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Advances in the Use of Nanoparticles as Anti-Cystic Echinococcosis Agents: A Review Article

Bushra Hussain Shnawa[1*]

[1]Department of Biology, Faculty of Science, Soran University, Kurdistan, Iraq.

Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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Review Article

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ABSTRACT

Echinococcus granulosus is the etiological agent of cystic echinococcosis, which is globally distributed and considered as a neglected tropical disease. It is one of the most important zoonotic parasitic infections in both humans and animals. This parasite forms hydatid cysts in various organs of numerous hosts including humans. Surgery remains the predominant therapeutic modality, but other methods also play important role in this disease management. Several scolicidal agents are used for inactivation of the protoscoleces within the hydatid cyst during surgery because spillage of hydatid fluid is the major reason for recurrence. Till now, no effective and safe agent is available. Benzimidazole is the only chemical synthetic drug licensed for the treatment of this disease. Usage of this medication is limited owing to its poor water solubility and low bioavailability, as well as its severe adverse effects. As a result, there is a constant motivation toward exploring a novel alternative to prevent the recurrence rate of the disease and to overcome the side effects of synthetic therapy. The current review focuses on the recent efforts toward obtaining better scolicidal compounds including the achievements in the frontiers of Nanomedicine technique. This review highlights the result of newer therapeutic attempts such as, the introducing of biogenic selenium, silver, gold and chitosan nanoparticles as potential agents against cystic echinococcosis in addition to the applying of Nano-carriers drug delivery system that promises to further extend the treatment options.

**Corresponding author: E-mail: Bushra.shnawa@bio.soran.edu.krd, bushra.shnawa@gmail.com;*

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1. INTRODUCTION

Cystic echinococcosis (CE) is a chronic zoonotic disease caused by the larval stage of the dog tapeworm *Echinococcus granulosus.* Many studies considered the disease as emerging or re-emerging with an increasing medical and public health concern in several countries [1,2]. Echinococcal infection was identified by the World Health Organization as a neglected tropical disease with other twelve diseases [3]. The highest number of cases is reported from rural sheep-raising regions where dogs are allowed to feed on raw animal viscera. In Iraq including Kurdistan the disease is classified as hyperendemic and one of the countries' most important parasitic infection with significant socio-economic effect, because both human and their livestock are infected [4,5]. Another researcher [6] pointed out that CE is highly prevalent in Arabic North Africa and the Middle East including Iraq. Nowadays, there are three methods for treating hydatid cysts of the liver including surgery, percutaneous aspiration and chemotherapy [7]. Surgery remains the predominant therapeutic modality, but other methods also play an important role in echinococcosis management [8]. Several scolicidal agents are used for inactivating the protoscoleces within the hydatid cyst during surgery because spillage of hydatid fluid is the major reason for recurrence [1]. All scolicidal agents have adverse effects [9]. For instance, presently hypertonic saline is used as scolicidal agent globally. Nevertheless, it can induce hypernatremia which leads to convulsions, intracranial bleeding, necrosis and myelinolysis [7,10]. Treatment of CE still depends on benzimidazole. this drug showed severe adverse effects like leucopenia, alopecia, hepatotoxicity, and thrombocytopenia [11]. Furthermore, usage of benzimidazole is mainly limited owing to its low aqueous solubility and poor bioavailability. As a result, poor gastrointestinal absorption makes it inadequate for systemic availability and decreases its efficiency against hydatidosis [12]. Therefore many attempts were done to improve the efficacy of albendazole like the trial of Shuhua et al. [13] who reformulated this drug in soybean oil emulsion and used it as therapy for CE disease in mice. On another aspect, efforts were made to discover new protoscolicidal bioactive materials from herbal sources. Kohansal et al. [14] reviewed most literature that achieved results during 1996-2015 and focused on some plant extracts that showed high efficiency against CE. In recent studies, Almalki et al. [15] and Shnawa et al. [16] investigated the scolicidal effects of *Curcuma longa*, *Zingiber officinale*, and *Cyperus rotundus* extracts respectively. Their results indicated the potential effectiveness of these plants as scolicidal agents against CE. Owing to unavailability of effective treatment strategies for CE, there is an important need for novel compounds. In this context, nanotechnology-based materials would be helpful in the management of diseases. Nanoparticles (NPs) have a wide range of applications specifically in medicine, which contributes to major advances in the progress of several techniques for increasing drug efficacy, drug delivery, decreasing toxicity of compounds and enabling programmed and sustained release of nanomaterial [17]. The present review highlights the Nanomedicine, particularly concentrating on the green biosynthesis of NPs. It also focuses on the efficacy of NPs as protoscolicidal agents through reviewing several recent published literature regarding this aspect. That may allow discovering of a new therapeutic alternative for the treatment of CE disease.

