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Ants and Human Health: What We Know and What We Don't

Muna A Mohamed[1], Awatif K Omer[2], Sulafa Z Mahmoud[3], Nura Z Mahmoud[4], Sally Z Mahmoud[4], El Frazdag A saad[5] and ZN Mahmoud[6]*

[1]*Department of Biology, Faculty of Science, Taibah University, Kingdom of Saudi Arabia, Institute of Environmental Studies, University of Khartoum.*

[2]*Department of Life Sciences and Environmental Sciences, Nile Valley University, Sudan.*

[3]*Faculty of Pharmacy, Ahfad University, Omdurman, Sudan.*

[4]*No. 22/Block 2AE, Khartoum, Sudan.*

[5]*Faculty of Medicine, Taibah University, Kingdom of Saudi Arabia.*

[6]*Department of Zoology, Faculty of Science, University of Khartoum, Sudan.*

***Corresponding author:** ZN Mahmoud, Department of Zoology, Faculty of Science, University of Khartoum, Sudan.

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ABSTRACT

Ants are increasingly recognized as nutritionally valuable and biologically active resources with considerable potential for food, pharmaceutical, and nutraceutical applications. Their lipid contains fatty acids, phospholipids, sterols, and triglycerides that contribute to their nutritional and functional properties. In traditional medicine, various ant species have been used for their potential antioxidant, immunomodulatory, anti-inflammatory, antimicrobial, and aphrodisiac properties. The black ant Polyrhachis vicina has received particular attention in China and neighboring regions because of its diverse bioactive constituents, including alkaloids, superoxide dismutase, and unsaturated fatty acids, which may contribute to its reported medicinal effects. Ant-derived preparations have also been traditionally associated with supporting immunity, vitality, and general health. Furthermore, edible insects are gaining recognition as sustainable sources of nutrients for both human and animal nu. Numerous ant species are consumed, particularly in tropical and subtropical regions, where they provide proteins, lipids, carbohydrates, minerals, and other bioactive compounds. These attributes highlight ants as promising resources for functional foods, nutraceuticals, pharmaceutical products, and value-added food ingredients, and sustainable health-promoting products for diverse applications.

Keyword: Ants; Pharmaceutica Health; Nutraceuticals; Functional foods; Ethnoentomology.

Introduction

Many animals hold significant medical importance. Some are directly used as food or indirectly as a source of nutritive products (egg, honey and milk) or curative products (camels' urine) (Ho, et al. [1-4]); and camel milk (Ho, et al. [1]) Some are medically hazardous (e.g. scorpions, snakes and spiders), causing potentially fatal consequences in humans (Whiley, et al. [5,6]). Laboratory animals, such as the domestic guinea pig (*Cavia porcellus*) and New Zealand rabbit *(Oryctolagus cuniculus)*, are widely used as biomedical models that inspire new treatments and antibiotics production, atherosclerosis, cancers, diabetes mellitus, musculoskeletal studies, immunodeficiencies, cardiovascular diseases and ophthalmological research (Everds and Brayton [7-9]). Throughout human history, people have used various plants and animals as an extensive traditional pharmacopoeia to cure illnesses and promote health (Alves and Rosa [10]). Approximately 80% of rural populations in developing countries depend on traditional medicine for primary healthcare (WHO, 2002), largely because it is accessible and affordable (Alves and Rosa [11]). More than 200 ant species are known to cause medically relevant bites or stings, while some species can also release irritant chemicals. Although most encounters result in mild, self-limiting effects, certain species can cause severe local injury, systemic toxicity, or potentially fatal anaphylactic reactions, particularly following multiple stings or

in susceptible individuals (Klotz, et al. [12-14]). Ant secretions and venoms contain diverse bioactive compounds, including acids, hydrocarbons, peptides, and proteins, exhibiting antimicrobial, anti-inflammatory, analgesic, and cytotoxic activities, highlighting their potential as sources for novel pharmaceutical and therapeutic agents (Schmidt, [15-18]). This work examines the current understanding, emerging medical relevance, and knowledge gaps concerning the biological, ecological, pathological, and therapeutic implications of ants for human health.

Study Methodology

The methodology of this study was partially based on field observations (Omer and Mahmoud [19]); relevant literature identified through Google Scholar and other online scholarly information resources, and oral accounts concerning the use of ants as a potential indicator of diabetes mellitus.

Results and Discussion

Different ethnic and cultural groups across Africa, Australia, South America and southeast Asia have utilized different ant species and their byproducts in traditional medicine, with whole ants, larvae, eggs and venom used to treat rheumatism, infections and pain (Chakravorty, et al. [20]), and in folk medicine in Brazil (Costa-Neto, [21]) and Africa (Mntambo, et al. [22]). Matabele ants (*Megaponera analis*) exhibit sophisticated medical behavior, using metapleural gland secretions to treat infected wounds in nestmates, dramatically reducing mortality by 90% and providing valuable insights into natural wound-healing mechanisms (Frank, et al. [23]).

