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Hemionitis calomelanos (Sw.) Christenh.: From traditional medicinal uses to chemical identification of active principles

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Abstract

Hemionitis calomelanos (Sw.) Christenh. is a fern widely used as a traditional medicine throughout its distributional range. This study aims to record, analyze, and provide insights into the historical, scientific, and ethnopharmacological properties of *H. calomelanos*. Multiple searches on existing literature on the medicinal, phytochemical, and pharmacological properties of *H. calomelanos* were conducted in online databases such as Scopus, JSTOR, PubMed, Google Scholar, and Science Direct as well as using pre-electronic literature sources obtained from the university library. This study revealed that the leaves, rhizomes, roots, stems and whole plant parts of *H. calomelanos* are mainly used as ethnoveterinary medicines, lucky and protective charm, and traditional medicine for colds, boils, cough, sores, and diarrhoea. Phytochemical research showed that the species is characterized by flavonoids, steroids, tannins, esters, alcohols, ketones, and alkanes. Ethnopharmacological research revealed that the extracts of the species demonstrated antibacterial and antifungal activities. *H. calomelanos* is an important medicinal plant species in several countries with numerous medicinal applications. Despite its historical and traditional medicinal uses, many questions regarding the species' ethnopharmacological properties and potential therapeutic effects remain to be answered. Therefore, future research should focus on validating the medicinal uses of *H. calomelanos* through elucidation of phytochemical composition, pharmacology, clinical application, toxicology, and safety.

Keywords

adiantaceae; *Hemionitis calomelanos*; indigenous pharmacopeia; pteridaceae; sinopteridaceae; traditional medicine

Introduction

Hemionitis calomelanos (Sw.) Christenh. is a fern that belongs to the subfamily Cheilanthoideae within the Pteridaceae family. Evidence from recent molecular analysis established that the subfamily Cheilanthoideae composed of genera such as *Cheilanthes* Sw., *Doryopteris* J. Sm., and *Pellaea* Link is polyphyletic (1) and therefore, the entire subfamily has been merged into a single genus *Hemionitis* L. which has nomenclatural priority over the other genera (Fig. 1) (2). The nomenclature of *H. calomelanos* is complicated and proper species name is further hampered by historical references to invalid names and it therefore seems appropriate to include the full synonymy of the species. In literature, synonyms of *H. calomelanos* which are often used include *Allosorus calomelanos* (Sw.) C.Presl, *Notholaena calomelanos* (Sw.) Keyserl., *Pellaea calomelanos* (Sw.) Link, *P. calomelanos* (Sw.) Link var. *swynnertoniana* (Sim) Schelpe, *P. hastata* (Thunb.) Prantl, *P. swynnertoniana* Sim, *Platyloma*

calomelanos (Sw.) J.Sm., *Pteris calomelanos* Sw., *Pteridella hastata* (Thunb.) Mett. ex Kuhn, *Pteris codinae* Cadevall & Pau ex Bonap. and *P. hastata* Thunb. (2-4). Similarly, *H. calomelanos* has also been associated with Adiantaceae (5) and Sinopteridaceae (3) families. Leathery hard fern is the English common name used all over the world for *H. calomelanos*.

Medicinal plants such as *H. calomelanos* and other related Pteridophytes are often neglected as a result of inadequate research and pharmaceutical development (6). Pteridophytes have been considered excellent sources of traditional medicines by various indigenous communities since ancient times and remain underexplored in ethnopharmacological aspects when compared with other vascular medicinal plants (7). Pteridophytes are rich in various secondary metabolites such as terpenoids, alkaloids, saponins, tannins, phenolic acids, anthraquinones, lignans, steroids, glycosides, amino acids, fatty acids, and flavonoids which are known to have medicinal properties (8-11). Various extracts and isolated compounds from the Pteridophytes are characterized by diverse biological activities such as antioxidant, antibacterial, anti-inflammatory, antiviral, anticancer, analgesic, antimutagenic, antifungal, immunomodulatory, neuromodulatory, hepatoprotective, antidiabetic and wound healing (12-14). Therefore, in-depth ethnopharmacological studies are needed to adequately record the wealth of cultural, ethnomedicinal, and pharmacological properties of Pteridophytes. Such documentation is particularly important for this ancient evolutionary lineage which could potentially become extinct if used and harvested unsustainably. It is therefore, within this context that the current study was undertaken aimed at recording, analyzing, and providing insights into the historical, scientific, and ethnopharmacological properties of *H. calomelanos*. Such a historical perspective focusing on the medicinal uses, phytochemical properties, and biological activities of *H. calomelanos* is aimed at tapping into the pool of medicinal use records of the species and comparing this historical data with current data and practices. Moreover, about 25-50 percent (5) of the natural health products and their pharmaceutical derivatives are obtained from plants via traditional use records.