2. LIFE-CYCLE OF *E. granulosus*

The echinococcal parasite needs two mammalian hosts to complete its life cycle. The protoscolex plays a key role in the life cycle of the parasite being the only infective stage for carnivores like dogs which are known as the definitive host for it [18]. In the definitive host, the adult worms attach to the small intestinal epithelium and released eggs, shedding into an environment with faeces which represent the infective stage for humans and other appropriate intermediate hosts including sheep, cattle and other herbivores [19]. The life cycle of *E. granulosus* is shown in Fig. 1. Humans become infected through accidental ingestion of infective embryonated eggs; humans are dead-end hosts for this parasite. Eggs hatch in the intermediate host's intestinal tract and release hexacanth embryos that penetrate the intestinal wall and migrate through blood and lymphatic channels to the liver, lungs, and other organs to form unilocular hydatid cyst. The cyst structure contains pericyst, an outer layer of reactive host tissue; exocyst, a carbohydrate-rich acellular laminated layer; and the endocyst, an inner germinal layer that produces the brood

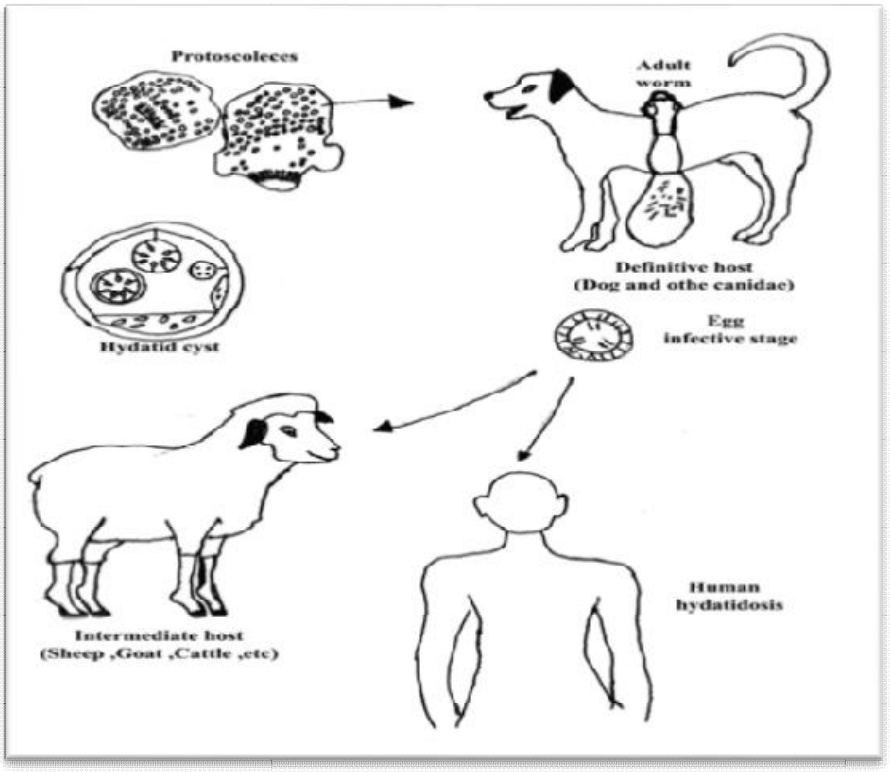

Fig. 1. Schematic representation of life cycle of *E. granulosus*

capsules or "daughter" cysts. As the cyst grows, it produces brood capsules containing protoscoleces and filled with clear fluid and may contain several daughter cysts. Parent and daughter cysts have protoscoleces, which are estimated as thousands [20,21]. When the definitive host ingests the cyst-containing organs of the infected intermediate host, the protoscoleces evaginate their scolex and attach to the intestinal wall, and develop to adult worms.

