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Echinodermata as a Promising Source of Antiparasitic Agents: A Review

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ABSTRACT

Marine invertebrate natural products are a potential major source of new drugs for treating diseases, including parasitic infections. Echinodermata is an important invertebrate phylum with approximately 13,000 extinct species known from the fossil record and about 7000 described living species. In order to develop more effective, targeted, and specific innovative antiparasitic medications, this article reviewed the antiparasitic properties of crude extracts and bioactive chemicals isolated from echinoderms. Articles concerning echinoderm antiparasitic activity published since 1970 have been retrieved, studied, and discussed. Echinoderms appeared to exhibit antitrypanosomal, antileishmanial, antimalarial, antitrichomonal, antigiardial, antischistosomal, and scolicidal activities, and some of the obtained chemicals can be turned into novel antiparasitic drugs in the future.

INTRODUCTION

Even with all of the progress made in the biomedical sciences, parasites still constitute a serious threat to humankind. Globally, parasitic illnesses cause a considerable amount of morbidity and mortality and have a great socioeconomic impact, especially in low- and middle-income nations. A parasite spends all or a portion of its life cycle living within one or more hosts **(Cable *et al.*, 2017)**. The World Health Organization (WHO) estimates that globally, 3 billion individuals have one or more parasite infections. A group of diseases called Neglected Tropical Diseases (NTDs) are described by the WHO as "underrated tropical illnesses that debilitate the health of millions of people living in low socioeconomic conditions." Out of the seventeen neglected tropical diseases, eleven are caused by parasite infections **(Brahmachari, 2019)**.

Unfortunately, vaccines against the most common human parasite illnesses, such as schistosomiasis, leishmaniasis, amoebiasis and malaria, do not yet exist **(Versteeg *et al.*, 2019)**. Several logistical and technical problems have contributed to the lack of antiparasitic vaccinations. It is difficult and even impossible to cultivate enough parasites for vaccine manufacturing. Furthermore, antigens of the parasite are difficult to identify,

and parasites have various stages in their life cycle as well as sophisticated strategies for immunological evasion **(Mutapi *et al.*, 2013; Folliero *et al.*, 2021)**.

Chemotherapy is the primary treatment choice in the absence of successful vaccinations **(Sharma *et al*., 2015)**. However, therapeutic alternatives are at risk due to issues with efficacy, side effects, high costs, and medication resistance. Transmembrane export, decreased absorption, loss of effect, genetic changes, and target modification are the most common mechanisms of drug resistance **(Ertabaklar *et al.*, 2020; Folliero *et al.*, 2021)**. Therefore, no safe and effective antiparasitic medications are currently available **(Caminade *et al.*, 2018)**. The high cost of infections to public health, the scarcity of effective and safe medications, the rapid emergence of drug resistance, and the absence of effective immunizations have made the discovery of novel antiparasitic medications imperative **(Folliero *et al.*, 2021)**.

The marine ecology has greater biodiversity than the land ecosystem, which gives several resources to human societies **(Hill & Fenical, 2010)**. The varied group of marine invertebrates is present in all marine environments, from the intertidal region to the deep sea **(Thorpe *et al.*, 2000)**. In order to develop new treatments, marine invertebrates are increasingly being employed for screening bioactive marine natural products (MNPs) **(Hill & Fenical, 2010)**. **Hu *et al.* (2011)** reported that marine invertebrates account for approximately 75% of the 20,000 MNPs extracted from all marine animals.

The important invertebrate phylum Echinodermata contains about 13,000 known extinct species from the fossil record and 7000 recognized extant species. Echinodermata is the largest invertebrate phylum without any freshwater or terrestrial forms **(Siddall, 2004)**. Moreover, the echinoderms are a valuable source of biomaterials that can be used in a variety of biomedical applications **(Romano *et al*., 2022)**.

In this work, the antiparasitic properties of crude extracts and/or compounds isolated from Echinodermata were explored; particular attention was paid to the most promising compounds that could one day be developed into novel antiparasitic medications.