Methodology

The literature review of the historical or traditional medicinal uses, phytochemical properties, and biological activities of *H. calomelanos* within its geographical range was conducted using online databases such as Scopus, JSTOR, PubMed, Google Scholar, and Science Direct. In addition to this, pre-electronic literature sources were used which included books, book chapters, journal articles, dissertations, theses, and other scientific articles obtained from the University of Fort Hare library. The keywords which included scientific and common plant names such as "*H. calomelanos*", "*Pellaea calomelanos*", "*Pteris calomelanos*", "leathery hard-fern", "biological activities", "pharmacological properties", "ethnobotany", "taxonomy", "nomenclature", "ecology", "chemistry", "biochemistry", "medicinal uses", "phytochemistry", "toxicology", and "traditional uses of *H. calomelanos*, *Pellaea calomelanos* or *Pteris calomelanos*" were used to search for relevant articles as shown in the flow diagram (Fig. 2).

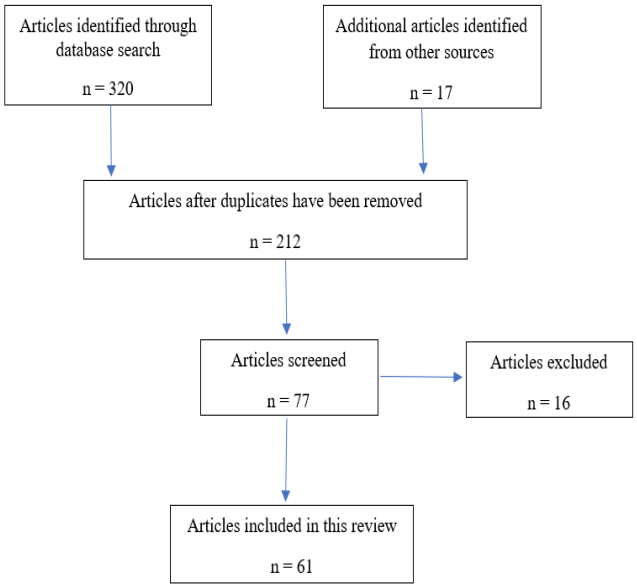

Fig. 2: Flow diagram showing identification and screening of articles used in this review