3. TREATMENT AND EXISTING ANTI-*E. granulosus* DRUGS

Management of CE should be individualised and guided by disease stage. Surgery is the primary therapeutic modality and continues to be the gold standard treatment of large complex cysts [21]. In spite of the progress in surgical technique, secondary infection due to spillage of viable protoscoleces during the intervention may occur. Prevalence of recurrence was recorded in 2-25% of cases [22]. Also, anaphylactic reaction represents a further risk, therefore protoscolicidal agents are often applied, owing to the risk of spillage of cyst fluid [23]. Later new technique was introduced, Puncture, Aspiration, Injection, and Re-aspiration (PAIR). This method includes percutaneous puncture of the cyst under ultrasonic guidance, aspiration of substantial amounts of cyst fluid, injection of scolicidal substance (eg.95% ethanol) and re-aspiration of fluid after 5-20 min [24]. This technique targeted the germinal cyst layer, minimising cyst size, and finally collapsing and solidifying the cyst [21].

Chemotherapeutic of CE has been developed in several animal models studies, both albendazole and mebendazole are considered to have identical efficiency [19] with mild adverse effects. Treatment of CE routinely depend on surgery and/or chemotherapy, according to various factors such as cyst size and location, viability, microbial infection, and potentially dangerous complications related to cyst rupture [25,26]. Surgery has limitations such as recurrence of cysts and contraindications in cases of inactive symptomless cysts, difficult to contact cysts, and the too small cysts [27]. Drugs classically used against CE with its adverse effect are summarised in Table 1.

Table 1. Anti-echinococcal drugs and scolicidal agents with associated limitations

Drugs	Adverse effects	Reference
Benzimidazoles	Hepatotoxicity, leukopenia, and thrombocytopenia. contraindicated in pregnancy(teratogenic)	[21]
	20-40% of cases failed to respond favourably	[1]
Albendazole	Liver function abnormalities in 20%.	[29]
	Raised transaminases.	[30]
	Teratogenicity has been reported when albendozole is administered to laboratory animals in early gestation	[31]
	Hematuria, leukopenia, teratogenic in rats, and not recommended for pregnant women.	[32]
	May induce embryo-toxic and teratogenic in animal experimentation. Should be avoided during pregnancy and lactation. It is slow.	[24], [35]
		[34]
Mebendazole and albendazole	20-40% of hydatidosis don't respond to treatment.	[33]
	High cost, lifelong consumption, Parasitostatic rather than parasiticidal, high recurrence.	
	Hepatotoxicity, severe leukopenia, thrombocytopenia, and alopecia.	[36]; [24]
	Neutropenia, liver toxicity, alopecia. Contraindications in pregnancy, chronic hepatic disease, and bone marrow depression.	[11]
		[1]
	Raised transaminases, abdominal pain, headache, vertigo, urticaria, and jaundice.	[28]
Formalin	Toxic	[37]
Ethyl alcohol	Cause damage in the epithelium of bile ducts leading to sclerosing cholangitis	[38]
	Deleterious effect on hepatopancreatic biliary system	[39]
Hydrogen peroxide	low efficacy and with complications	[40]
Hypertonic saline	Hypertonic saline can cause acute hypernatremia.	[7]
	Iatrogenic acute hypernatremia (200 mmol/L) which exposed the patient to neurological damage or death	[41],[10]

4. NANO-MEDICINE

Nanotechnology is a combination of dual words; nano and technology. Nano created from Greek word 'nanos' that means 'dwarf' and mentions to one billionth part 10^{-9}. American Society for Testing and Materials well-defined 'nanoparticles' as particles having at least coupled or more dimensions with a size of 1 to 100 nm [42].