Ants as Functional Foods and Nutraceuticals for Human Health

Ants are a rich source of food-derived products 'nutraceuticals' such as proteins, amino acids, lipids, polyunsaturated fatty acids, and essential trace minerals like zinc and selenium, that provide health benefits beyond basic nutrition. Ants are traditionally consumed raw, cooked, and preserved across regions. Many ant species are consumed widely in various parts of the world due to their high protein content (Pattarayingsakul, et al. [24]). In India, tribal communities consume *Oecophylla smaragdina* either raw or cooked, while its eggs and larvae are incorporated into cooked soups and/or eaten raw in spicy salads in Thailand in Thailand its (Srivastava, et al. [25]). In Mexico, the brood of *Liometopum apiculatum* and *Pogonomyrmex barbatus* is consumed as cooked food, whereas the repletes of *Myrmecocystus melliger* and *Myrmecocystus mexicanus* are eaten directly (Bodenheimer [26,27]). Likewise, in Zambia and Zimbabwe, winged sexual stages of *Carebara vidua* are consumed raw or after boiling, roasting, or frying, while winged adults of C. *vidua* and *Oecophylla* spp. are also consumed in Congo (Mbata, 1995). For preservation, O. *smaragdina* is roasted and processed into sauce or sun-dried and powdered for later consumption among the Muria of Chhattisgarh, India (Roy and Rao [28]). Its brood is also harvested and marketed for human consumption in Thailand and the Philippines (Offenberg and Wiwatwitaya [29]).

Toasted gravid females of Atta spp. are valued delicacies in parts of South and Central America (Bodenheimer, [26,30]). Amerindian groups in the Amazon basin have also been documented using large leaf-cutting ants as protein sources (Paoletti, et al. [31]). Ant larvae, workers, and egg-laden queens of various ant species are consumed directly, with alate ants noted to contain a higher proportion of fat than workers (Redfo rd and Dorea, 2009). In central Kalahari, worker ants of Camponotus sp. are used as salad seasoning and relished for their sweet-sour flavour (Nonaka, [32]). The nests of this ant species are located only in termite mounds. In Congo, winged adults of C. vidua and all stages of Oecophylla ants are used as food (DeFoliart, [30]). Aborigine of Australia use *Melophorus bagoti* and C. inflatus for food (Islam, et al. [33]). The nutritional composition of edible ants has been investigated across several species, revealing considerable variation in ant-derived nutraceuticals. Larvae and pupae of *Oecophylla smaragdina* are associated with nutritional support and antioxidant potential and contain approximately 12.7 and 12.5 g/100 g of protein and fat, respectively, based on dry/wet weight measurements (Yhoung-aree and Viwatpanich [34]). Similarly, dried powder of *Polyrhachis* dives contains 57 g/100 g protein, 9.0 g/100 g fat, and 13 g/100 g volatile oil (Shen, et al. [35]). Reproductive adults of Atta Mexicana, Atta laevigata and brood of *Liometopum apiculatum* are notable sources of essential amino acids, particularly lysine, leucine, isoleucine, valine, and phenylalanine with nutritional and antioxidant value (Ladrón, et al. [36]).

In *Myrmecocystus melliger*, carbohydrates constitute approximately 78% of the composition, representing a relatively high proportion among insects (Ramos-Elorduy [27]). Furthermore, P. dives extracts contain more than 50 nutritional elements, including 26 amino acids (Chen [37]). *Polyrhachis* dives also provides 77,000 IU/100 g superoxide dismutase and 16 minerals, including nutritionally important K, Ca, P, Mg, Fe, Mn, and Zn (Shen, et al. [35] *P*olyrhachis), demonstrating experimentally antioxidant and immunomodulatory effects. Whereas, *Polyrhachis* vicina exhibit antioxidant and antimicrobial activities.

Bio-Diabetic Indicator

In traditional medicine in Sudan, women from villages remote from medical centers use a chamber pot for urination. They scatter the urine in shaded areas and observe ant activity around urine. These observations were treated as a potential indicator of diabetes mellitus. When blood sugar gets too high, the kidneys push extra sugar into the urine (glucosuria), which may attract ants. Finding of ants (e. g. *Lepisiota affinis* (Figure 1), commonly known as the small black sugar ant and/or the spotted sugar ant *Camponotus maculatus, Camponotus oasium, Camponotus sericeus*, (Figure 2)) near urine can suggest high sugar levels, but it is not a definite proof of diabetes, as glucosuria can also occur for reasons other than diabetes. Ideally, this

simple indicator is useful when linked to the unique clinical presentation of diabetes mellitus, such as polyphagia, polydipsia, and polyuria (Kannan [38]). This reservation is based on the principle that interspecific communication in ants is primarily mediated through chemical signaling (Hölldobler and Wilson [39]). These 'sugar' ant species are wide-spread and recorded from at least 14 different Sudanese ecozones (Omer et al. [40]).