Echinodermata biology and systematic

There are three subphyla in the phylum Echinodermata: Asterozoa, Echinozoa, and Crinozoa. Asteroidea (sea stars, sea daisies) and Ophiuroidea (brittle and basket stars) are the two extant classes that make up the Subphylum Asterozoa. Two classes of Echinozoa are currently recognized: Holothuroidea (sea cucumbers) and Echinoidea (sea urchins and sand dollars). The only class of the subphylum Crinozoa that is still in existence is Crinoidea (sea lilies, feather stars). A tricoelomate body cavity, radial symmetry (pentamerous symmetry), and a body wall made of calcite endoskeletal plates (dermal ossicles) joined by "flexible collagenous tissue" are characteristics shared by all

echinoderms. Ten divisions make up the classic echinoderm body plan: five radii, or rays or arms, alternate with five interradii, or interrays. Usually, there is an aboral surface that contains the anus and an oral surface with the central mouth. Even with these similarities, each subphylum's morphology varies greatly. The majority of internal structures throughout the subphyla are identical in basic plan, including the reproductive, nervous, respiratory, and alimentary systems as well as distinct water vascular system.

All echinoderms are aquatic, and nearly all are benthic. Some subphyla are movable (Echinozoa, Asterozoa) and others are sessile (Crinozoa), even though it has been reported that some sea lilies can swim some distances. Among other invertebrate phyla, echinoderms do not seem to have any close relatives. A few species of Echinodermata reproduce asexually, while the majority of its members are dioecious and engage in sexual reproduction. Some members of the Asteroidea and Holothuroidea may reproduce asexually through fragmentation as a result of damage or predation. The diets of the various classes differ greatly, Echinozoa and Crinozoa being filter feeders and vegetarian browsers, Asterozoa being carnivorous, and Holothuroidea being detritivores **(Newton & Dennis, 2021)**. The antiparasitic activities of phylum Echinodermata is reviewed in detail below; Table (1) summarizes these activities.

Antitrypanosomal activities

Humans can contract African trypanosomiasis, often known as sleeping sickness, or American trypanosomiasis, sometimes called Chagas disease. Tsetse flies are the intermediate host by which trypanosome parasites, which cause human African trypanosomiasis (HAT) or sleeping sickness, are spread. Only in sub-Saharan Africa can one find HAT. *Trypanosoma brucei* has two subspecies that produce disease: *T. b. gambiense* in West and Central Africa and *T. b. rhodesiense* in East Africa. About 25,000 cases were reported in 1995, 300,000 instances were thought to be undiscovered, and 60 million people were thought to be at risk of contracting a HAT infection. Following the WHO's 2001 initiative to strengthen control and surveillance, there was a noticeable decline in HAT in the years that followed. Less than 1000 cases are recorded annually as of 2019. This decrease does not indicate a lack of control measures, since annual screening rates for both active and passive screening have remained roughly the same (around 2.5 million persons). The potentially fatal protozoan parasite *Trypanosoma cruzi* is the cause of Chagas disease, commonly referred to as American trypanosomiasis. *T. cruzi* is thought to infect 6–7 million people worldwide. Chagas disease is mostly found in endemic regions of 21 continental Latin American countries. Humans contract the disease primarily by contact with the feces of infected blood-sucking triatomine bugs. About 75 million people are thought to be at risk of infection because of the large number of persons who go undiagnosed or untreated in addition to the locations where there is still active transmission occurring **(WHO, 2024)**.

Few studies have been conducted using echinoderm extract to treat trypanosomiasis, an early investigation has been done by **Styles (1970)** on the effect of crude holothurian toxin extracted from the Bahamian sea cucumber *Actinopyga agassiz* on *Trypanosoma lewisi* infections in rats. The extract was administered intraperitoneally into rats prior, simultaneously, and post-infection. A low level of parasitemia was observed in rats treated prior to infection, followed by those treated simultaneously, and the highest parasitemia was observed in rats treated after infection. The author suspected that results might be related to potential pharmacologic properties of holothurian or some of its derivatives and its effect on the reticuloendothelial system. **Sen *et al.* (1981)** studied the effect of holothurian on *T. musculi* that infected three strains of mice: the Swiss Webster (SW), Beige (BG), and Black (BL). Their results were corralled with that of **Styles (1970)**, since they observed a high level of parasitemia in mice treated after infection. Moreover, BG mice appeared more susceptible to *T. musculi* infection than other strains studied.