There are two alternative approaches for the synthesis of metallic nanoparticles: the "bottom-up" approach and the "top-down" one [43]. These methods make nanoparticles diverse from their original ones either in surface related properties or quantum characters [44]. Recently, nanotechnology has emerged as a promising field due to the application in different branches of science [45]. Metal nanoparticles including silver and gold nanoparticles (AgNPs & AuNPs) are being tested for many diseases as medicinal agents [46]. Some disadvantages of these NPs are being expensive and are harmful to the biological system. So, biological approaches such as using microorganisms [47] and enzymes [48] are suggested as probable eco-friendly options for the synthesis. The advantages of the current Nanomedicine includes high

bioavailability and stability, different routes of administration, targeted delivery, organised release, and low toxicity, whereas the disadvantages are safety and ethical concerns, and cost efficiency [49]. Reddy and Couvreur mentioned that Nanomedicines are usually using phospholipids (i.e. liposomes), polymers (i.e. NPs or micelles), or iron resources (i.e. small iron oxide NPs) in their review about nanotechnology and liver diseases [50]. In the previous study, Alving et al. used liposomes for improving the efficacy of drugs in experimentally infected hamsters with *Leishmania donovani* [51]. Nano-biotechnology is a branch of nanotechnology that enables creating NPs for specific applications with less dangerous impacts from biological materials. So, Nano-biotechnology is a general term that covers the synthesis and consequent utilisation of tiny particles less than 100 nm in size [52]. There are numerous biological resources in nature like plants, algae, fungi, yeast, bacteria, and viruses that could all be depend used for the synthesis of NPs. Recently, scientists tried to use microorganisms as possible eco-friendly resources for the synthesis of metallic NPs, such as cadmium, gold sulfide, and silver [52,53]. Green technology is followed nowadays; that makes use of plants and their extracts for producing the NPs 54]. For instance, the ability of black tea leaf extracts to produce Au and Ag NPs, this ability related to biomolecules which identified as tea polyphenols [54]. Moreover, AuNPs synthesised by plants are found to be more stable than those produced through other ways. Phytochemicals present in the plants contain active compounds such as terpenes, polyphenols and functional groups like carboxyl, hydroxyl and aldehydes that have the ability of reduction of gold salt HAuCl4 to AuNPs [55]. Their finding confirmed the capability of non-toxic cinnamon -Au NPs as a signal for diagnosing cancerous cells, which may be clinically beneficial as a new diagnostic tool [55].

Many researchers pointed out that microorganisms can be essential Nano-factories. Microorganisms have the capability to gather and detoxify heavy metals owing to different reductase enzymes, which are capable to reduce metal salts to metal NPs [56]. During the past few years, bacteria, Actinomycetes, filamentous fungi, and yeasts, were investigated for the production of metal NPs [56]. The bacterial enzymes or the plant phytochemicals with anti-oxidant or reducing features are accountable for the reduction of metal compounds into their corresponding NPs [57]. The NPs are attractive for medical applications because of their significant and unique characters such as surface to mass ratio that is much larger than that of other particles, their quantum features and their capabilities to adsorb and carry other materials such as drugs, probes and protein. Metal NPs had specific attention owing to their wide application in catalysis, electronics, biosensing, photonics, cosmetics, environmental cleanup, photo- imaging, and drug delivery [56,58,59]. Recently, studies are focusing on the development of most efficient and eco-friendly green chemistry for the production of metal NPs. Green synthesis of metal NPs has several advantages, for instance, it is very simple, clean, effective, safe and economically cheap as they use bio-resources (plants, fungi, algae, and microorganism) that can act as reducing and stabilising agents [60-62]. Nowadays, NPs of some metals or metal oxides are widely used as a medication to treat various diseases and improve human health owing to their antimicrobial activity; these NPs showed antibacterial, antiviral and anti-parasitic efficiencies [63,64]. Nanotechnology represents beneficial drug delivery systems to improve the pharmacokinetic action of the medication. In this context, researchers have been achieving studies to develop new drugs to ensure safety and efficacy against the parasite. Several drug delivery systems were used including Nano-emulsions, liposomes and NPs against *Schistosoma spp.* with promising results [65].

In recent years, metal NPs particularly AuNPs and AgNPs are frequently used as medicinal agents for therapeutic applications of numerous diseases such as cancer, diabetes, Parkinson's, Alzheimer's, HIV/AIDS, arthritis, hepatitis, cirrhosis, spinal cord injury, tuberculosis and cardiovascular diseases as a result of its optoelectronic and physicochemical properties [46,66]. Also, Aly et al. found that silica coated NPs with polyclonal antibody increased the sensitivity and specificity of Nano-sandwich ELISA for detection *Toxoplasma gondii* antigens in serum and urine due to their high surface to volume ratios and crystallographic surface building [67].