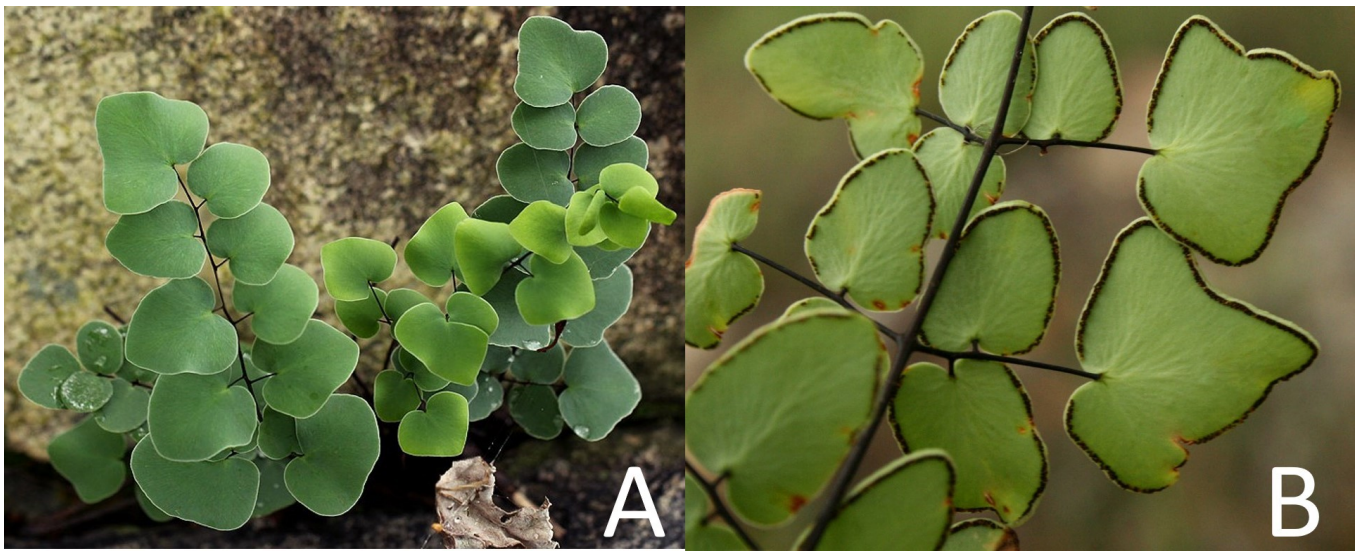

Fig. 1: *H. calomelanos*. A: entire plant growing on rock crevices (photo: B Wursten) and B: sori (Photo: P Ballings)

Results

Morphological description and taxonomy of the species

The genus *Hemionitis* comprises over 400 species (2, 15, 16). The genus name "*Hemionitis*" is derived from the Greek word "*hemionos*", meaning "mule" about the general belief in the early years that plants were sterile (17). The species name "*calomelanos*" is derived from the Greek words "*calos*" which means "beautiful" and "*melanos*" which means "black" about the shiny black stipe and rachis of the species which forms a striking contrast to the grey-green pinnules (3). *H. calomelanos* is a hard-textured, grey-blue to blue-green fern growing to about 40 cm in height (4). This fern has an underground rootstock of about 6 mm in diameter covered with small brown scales (5). The leaves are tufted on a short rhizome with an almost black leaf stalk. The leaf blade is narrowly triangular in outline with rounded to triangular pinnules (Fig. 1). The leaf blade has two spreading basal lobes and a blunt apex bearing sporangia in a line along the margin below (Fig. 1B). *H. calomelanos* has been recorded in rock crevices and at the foot of boulders, occasionally on vegetation islands on bare rock, in the shade, and in the sun at an altitude ranging from 100 m to 2100 m above sea level (3). *H. calomelanos* has been recorded in Angola, Botswana, Burundi, China, Comoros, the Democratic Republic of Congo (DRC), Eswatini, Ethiopia, Kenya, Lesotho, Madagascar, Malawi, Mauritius, Mozambique, Namibia, Nepal, Pakistan, Rwanda, Réunion, Somalia, South Africa, South Sudan, Spain, Sudan, Tanzania, Uganda, West Himalaya and Zimbabwe (Fig. 3). *H. calomelanos* is categorized as Critically Endangered in Spain (18, 19), threatened by general habitat degradation due to wildfires, changes in land use, and competition with weedy plants. Further research is needed to assess the causes of the threats the species is currently facing, and measures should be taken to protect these subpopulations in Spain, as they represent an isolated outlying population of the species (18, 19).

Medicinal uses of the species

H. calomelanos is an important source of traditional medicines in several countries throughout its distributional range. In both historical, modern, official, and non-official traditional pharmacopeia, the preparations of *H. calomelanos* as traditional medicine are well-defined and extensively studied. Despite this rich historical and traditional medicinal applications and therapeutic effects, recent studies categorized *H. calomelanos* as neglected and often underutilized as traditional medicine (5, 6). In South Africa, the leaves and stems of *H. calomelanos* are traditionally used to make herbal tea used against colds and chest ailments (5, 20-22). The early settlers and colonists around the Cape region in South Africa used *H. calomelanos* for similar medicinal applications as *Adiantum capillus-veneris* L. (maiden-hair fern), a traditional European remedy used as a mild diuretic and traditional medicine against asthma, coughs, and kidney problems (5). Therefore, the practice of making *H. calomelanos* herbal tea decoctions was probably introduced by the early settlers and colonists, and the practice was adopted by the local communities. Such popularity as a source of traditional medicines led to the inclusion of the species in the monograph Medicinal Plants of South Africa (5), Sesotho: plant and animal names and plants used by the Basotho (23), and Medicinal and magical plants of southern Africa: an annotated checklist (24). Similarly, the different plant parts of *H. calomelanos* are sold as sources of traditional medicines in informal herbal medicine markets in South Africa (25) and Zimbabwe (26). In literature, it is clear that wild harvesting of *H. calomelanos* is of economic importance for local communities and cultivation of the species plays a limited role in the livelihoods of local communities (6).