The sand sifting starfish or comb sea star *Astropecten polyacanthus* and sea urchin *Diadema savignyi* were collected at Quangtri, Khanhhoa, Hue, and Haiphong, Vietnam. The methanolic crude extracts of both echinoderms exhibited potent activities with EC_{50} < 5.0μg/ mL against the cultures of *T. brucei* and *T. cruzi.* Concerned with the compounds isolated from these methanolic extracts, astropectenol A from *Astropecten polyacanthus*, and cholest-8-ene-3*β*,5*α*,6*β*,7*α*-tetraol from *Diadema savignyi* showed inhibitory activity against the bloodstream forms of *T. brucei*, with EC_{50} values of 1.57 and 14.6μM, respectively. Although, these two compounds showed insignificant activity (less than 30% inhibition at 50.0μM) against the intracellular form of *T. cruzi*. None of both astropectenol A and cholest-8-ene-3*β*,5*α*,6*β*,7*α*-tetraol exhibited any significant cytotoxicity. Therefore, these compounds might provide a new approach to developing drugs to treat African sleeping sickness in the future **(Thao *et al.*, 2014)**.

Antileishmanial activities

The causative agents of leishmaniases are the protozoan parasites of more than 20 different *Leishmania* species, which can infect both humans and animals. The bite of an infected female phlebotomine sandfly transmits these parasites to humans. The disease is classified into three types: cutaneous leishmaniasis (CL), visceral leishmaniasis (VL), and mucocutaneous leishmaniasis (MCL). CL is the most frequent form of the disease; VL is the most severe, and MCL is the most devastating. In 2018, 92 and 83 nations or territories, respectively, were considered endemic for, or had previously documented occurrences of CL and VL. More than 1 billion people live in leishmaniasis-endemic areas and are at risk of infection. Every year, an estimated 30,000 new cases of VL and over 1 million new cases of CL are diagnosed **(WHO, 2024)**.

Compared to trypanosomiasis, leishmaniasis attracted the interest of more authors who investigated how echinoderm extracts affected it. **Encarnacion-Dimayuga *et al.***

(2006) isolated three compounds from the body walls of the sea cucumber *Neothyone gibbosa,* named Neothyosides A, B and C. The antiparasitic activity of these compounds was tested *in vitro* against promastigote stages of two strains of *Leishmania mexicana*: MHOM/MX/84ISETGS and MHOM/MX/88HRCMC. The IC_{100} (100% inhibitory concentration) of Neothyosides A, B and C was 100, >100 and 5, respectively, for MHOM/MX/84ISETGS strain; however, it was 100, >100 and 10, respectively, for MHOM/MX/88HRCMC strain.

Extensive investigations on the leishmanicidal activities of *Actinopyga lecanora* (the coral reef sea cucumber) extracts both *in vitro* and *in vivo* were done by **Singh *et al.* (2008)**. They observed that at a concentration of 100g/ mL, the crude methanol extract was able to lower the promastigotes and amastigotes populations by 88.5 and 72.45%, respectively. On other hand, the ethyl acetate soluble fraction, when used at the same dose, proved ineffective, suppressing less than 22.0% of both parasite forms. However, the butanol soluble fraction inhabited 76.4 and 98.5% of the amastigote and promastigote growth, respectively. Moreover, a 500mg/ kg dose of the butanol soluble fraction reduced parasite load in *L. donovani*-infected hamsters by 26%. The same authors isolated and identified two glycosides, namely holothurin A and B from the n-butanol fraction. *In vitro*, holothurin A was found to be less active than holothurin B; since at 50µg/ mL concentration, the two compounds were able to decrease the viability of amastigote intracellular stages by 45 and 57.65%, respectively. *In vivo,* applying holothurin B at a dose of 100mg/ kg/ day for 5 days reduced parasite burden by 71.5%, compared to holothurin A, which reduced parasite burden by around 50% in *L. donovani* infected hamsters. Authors expected that increasing the number of glicosyl groups in holothurin A would reduce its antileishmanial activity both *in vitro* and *in vivo*. Unfortunately, the toxicity tests have not been conducted for these extracts and compounds.