5. SCOLICIDAL EFFECTS OF NANO-PARTICLES

At present, several studies investigated the scolicidal effects of biogenic NPs against

protoscoleces of *E. granulosus* within in vitro model. Among them the study of Mohmoud et al. who studied for the first time the scolicidal activity of biogenic selenium nanoparticles (Se NPs) which was synthesized by *Bacillus* sp.MSh-1 against protoscoleces [68]. Their finding showed that Se NPs have a potent scolicidal effect at 500 and 250 mg/ml as 100% mortality rate after 10 and 20 min of incubation The activity of Se NPs at 500 mg /ml was comparable to scolicidal effect of other scolicidal agents that were previously proved [7,69-71]. Moreover, biogenic Se NPs can be considered as a novel therapeutic agent for treatment of the localised lesions of cutaneous leishmaniasis also. They revealed its activity against promastigote and amastigote stages of *Leishmania major* [72].

Recently, owing to higher biological activity, higher anti-oxidant role and lower cytotoxicity of Se NPs compared to those of Se ions, view of studies is nowadays directed to synthesis and biological applications of it [68,72]. Regarding cytotoxicity of SeNPs, Shakibaie et al. mentioned that no death was observed in mice treated with 2.5, 5 and 10mg kg−1 of Se NPs produced by *Bacillus spp*, while mice receiving 20 mg kg−1 of Se NPs showed 20% mortality with alteration in both biochemical and haematological parameters [73]. Moreover, the toxicity of biogenic Se NPs was fewer than that of synthetic Se NPs and much less (26-fold) toxic than that of SeO_2, which confirmed the role of *Bacillus* sp. MSh-1 in changing the very toxic Se compound to less toxic Se NPs [73]. In addition, Guisbiers et al. proved the role of Se NPs in inhibition of *Candida albicans* biofilm. It was found that Se NPs appear to be a good candidate and they could be coated on the surface of medical devices and act as antibacterial and antifungal material [74].

Selenium is a trace element that is also necessary for life (adult nutrition need ~40 µg Se/day), whereas it is toxic at high concentration (N3200–6700 µg Se/day) [75]. Seleno-proteins have an essential role in the human body by achieving several biological functions such as oxido-reductions, antioxidant defence, thyroid metabolism and immune response; so, the probability to synthesis selenium NPs without any contaminants is important for further applications in Nanomedicine [74] Up-to-date selenium is being evaluated as a potential anticancer and antioxidant agent in many publications as reviewed by Skalickova et al. [76] Selenium is required for maintaining health and growth; however, its toxicity could cause serious damage depending on dose. SeNPs represent what we believe to be a novel prospect for a nutritional supplement because of their lower toxicity and ability to gradually release selenium after ingestion [76]. Moreover, Rahimi et al. [77] conducted a study on scolicidal effects of biosynthesised silver NPs that derived from *Penicillium aculeatum* against *E. granulosus* protoscoleces. The results showed that all concentration of the AgNPs (0.025,0.05,0.1 and 0.15 mg /mL) had high scolicidal activity. The highest activity was recorded in 0.15 mg/ml of AgNPs after 120 min of the application as 90% mortality. Those researchers concluded that biogenic AgNPs may be considered as a potential scolicidal agent against CE owing to eco-friendly source and its safety which involve non-toxic substances in comparison with the existing chemical procedure. Furthermore, they mentioned that the scolicidal activity of AgNPs at a concentration of 0.15 mg/ml was analogous with that of scolicidal agents that were previously recorded by several studies [7,69-71]. In addition, Lashkarizadeh et al. studied the scolicidal activity of amphotericin B, colloidal silver NPs, essential oil of *Foeniculum vulgare Mill*, and hypertonic saline versus *E. granulosus* within *in vitro* experiments. This research recorded protoscolicidal activity of colloidal Ag-NPs, its maximum effect was detected at concentrations of 4 mg/mL that led to killing 71.6% of the protoscoleces after 60 min of incubation time [78].

