*Ctenocephalides canis*) spreads the flea tapeworm (*Dipylidium caninum*). Human fleas transmit numerous microorganisms, including the plague-causing *Yersinia pestis*, typhoid *Salmonella typhi*, tularemia-causing *Francisella tularensis*, and *Staphylococcus aureus*. A very large number of bites can cause anemia, especially in children. Within about 80 days from one flea, under favorable conditions, millions of fleas can develop in the form of eggs, larvae, pupae and adult insects. Depending on the species, one flea can lay 600–2000 eggs during its lifetime [50]. Fleas adversely affecting their hosts. They are bothersome and difficult to exterminate. They transmit serious diseases that can even be fatal. *Rickettsia typhi* is a typhus bacterium and is transmitted primarily by rat and cat fleas. People get infected through feces and crushed flea bodies. *Y. pestis* causing the plague was not discovered until 1894. This made it possible to understand the link between hygiene, transmission and disease. Old books mention plants that were used to protect against infection, including common juniper (*Juniperus communis*), healing angelica (*Angelica archangelica*) and saxifrage (*Pimpinella saxifraga*). To get rid of the source of the infection, focus on eliminating fleas. The prevention of bites of blood-sucking insect species relies heavily on the use of chemical repellants and pesticides. However, their effectiveness is currently under threat due to the rapidly increasing levels of resistance in target vectors. There are many examples of insect control strategies using natural products and herbal remedies. The anti-flea effect of lemon and eucalyptus oil has been observed. Fleas also do not like the smell of mint, fern leaves, rose petals and cloves, so it is worth helping them directly (e.g. by spreading them on plates around the bed) or indirectly (creating, for example, infusions). Plants vary in chemical content depending on soil nutrition, stress exposure, water availability, and many other environmental conditions. Thus, it can be dangerous to assume that all plants are the same or „natural is safe" [50]. Linalool or linalool (3,7-dimethyl-1,6-octadien-3-ol) is a compound extracted from many plants, including basil

(*Ocimum* spp.) and lavender (*Lavandula angustifolia*) [51,52]. It is distinguished by a different smell, reminiscent of the aroma of lily of the valley. This ingredient can be found in flea preparations for dogs and cats. It acts on the nervous system, interferes with ion transport and the release of acetylcholine esterase [53]. Linalool has been found to be a strong allergic ingredient. A possible rash on the skin does not manifest itself under the influence of the direct action of this substance. It is the product of its decay that has such toxic properties. Linalool hydroxide, which may irritate and cause contact rash. Insects dislike tea tree oil (*Melaleuca alternifolia*). It brings relief from mosquito and flea bites. Its combination with other essential oils is used to combat ectoparasites in pets and humans. It is enough to apply in the form of a spray. The most active ingredients of the oil are terpenes and sesquiterpenes. 1,8-cineole is another type of terpene found in tea tree oil that has been shown to be relatively effective at killing various types of parasites. Limonene, also a type of terpene, specifically kills *Ctenocephalides felis*, the most common flea species found in pets. The intense fragrance of this oil causes fleas and ticks to fall off the skin. The research proved that the plants *Tithonia diversifolia* and *Senna didymobotrya* show a strong activity against fleas. Aqueous extracts of the flowers of these plants they are very effective against fleas. Appropriately high concentration (100 mg/ml) shows efficiency oscillating around 90%. So far, the focus has been on the leaves of the tree marigold (*Tithonia diversifolia*), but flowers have now been found to be more effective. The extract does not significantly affect the blood profile. More emphasis should be placed on research into this plant, which has been shown to be both effective and safe. The essential oils of thyme and myrtle are also deterrents. The main ingredients of these oils were thymol and α-pinene, respectively. These plants show promising results and research and field trials should be continued to assess long-term dermal toxicity [54]. Fleas are carriers of human and animal diseases, so measures are needed to protect against their bites and thus prevent flea-borne diseases. Many substances of plant origin have been found to be effective in repelling and killing insects. The more important ones include, among others, linalool, terpenes and sesquiterpenes.

In summary, parasites, despite more and more knowledge about them, better methods of combating and improving sanitation, still pose a great threat to humans, and the known methods of treatment do not always bring the expected results. As a result, there is a high incidence of parasitic diseases, which were not only a medical problem, but also a social and economic one. Phytotherapy is therefore an alternative way of treating certain parasitic diseases, as we presented in the above article. It involves the search for new plant medicines and the discovery of new therapeutic applications of already known plants. Thus, the activity of „herbal pharmaceuticals" has become the subject of various studies, experiments and analyzes. Research shows that the use of phytotherapy can be as effective as the use of expensive pharmaceuticals, which is why it is used more and more often.

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Received 25 May 2023
Accepted 15 December 2023