The antileishmanial activities of methylene chloride/methanol (1:1) extracts of the body wall of 11 out of 22 species of sea cucumbers collected along the Egyptian coasts of the Red Sea were investigated by **Lawrence *et al.* (2010)**; the extracts of *Holothuria fuscogilva, H. leucospilota, Stichopus hermanni, Actinopyga crasa, Pearonothuria graeffei, Bohadschia cousteaui* and *B. vitensis* appeared active against *Leishmania* sp. with IC_{50} values of 402, 432, 364, 371, 92, 200 and 127µg/ mL. *H. nobilis* extract was inactive with $IC_{50} \geq 500$µg/ mL. The same authors verified that gathering organisms from different locations can result in intraspecific variability in the synthesis of bioactive metabolites; since antileishmanial activity of extracts of *A. mauritiana, B. tenuissima,* and *H. atra* from northern sites differed significantly from those of the same species from southern sites.

The efficacy of the methanolic extract of the sea star *Echinaster* (*Othilia*) *echinophorus,* which was obtained from the north coast of Pinar del Rio, Cuba, against *Leishmania amazonensis*, was assessed by **Parra *et al.* (2010)**; with IC_{50} values of 62.9 and 37.5µg/ mL, respectively, the extract demonstrated activity against promastigote and

amastigote forms *in vitro*. With an IC_{50} value of 348.6µg/ mL, this extract demonstrated a moderate toxicity on macrophages from BALB/c mice. *In vivo*, a dosage of 100mg/ kg/ day delivered intraperitoneally to experimentally infected BALB/c mice for 15 days proved effective.

Antimalarial activities

Through the bites of female *Anopheles* mosquitoes carrying the parasite that causes malaria, people suffer from this potentially fatal disease. There are five parasite species that cause malaria, but *Plasmodium falciparum* and *Plasmodium vivax* are the two that do the most harm. An estimated 247 million people had malaria in 2021, and 619 000 people died from the disease overall. A disproportionately high amount of the malaria burden worldwide falls on the WHO's African Region. 95% of malaria cases and 96% of malaria deaths in 2020 occurred in that region. Children under five are the most susceptible to malaria; in the WHO African Region in 2021, they accounted for over 80% of all malaria-related deaths **(WHO, 2024)**.

Seven echinoderms were among the 27 species of marine invertebrates that were collected by **Mendiola *et al.* (2006)** from the northwest Cuban coast to investigate their antimalarial activity. The aqueous extracts from these seven species were tested against F32 strain of *Plasmodium falciparum*. Five extracts of *Echinometra lucunter, Echinaster spinulosus, Echinaster* sp., *Luidia senegala* and *Lebrunia danae* were considered inactive as showing minimum inhibitory concentrations (MIC) value of >500µg /ml; while two extracts of *Holothuria* sp. and *Echinaster echinophorus* appeared active with MIC value of 136.5 and 500µg/ ml, respectively. Minimum cytotoxic concentration (MCC) for U937 macrophage cells was 68.25 and 2000µg/ ml for *Holothuria* sp. and *Echinaster echinophorus* extracts, respectively.

To impair the growth of malaria parasite in the midgut of female mosquito, **Yoshida *et al.* (2007)** applied the genetic engineering techniques and generated transgenic *Anopheles stephensi* that express the C-type lectin CEL-III from the sea cucumber, *Cucumaria echinata.* In the presence of serum, CEL-III has powerful and quick hemolytic activity toward rat and human RBCs. Sporogonic development of *Plasmodium berghei* was severely inhibited in transgenic mosquito. On other hand, it was found that *P. falciparum* affected moderately but significantly. Moreover, authors observed that CEL-III exhibits hemolytic and cytotoxicity toward ookinetes; since *in vitro* with an IC_{50} of 15 nM, CEL-III binds to ookinetes leading to effectively inhibition of ookinete production.