The smoke or herbal concoctions prepared from the leaves, rhizomes, roots, stems, and whole plant parts of *H. calomelanos* are used to treat and manage 30 human and animal diseases and ailments (Table 1). The

Fig. 3 Distribution of *H. calomelanos* in the world (https://www.gbif.org/occurrence/map?has_coordinate=true&has_geospatial_issue=false&taxon_key=7335563)

major diseases and ailments treated by *H. calomelanos* extracts include colds recorded in three countries based on 14 literature records (Fig. 4), followed by lucky and protective charm (three countries and seven literature records), boils (two countries and 18 literature records), cough (two countries and eight literature records), ethnoveterinary medicine (two countries and six literature records), sores (two countries and three literature records) and diarrhoea (two countries and two literature records). Other medicinal applications of *H. calomelanos* supported by at least five literature records include the use of the leaves, rhizomes, roots, stems, and whole plant parts as traditional medicines against abscesses, asthma, chest colds, chest pains, convulsions, headaches, head colds, and intestinal parasites or worms (Table 1). In Zimbabwe, the whole plant parts of *H. calomelanos* are mixed with the roots of *Peltophorum africanum* Sond. (family Fabaceae) and taken orally as a remedy for abdominal pains (27). The Kgatla people of Lesotho and South Africa as well as the Kwena people of southern Africa, that is, Botswana, Eswatini, Lesotho, South Africa, and Zimbabwe traditionally used milk decoctions of the rhizome of *H. calomelanos* to calm frightened children at night (27). Other species related to *H. calomelanos* widely used as sources of traditional medicines include *H. atropurpurea* (L.) Christenh. (28-30), *H. longipilosa* (Bonap.) Christenh. (6, 31), *H. nivea* (Poir.) Christenh. (32, 33), *H. ternifolia* (Cav.) Christenh. (34, 35), *H. tomentosa* Raddi (7, 36), *H. viridis* (Forssk.) Christenh. (37-40) and *H. yikka* Christenh. (6, 41). This data on other *Hemionitis* species characterized by medicinal properties is useful for comparative analyses on ethnomedicinal uses of *Hemionitis* species.

Phytochemical compounds of *H. calomelanos*

The phytochemical compounds identified from the leaves of *H. calomelanos* (Table 2) include flavonoids, steroids, tannins, esters, alcohols, ketones, and alkanes (52). These findings corroborate previous research which showed that Pteridophytes contain flavonoids, steroids, tannins, esters, alcohols, ketones, and alkanes (8-11). Some of these phytochemical compounds may be responsible for the biological activities exhibited by the species. There is very little information on the phytochemistry of *H. calomelanos* but Pteridophytes are characterized by triterpenoids of the hopane type, such as adiantone and related compounds as well as a wide range of flavonoids (5, 78).