Allahverdiyev et al. for the first time proved that Ag_2O NPs were activated by visible and UV light and showed significant antileishmanial effects under both conditions. Since visible light is harmless to human tissues in contrast to UV light, it was summarised that Ag_2O NPs exposed to visible light are promising for further investigations. Also, their results outlined that metal oxide NPs can also be effective on eukaryotic pathogenic agents [79].

Recently, Barabadi et al. documented that the green synthesised AuNPs from *Penicillium aculeatum* exhibited scolicidal effects against *E. granulosus.* Different concentrations (0.05, 0.1, 0.2, and 0.3 mg / m L) of these biosynthesised NPs for various exposure times (10, 30, 60, and120 min.) were tested against protoscoleces [80]. The highest percentage of protoscoleces mortality was observed in the group which was treated with 0.3mg/mL AuNPs for 120 min. This study indicated that usage of AuNPs may be considered as a possible anti protoscoleces

agent for *E. granulosus* and recommended it for pharmaceutical application [80]. These results showed that the scolicidal activity of AuNPs at the effective concentration was analogous with scolicidal effects of methanolic extract of *Berberis vulgaris*, silver NPs, selenium NPs, and other as formerly described by some researchers [7,68,77]. They reasoned this anti-parasitic activity of AuNPs by their large surface area to volume percentage, which gave it novel mechanical, chemical, electrical, optical, magnetic, electro-optical, and magneto-optical characters which are lacking in them originally. Actually, lesser agglomeration offers a more available surface area for contact with parasitic membranes which results in high toxicity [80]. Also, Wang et al. explained the antibacterial mechanisms of NPs by expressing several mechanisms including oxidative stress induction, metal ion release, and non-oxidative processes [81]. In recent years, Dkhil et al. [82] indicated the protective role of AuNPs from splenic destruction in an experimental animal infected with *Schistosoma mansoni.* The treated mice showed less histological damage and oxidative stress in spleen tissue, therefore, they documented that AuNPs have therapeutic affectivity against splenic damage that results from *S.mansoni*. Furthermore, AuNPs may act as new cell death regulators particularly apoptosis, necrosis, and autophagy, which are crucial for human health. As well as it exhibited potential application in curing several diseases through unique AuNP properties, like cancer disease [83]. In another study, albendazole sulfoxide loaded with solid lipid NPs were prepared and tested within i*n vivo* model against CE. The cysts of the treated mice exhibited decreased size and weight, but these decreases were not significantly different from that of the control group. Moreover, the cysts of the animals which were treated with albendazole sulfoxide loaded with lipid NPs for every 48 hr. exhibited more ultrastructural alterations. These modifications revealed the destructive effect of the compounds on the parasite [84]. The microtriches which are functionally related to nutrients absorption were shortened or even disappeared in several treated metacestodes, proposing that the parasites responded to adverse conditions by decreasing their absorption surface [84].

To date, Siles-Lucas et al. concluded that CE is still neglected disease for which the recommended treatment is benzimidazole. This drug seems to exhibit a parasitostatic, rather than parasitocidal effect against *E. granulosus* with limited bioavailability. Therefore, several attempts were done to increase solubility, absorption, and bioavailability of this compound. One of these attempts that enhanced drug effectively is by using NPs, which result in increasing intra-cystic drug concentration [85]. In more recent years, Torabi et al. proved that chitosan albendazole (ChABZ) and chitosan praziquantel (ChPZQ) NPs are more efficient than albendazole and praziquantel suspension against CE in both cultured hydatid cyst and experimentally infected mice [86]. Furthermore, this investigation showed that the number of hydatid cysts was significantly reduced in mice which treated with ChABZ and ChPZQ in both therapeutic and chemoprophylactic experiments. They also proved that ChPZQ NPs were more effective than ChABZ in damaging the micro cysts, which may be reasoned by the small size and the high stability of ChPZQ NPs in comparison to ChABZ NPs [86]. In another previous paper, the anti-parasitic activity of albendazole loaded chitosan microspheres (ABZ-CS-MPs) as a new carrier in mice infected with *E. multilocularis* was evaluated. ABZ- CS-MPs showed better absorption and improved bioavailability of ABZ in the curing of *E. multilocularis* infestation in the murine model in comparison with those treated with liposome–albendazole and albendazole tablet. Therefore, ABZ-CS-MPs are considered as a promising candidate to treat alveolar echinococcosis also [87]. Moreover, there is another investigation that evaluated and compared in vitro apoptotic activities of Albendazole sulfoxide and Albendazole sulfoxide -loaded poly (lactic-co-glycolic acid) (PLGA)-PEG as a novel Nano polymeric particle against *E. granulosus* protoscoleces They concluded that ABZs and ABZs-loaded PLGA-PEG were capable to induce cell death of protoscoleces with aspect of oligonucleosomal DNA fragmentation which is suggestive the occurrence of late stages in the apoptosis process [88]. These apoptotic effects of ABZs on protoscoleces were assessed by caspase-3 mRNA expression of the *E. granulosus* genome. Also, it was observed that albendazole and albendazole sulfoxide loading solid lipid NPs expressed good physicochemical properties and controlled releasing by using solid lipid NPs as drug delivery carrier [89]. This finding suggested that these compounds are promising for curing CE. Table.2 summarises the scolicidal effects of nanoparticles.