Marques *et al.* (2016) explored the antimalarial activity of heparin-like sulfated polysaccharides from the sea cucumbers *Isostichopus badionotus* and *Ludwigothurea grisea*. Two compounds were extracted from these cucumbers called sulfated fucan and fucosyloted chondroitin sulfate (FucCS). *In vitro* assay demonstrated that compounds induced significant inhibition of *Plasmodium falciparum* growth at low-anticoagulant

concentrations. This action was discovered to function by preventing *Plasmodium* from invading erythrocytes, most likely through a coating of the parasite like that shown for heparin. Moreover, it was found that sulfated polysaccharides increased the lifespan of *Plasmodium yoelii*-infected mice according to *in vivo* four-day suppression tests. The parasitemia dropped from 10.4% to undetectable levels in one of *P. yoelii*-infected mice treated with *I. badionotus* sulfated fucan; however, Western blot analysis revealed the presence of antibodies against *P. yoelii* antigens in the plasma of that mouse. **Marques *et al.* (2016)** concluded that it is possible to investigate the delayed invasion caused by sulfated polysaccharides and the subsequent prolonged exposure of *Plasmodium* to the immune system in order to develop new therapeutic strategies against malaria, in which heparin-related polysaccharides with low anticoagulating activity could function both as therapeutic agents and immune response potentiators.

Other antiprotozoal activities

From the entire body of the sea cucumber *Cucumaria echinata*, **Miyamoto *et al.* (1990)** extracted and discovered six authentic holostane-type triterpenoid glycoside sulfates, which they named cucumechinoside A (l), B (2), C (3), D (4), E (5), and F (6). The antiprotozoal activity of cucumechinoside, their solvolized compounds and holotoxin A were assayed *in vitro* against *Trichomonas foetus*. Compounds 6, 10, 12 and holotoxin A appeared inhibitory against *T. foetus* active at concentrations 10, 2.5, 2.5 and 1.0µg/ ml, respectively.

Encarnación *et al.* (2000) assayed the antifungal and antiparasitic of some marine organisms including members of class Asteroidea collected in the Complejo Insular La Partida-Espiritu Santo Island B.C.S., México. Unfortunately, none of Echinoidea ethanolic extracts appeared active against *Giardia lamblia* and *Entamoeba histolytica*.

Asadi *et al.* (2022) evaluated the anti-protozoal activities of *Holothuria leucospilota* crude extract *in vivo* and *in vitro* against *Toxoplasma gondii*. They reported that *H. leucospilota* extract inhibits the proliferation and invasion of *T. gondii* tachyzoite. Additionally, mice treated with *H. leucospilota* extract showed a significant drop in IL-5 levels aligned with an increase in the production of TNF-α and IFN-γ. Additionally, these mice exhibited a highly significant increase in the levels of ALP, AST, and ALT.

Antischistosomal activities

Schistosomiasis has been recorded in 78 countries. Schistosomiasis is common in tropical and subtropical regions, particularly in impoverished communities lacking access to safe drinking water and proper sanitation. It is believed that at least 90% of persons in need of schistosomiasis therapy reside in Africa. There are two types of schistosomiasis caused by five different species of blood fluke: intestinal (caused by *Schistosoma*

intercalatum, *S. mekongi*, *S. japonicum* and *S. mansoni*) and urogenital (caused by *Schistosoma haematobium*). According to estimates, at least 251.4 million people will require preventative treatment in 2021. Preventive care, which should be repeated over time, will reduce and prevent morbidity **(WHO, 2024)**.

Both *In vitro* and *In vivo*, **Mona *et al.* (2012)** examined the antischistosomal activity of the holothurin extracted from three different species of the sea cucumber: *Actinopyga mauritiana*, *Bohadschia vitiensis*, and *Holothuria polii*. The first species was collected from the Red Sea's Hurgada coast, Egypt, while the other two species were collected from the Mediterranean Sea's Abu-Kir coast, Egypt. Authors suggested that *Holothuria polii* can be regarded as a promising natural source for a new antischistosomal drug since the results indicated a significant decrease in worm recovery and the egg count in mice treated with *H.polii* extract.

Melek *et al.* (2012) assayed *in vitro* the methanol extracts of 79 marine organisms for their antischistosomal activities against adult worms of *Schistosoma mansoni* and the most active extracts were subjected for further investigations for identification and isolation of their active compounds using 1D and 2D NMR analysis. The crude extracts of three cucumbers *Actinopyga echinites*, *Holothuria nobilis* and *Holothuria polii* and one sea star *Ophiarachnella septemspinosa* appeared active against *S. mansoni* with LC_{50} values of 0.33, 66.3, 17.3 and 41.2µg/ ml, respectively. Moreover, *Actinopyga echinites* and *Holothuria polii* were used to produce two highly antischistosomal active compounds, echinosides A and B, whose LC_{50} values were 0.19 and 0.27µg/ ml, respectively.