Biological activities of *H. calomelanos*

The leaf extracts of *H. calomelanos* demonstrated antibacterial and antifungal activities. Braithwaite et al. (45) evaluated the antibacterial activities of methanol and acetone extracts of *H. calomelanos* leaves and smoke fraction against *Staphylococcus aureus* (ATCC 25923), *Bacillus cereus* (ATCC 11778) and *Klebsiella pneumoniae* (ATCC 9633) using the microtiter plate technique with ciprofloxacin as a positive control. The extracts exhibited activities with minimum inhibitory concentration (MIC) values ranging from 0.53 mg/ml to >16.0 mg/ml (45). Mabona (48) and Mabona et al. (50) evaluated the antibacterial activities of aqueous and dichloromethane: methanol (1:1) extracts of *H. calomelanos* leaves and rhizomes against *Brevibacillus agri, Propionibacterium acnes, Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Staphylococcus epidermidis* using the microtiter plate assay with ciprofloxacin as a positive control. The extracts exhibited activities with MIC values ranging from 0.02 mg/ml to >16.00 mg/ml (48, 50). Dumisa et al. (79) evaluated the antibacterial activities of a 1:1 mixture of dichloromethane and methanol extracts of *H. calomelanos* leaves against *Staphylococcus aureus* and *Pseudomonas aeruginosa* using the microdilution assay with ciprofloxacin as a positive control. The extracts exhibited activities with MIC values ranging from 2000.0 µg/ml to >8000.0 µg/ml (78). Mahlangu and Serepa-Dlamini (54) evaluated the antibacterial activities of methanol, ethyl acetate, and supernatant extracts of *H. calomelanos* leaves against the Gram-negative bacteria *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 27853) and *Klebsiella pneumoniae* (ATCC 13182) and Gram-positive *Staphylococcus aureus* (NCTC 6571) and *Bacillus cereus* (ATCC 10876) using the disk diffusion method with streptomycin used as a positive control and dimethylsulfoxide (DMSO) as a negative control. The methanol extract exhibited activities against the tested