Table 2. Scolicidal efficacy of nanoparticles

Compound	Disease	Experiment setting	Dosage	Treatment duration	Efficiency assessment	References
Selenium NPs	CE	*In vitro*	500 mg/ml	10 minutes	100%	[68]
Silver NPs	CE	*In vitro*	0.15 mg/ml	120 minutes	90%	[77]
Colloidal silver	CE	*In vitro*	4 mg/ml	60 minutes	71.6%	[78]
Gold NPs	CE	*In vitro*	0.3 mg/ml	120 minutes	94%	[80]
Solid lipid NPs Loaded on albendazole sulfoxide	CE	*In vivo*	0.5 mg/kg BID 2 mg/kg	Every 48 hr for 15 days	Economic & shortening time	[84]
Chitosan albendazole NPs	CE	*In vivo* & *In vitro*	25 mg/ml	21 days	Significant effects	[86]
Albendazole-chitosan microsphere.	Alveolar E	*In vivo*	150 mg/kg		Efficient	[87]
Albendazole sulfoxide-loaded PLGA-PEG	CE	*In vitro*	150 & 200 µg/ml	5-60 minutes	100%	[88]
Albendazole & Albendazole Sulfoxide-Loaded Solid Lipid NPs	Alveolar E	*In vitro*	2,000 g/L 2,500 g/L	48hr. 72hr.	ABZ and ABZSO achieved good physicochemical characterizations, controlled release, higher permeability and efficacy by loading SLNPs	[89]

6. CONCLUSIONS AND PERSPECTIVES FOR FURTHER WORK

Human and animals' CE is a disease caused by the larval stage of *E. granulosus.* This disease is known as chronic, neglected, orphan, and zoonotic by the WHO. The only synthetic chemical drug licensed for human treatment is Benzimidazole. These compounds considered as parasitostatic rather than parasiticidal agents. In addition, curing failure of CE with Benzimidazole have attributed mainly to its low aqueous solubility and poor drug absorption level, besides having several adverse effects. Therefore, new alternatives are urgently required to overcome this therapeutic deficit. Usage of scolicidal agents during surgery is essential to minimize the risk of recurrence of the disease. Routinely, many compounds were used as scolicidal agents, but unfortunately, all showed adverse effects. In recent year, nanotechnology has emerged as a promising field due to the applications in various branches of science. Numerous studies investigated the scolicidal effect of NPs against CE, among them the biogenic NPs like selenium, silver, colloidal silver, and gold. Nowadays, usage of Nanocarriers for medication delivery is hypothesised to be an innovative method for curing many diseases. For instances, albendazole sulfoxide loaded with solid lipid NPs which tested against CE within *in vivo* design.

As a conclusion, biogenic NPs can be considered as an effective scolicidal candidate that may be used in the pharmaceutical application. Further investigations are needed to assess the *in vivo* safety and the efficiency of these NPs as a promising scolicidal agent in an animal model. Also, the cellular and molecular mechanisms of action of these biogenic NPs against CE should be clarified. These may help provide a new vision in NPs target, and perhaps give a chance for designing a new and more effective drug for human CE in the near future.

ETHICAL ISSUE

It is not applicable.

CONSENT

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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