Scolicidal activity

Human echinococcosis is a zoonotic disease caused by *Echinococcus* tapeworms. There are four types of echinococcosis; however, the two most significant ones, which have an impact on public and medical health, are alveolar echinococcosis (AE) produced by *Echinococcus multilocularis* and cystic echinococcosis (CE), which is caused by *Echinococcus granulosus* **(WHO, 2024)**. The agents used for the inhibition and treatment of the cystic infection are called scolicidal agents.

In vitro scolicidal impact of spines and shells extracted from the Persian Gulf sea urchins (*Echinometra mathaei*) against protoscolices of *Echinococcus granulosus* was studied by **Navvabi *et al.* (2019)**; 93.33% of the protoscolices were killed upon exposure to a concentration of 20µg/ ml of spine extract for 60 minutes; conversely, in the same incubation period, 20µg/ ml of shell extracts killed less protoscolices than did the spine extracts. The scolicidal activities were also studied by an ELISA assay for caspase activity. **Aryamand *et al.* (2019)** argued that CeO2 nanoparticles and the sea cucumber *Holothuria leucospilota* extract have potent scolicidal activity both *in vivo* and *in vitro*. The coelomic fluid extraction from sea urchin *Echinometra mathaei* have shown scolicidal effects on hydatid cysts protoscolices **(Navvabi *et al.*, 2022)**.

CONCLUSION

It can be concluded that there are good prospects for the ongoing study of echinoderms role for the treatment of parasitic infections, based on the numerous antiparasitic activities observed for crude extracts and natural compounds from them described here. This research would undoubtedly lead the scientific community to the discovery of more new efficient drugs for parasitic diseases. The world's poor people suffer greatly from parasitic infections, particularly neglected tropical diseases including schistosomiasis, malaria, leishmaniasis, Chagas disease, and the African trypanosomiasis. Regretfully, there hasn't been enough demand from communities affected by these illnesses to draw significant funding for the creation of new medications through research and development. Therefore, as part of the intense efforts of the international scientific community to tackle this economic and humanitarian crisis, this work call attention of parasitologists and encourage them to take an active role in the efforts required for the development of novel antiparasitic medications.

Table 1. Antiparasitic activity of echinoderms' extracts and compounds

Parasite targeted	Echinoderms	Extract/ compound	Experimental model	Country	References
Trypanosoma lewisi	Sea cucumber *Actinopyga agassiz*	Crude extract	*in vivo*: Rat	Bahama	Styles (1970)
T. musculi	Sea cucumber *Actinopyga agassiz*	Crude extract	*in vivo*: Three strains of mice Swiss Webster (SW), Beige (BG), and Black (BL).	Bahama	Sen *et al.* (1981)
T. brucei& *T. cruzi*	Sea star *Astropecten polyacanthus*	Methanolic crude extracts & astropectenol A	*in vitro*	Vietnam	Thao *et al.* (2014)
	Sea urchin *Diadema savignyi*	Methanolic crude extracts & cholest-8-ene-3β,5α,6β,7α-tetraol			
Leishmania mexicana (promastigote stages**)**	Sea cucumber *Neothyone gibbosa*	Neothyosides A, B, and C compounds	*in vitro*	México	Encarnacion-Dimayuga *et al.* (2006)
L. donovani (promastigotes and amastigotes**)**	Coral reef sea cucumber *Actinopyga lecanora*	Crude methanol extract- Ethyl acetate soluble fraction- Butanol soluble fraction- Two glycosides holothurin A and B from the n-butanol fraction	*in vitro* and *in vivo*	-	Singh *et al.* (2008).
Leishmania sp.	Sea cucumbers: *Holothuria fuscogilva, H. leucospilota, Stichopus hermanni, Actinopyga crasa, Pearonothuria graeffei, Bohadschia cousteaui B. vitensis, H. nobilis*, *A. mauritiana, B. tenuissima* & *H. atra*	methylene chloride/methanol (1:1) extracts	*in vitro*	Egypt	Lawrence *et al.* (2010)
Leishmania amazonensis (promastigote and amastigote forms**)**	Sea star *Echinaster (Othilia) echinophorus*	Methanolic extract	*in vitro* and *in vivo*	Cuba	Parra *et al.* (2010)