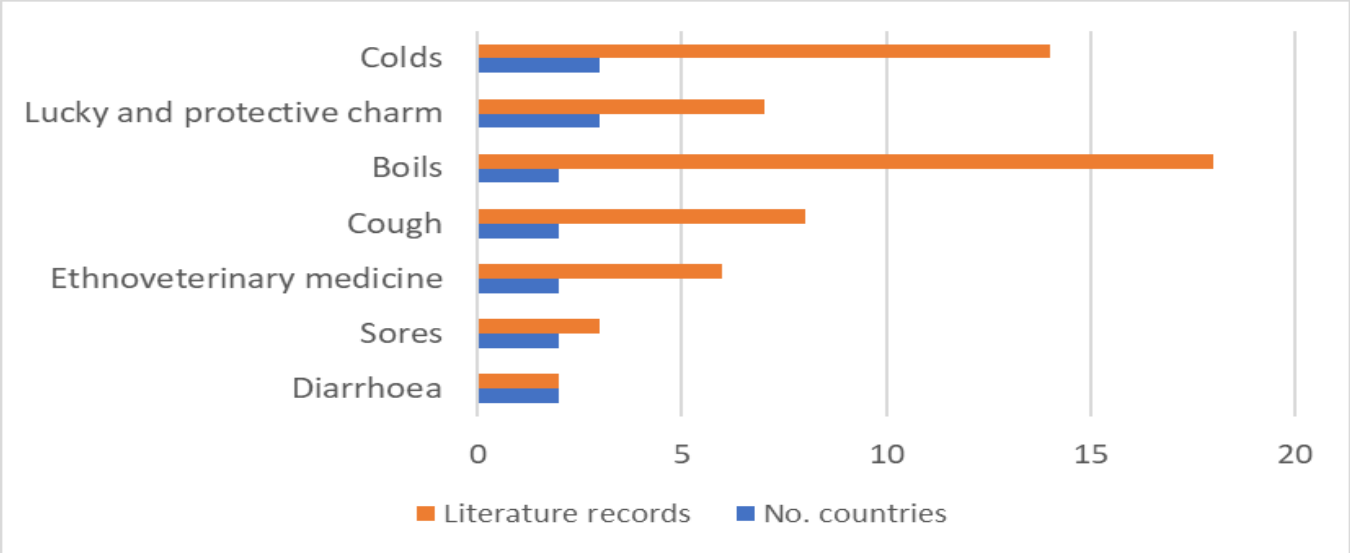

Fig. 4 Main diseases and ailments treated and managed by *H. calomelanos*

Table 1 Medicinal uses of *H. calomelanos*

Medicinal application	Parts used and application	Country	Reference(s)
Abdominal pains	The whole plant mixed with roots of *Peltophorum africanum* Sond. (family Fabaceae) and taken orally	Zimbabwe	(6, 27)
Abscesses	Leaf, rhizome, and root decoction applied topically	South Africa	(5, 6, 23, 41-53)
Asthma	Smoke of foliage, leaves, and rhizomes inhaled	South Africa	(5, 6, 23, 41, 42, 44-47, 51-56)
Boils	Leaf, rhizome, and root decoction applied topically	Eswatini and South Africa	(5, 6, 23, 41-53, 57, 58)
Bronchitis	The smoke of foliage, leaves, and rhizomes inhaled	South Africa	(59)
Chest colds	Leaf decoction is taken orally	South Africa	(5, 20, 44, 45, 47, 51-56)
Chest pains	Leaf and stem decoction taken orally	South Africa	(5, 20, 44, 47, 51)
Colds	Foliage, leaf, rhizome, and stem decoction taken orally	Lesotho, Pakistan, and South Africa	(5, 6, 23, 44, 46, 47, 51, 60-66)
Convulsions	Whole plant smoke inhaled	Zimbabwe	(6, 27, 67-71)
Cough	Leaf decoction is taken orally	Pakistan and South Africa	(6, 41, 42, 51, 52, 56, 62, 64)
Depressed fontanelle	Ointment of whole plant applied topically	Zimbabwe	(6, 27)
Diarrhea	Leaf decoction is taken orally	Lesotho and South Africa	(6, 72)
Dizziness	Leaf decoction is taken orally	Eswatini	(73, 74)
Fainting spells	Leaf decoction is taken orally	Eswatini	(73, 74)
Headaches	Leaf decoction is taken orally	South Africa	(6, 41, 42, 47, 51, 53-55, 70, 75)
Head colds	Leaf decoction is taken orally	South Africa	(6, 41, 42, 44, 45, 47, 51-54, 56)
Herbal medicine uses not specified	Not specified	Kenya	(6, 31)
Internal sores	Rhizome and root decoction taken orally	South Africa	(6, 41, 47)
Insomnia	Not specified	South Africa	(52, 53)
Intestinal parasites or worms	Rhizome decoction is taken orally	South Africa	(5, 6, 23, 43, 44, 46, 47, 52, 53)
Mouth and nasal ulcers	Rhizome decoction applied topically	South Africa	(6, 41, 47, 54)
Placental expulsion	Rhizome decoction is taken orally	Lesotho	(6, 61)
Lucky and protective charm	Rhizomes and whole plants used	Lesotho, South Africa and Zimbabwe	(5, 23, 27, 60, 61, 63, 65)
Prevent abortion	Powder of whole plant decoction taken orally or smoke directed into the vagina	Zimbabwe	(6, 27)
Skin problems	Leaf decoction applied topically	South Africa	(51-53)
Sores	Rhizomes and root decoction applied topically	Eswatini and South Africa	(51, 57, 58)
Sore throat	Rhizomes and root decoction taken orally	South Africa	(51)
Tuberculosis	Root decoction is taken orally	South Africa	(6, 59, 76, 77)
Uterine pains	Whole plant decoction is taken orally	Malawi	(6, 27, 55)
Ethnoveterinary medicine			
Placental expulsion in cows	Rhizomes used	Lesotho and South Africa	(5, 23, 60, 61, 63, 65)

Table 2 Phytochemical composition of *H. calomelanos* leaves (52)

Chemical components	Value (%)
Flavonoids	-
Steroids	-
Tannins	-
Caffeoylquinic acid	-
Caffeoyl-hexoside	-
p-Coumaroylquinic acid	-
Quercetin-O-hexose-O-rhamnoside	-
Benzoic acid, 4-ethoxy-, ethyl ester	0.79
Hexadecanoic acid, methyl ester	0.83
L-Proline, N-pivaloyl-, heptadecyl ester	1.74
Methyl stearate	0.47
N-Ethylpyrrolidine-2,2-dicarboxylic acid, dimethyl ester	0.60
Propanoic acid, 2-methyl-, 2-ethyl-3-hydroxyethyl ester	0.33
Succinic acid, but-3-yn-2-yl 2-methoxy-5-methyl phenyl ester	0.49
Phthalic acid, 2-chloropropyl hexyl ester	0.53
Phthalic acid, 3,3-dimethyl but-2-yl tetradecyl ester	0.18
Phenol, 2,5-bis(1,1-dimethyl ethyl)	0.46
Phytol	1.5
Ethanol, 2-(2-butoxy ethoxy)	1.7
1H-Isoindole-1,3(2H)-dione, 2-(2-hydroxyethyl)	0.16
2H-imidazole-2-thione, 1,3-dihydro-4-(2-methyl propyl)	0.47
Ergotaman-3',6',18-trione, 9,10-dihydro-12'-hydroxy-2'-methyl-5'-(phenylmethyl)-,(5'à,10à)	6.23
Cycloheptasiloxane, tetradecamethyl	2.2
Cyclohexasiloxane, dodecamethyl	0.48
Cyclooctasiloxane, hexadecamethyl	1.5
Dodecanamide	0.29
Cyclo-(l-leucyl-l-phenylalanyl)	0.40
2-Methylmercaptoaniline	0.03
3-Methyl-4-phenyl-1H-pyrrole	0.43
Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-3-(2-methyl propyl)	4.19
5,10-Diethoxy-2,3,7,8-tetrahydro-1H,6H-dipyrrolo[1,2-a:1',2'-d]pyrazine	9.08
Tetradecanamide	0.75