Plasmodium falciparum (F32 strain)	*Echinometra lucunter, Echinaster spinulosus, Echinaster* sp., *Luidia senegala, Lebrunia danae, Holothuria* sp., and *Echinaster echinophorus*	Aqueous extracts	*in vitro* and *in vivo*	Cuba	Mendiola *et al.* (2006)
Plasmodium berghei	Sea cucumber, *Cucumaria echinata*	-	Transgenic *Anopheles stephensi* express the C-type lectin CEL-III	-	Yoshida *et al.* (2007)
Plasmodium falciparum	Sea cucumbers *Isostichopus badionotus* and *Ludwigothurea grisea*	Two heparin-like sulfated polysaccharides:sulfated fucan and fucosyloted chondroitin sulfate (FucCS)	*in vitro* and *in vivo*	-	Marques *et al.* (2016)
Trichomonas foetus	Sea cucumber *Cucumaria echinata*	Triterpenoid glycoside sulfates	*in vitro*	-	Miyamoto *et al.* (1990)
Entamoeba histolytica and *Giardia lamblia*	Members of class Asteroidea	Ethanolic extracts	*in vitro*	México	Encarnación *et al.* (2000)
Toxoplasma gondii (Tachyzoites)	Sea cucumber *Holothuria leucospilota*	Crude extract	*in vitro* and *in vivo*	-	Asadi *et al.* (2022)
Schistosoma mansoni	sea cucumbers: *Holothuria polii*, *Bohadschia vitiensis*, and *Actinopyga mauritiana*	Ethanol extract	*in vitro* and *in vivo*	Egypt	Mona *et al.* (2012)
Schistosoma mansoni	sea cucumbers: *Actinopyga echinites*, *Holothuria nobilis Holothuria polii* and one Sea star: *Ophiarachnella septemspinosa*	Methanol extracts and two compounds echinosides A and B isolated from the sea cucumbers	*in vitro*	Egypt	Melek *et al.* (2012)
Echinococcus granulosus	Sea urchin *Echinometra mathaei*	Crude extract	*in vitro*	Iran	Navvabi *et al.* (2019)
Echinococcus granulosus	Sea cucumber: *Holothuria leucospilota*	Methanol extracts	*in vitro* and *in vivo*	Iran	Aryamand *et al.* (2019)
Echinococcus granulosus	Sea urchin *Echinometra mathaei*	Coelomic fluid	*in vivo*	Iran	Navvabi *et al.* (2022)

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Arabic Summary

تمثل المنتجات الطبيعية للافقاريات البحرية مصدرًا رئيسيًا محتملاً للأدوية الجديدة لعلاج العديد من الأمراض, البعض منهم لديهم نشاط مضاد للطفيليات. شوكيات الجلد هي شعبة مهمة من اللافقاريات تضم ما يقرب من 7000 نوع حي موصوف وحوالي 13000 نوع منقرض معروف من السجل الأحفوري. تهدف هذه المقالة إلى مراجعة الخصائص المضادة للطفيليات للمركبات النشطة بيولوجيًا المستخرجة من شوكيات الجلد والتي يمكن إستخدامها لإنتاج أدوية مضادة للطفيليات جديدة أكثر انتقائية ومحددة. ولتحقيق هذا الغرض، تم استرجاع وتحليل ومناقشة الأوراق البحثية المتعلقة بالأنشطة المضادة للطفيليات لشوكيات الجلد، والتي نُشرت بين عامي 1970 و2023. وقد ظهر أن شوكيات الجلد لها أنشطة مضادة للمثقبيات، ومضادة لليشمانيات، ومضادة للملاريا، ومضادة للمشعرات، ومضادة للجياردیات، ومضادة للبلهارسيا، وقاتلة ليرقات الاكينوكوكس، وبعض المركبات المستخرجة واعدة ويمكن تطويرها إلى منتجات تجارية في المستقبل.