pathogens with the diameter of each zone of inhibition ranging from 3.0 mm to 8.0 mm which was lower than the 10.0 mm to 15.0 mm exhibited by the positive control (54). The documented antibacterial activities appear to account for the therapeutic effects of *H. calomelanos*.

Braithwaite et al. (45) evaluated the antifungal activities of methanol and acetone extracts of *H. calomelanos* leaves and a smoke fraction against *Cryptococcus neoformans* (ATCC 90112) using the microtiter plate technique with amphotericin B as a positive control. The extracts exhibited activities with MIC values ranging from 0.53 mg/ml to >32.0 mg/ml (45). Mabona (48) and Mabona et al. (50) evaluated the antifungal activities of aqueous and dichloromethane: methanol (1:1) extracts of *H. calomelanos* leaves and rhizomes against *Candida albicans, Microsporum canis,* and *Trichophyton mentagrophytes* using the microtiter assay with amphotericin B as a positive control. The extracts exhibited activities with MIC values ranging from 0.5 mg/ml to >16.0 mg/ml (48, 50). Dumisa et al. (79) evaluated the antifungal activities of a 1:1 mixture of dichloromethane and methanol extracts of *H. calomelanos* leaves against *Candida albicans* using the microdilution assay with amphotericin B as a positive control. The extracts exhibited activities with MIC values ranging from 1000.0 µg/ml to >8000.0 µg/ml (78). These antibacterial and antifungal activities of *H. calomelanos* seem to account for the therapeutic effects of the species in humans suffering from microbial infections such as abscesses, asthma, boils, bronchitis, chest pains, colds, cough, diarrhoea, skin problems, sores, sore throat, and tuberculosis. Van Wyk et al. (5) argued that there is no clear link between the chemistry of *H. calomelanos* leaves and its reported therapeutic value but triterpenoids could be responsible for the ethnopharmacological effects. Research by Braithwaite et al. (45) showed that smoke of aromatic plants sometimes has higher antimicrobial activities than the essential oil or solvent extracts, and therefore, smoke inhalation may be a very effective therapy for respiratory infections such as asthma, bronchitis, chest pains, colds, cough, sore throat, and tuberculosis, see Table 1. The leaves of *H. calomelanos* are characterized by bacterial endophytes which demonstrate antimicrobial activities (52-54). Previous research showed that endophytes are capable of producing secondary metabolites with pharmaceutical properties meant to protect their plant host from harmful pathogens (80-83). Therefore, there is a need to understand the interactions between *H. calomelanos* and the symbiotic endophytes.

Conclusion

H. calomelanos is a well-established medicinal Pteridophyte. A large body of ethnomedicinal data exists and to some extent, preliminary phytochemical composition and biological activities have been established. However, the ethnopharmacological evaluations conducted so far are not sufficient to reach a final judgment on the therapeutic potential of *H. calomelanos* in both humans and animals. In addition to this, there are no *in vivo* nor clinical studies that have been conducted. Therefore, detailed studies focusing on pharmacological and phytochemical evaluations including toxicological, *in vitro*, *in vivo,* and clinical studies to corroborate the traditional medical applications of the species are recommended.

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Author's contributions

I conceived the study and wrote the manuscript

Compliance with ethical standards

Conflict of interest: : The author declares that there is no conflict of interest.

Ethical issues: Ethical standards were maintained in writing this article.

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