Figure 1: *Lepisiota Affinis.*

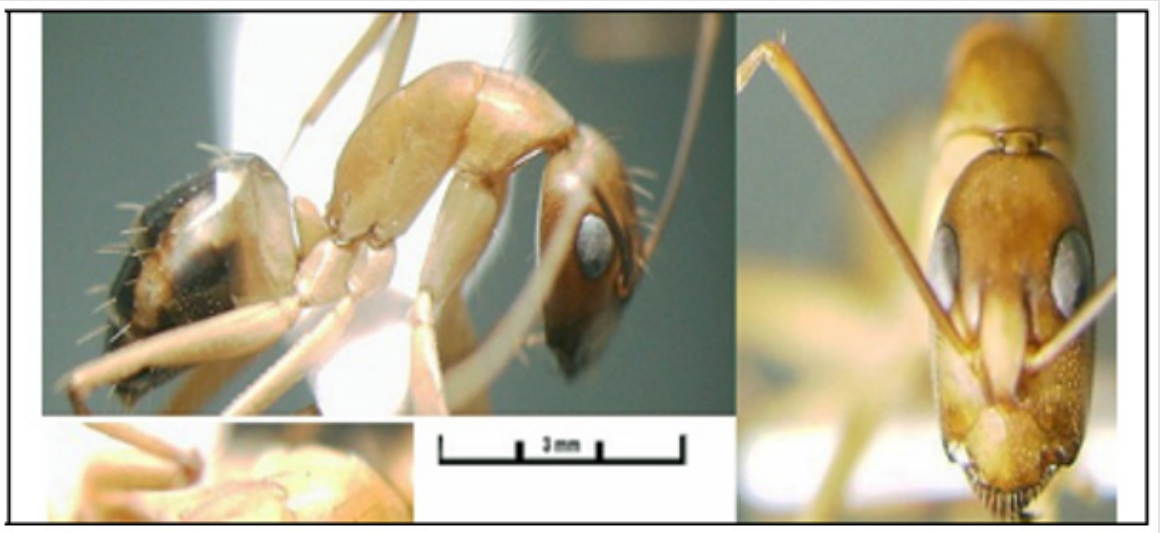


Figure 2: *Camponotus oasium*

Ant-Induced Micturition: A Historical Account

A relative described a historical episode of severe urinary retention that did not respond to conventional urinary-retention medications. He was subsequently advised to consult a traditional herbal practitioner, who instructed the patient's companion to prepare a small, condom-like cotton pouch and fill it with ants locally known as Shahmouta (*Camponotus* species). The patient's penis was inserted into the pouch, which was then tied around the penile shaft. According to the account, urinary flow increased markedly shortly thereafter. This procedure may succeed if the cause is not a physical block-

age, such as a urethral stricture, severe prolapse, or bladder stones (Selius and Subedi [41]). The mechanism remains uncertain. Defensive biting or stinging by confined ants may have produced intense mechanical and nociceptive stimulation, potentially activating autonomic or spinal reflexes involved in micturition. Alternatively, chemical or olfactory cues may have triggered ant activity. This anecdote is historical and does not establish therapeutic efficacy. Acute urinary retention requires prompt medical evaluation.

Medical Applications

According to (Nonaka [32,42]) insects including ant are of entomotherapy, or the medicinal uses.

1) Mud from the interior portion of an anthill and/or crushed black ants, *Bothroponera* rufipes is applied topically for the scabies (Chakravorty, et al. [20]). Scabies is a contagious skin condition caused by a tiny mite called *Sarcoptes* scabiei that burrows into the outer layer of the skin. *Oecophylla smaragdina* is used by Aborigine of Australia as a topical ointment to treat skin infections (Islam, et al. [33, 43]). The indigenous tribes in the Bastar District of India apply live fire ants (Solenopsis species) stings directly to the skin over painful areas (Kumari, et al. [44]). According to (Anal, et al. [45]) Weaver Ants (*Oecophylla species*) is applied to localized pains and skin afflictions. Nest of *Eumeninae* spp. is used in sub-Saharan Africa for curing boils, headache, inflammation, mumps and ulcers (Van Hus [46]).

2) Traditional sutures-based wound management

Indigenous groups in parts of East and Sub-Saharan Africa historically used large driver ants or army ants (*Dorylus* species) as natural surgical staples (Gudger [47,48]). An ant is placed along the edges of an open wound. Once the ant bites down and locks its powerful mandibles (Figure 3) into the skin, its body is twisted off. The detached head and jaws remain clamped shut, effectively holding the wound margins together to close tissue and reduce bleeding until healing occurs (Gudger [47,48]). *Companoutus brutus* and Formica sp. ants are also used as topical application for teatment of wounds (Lawal and Banjo [49]).



Figure 3: Dorylus brevipennis.

Ant-Derived Compounds: Anticancer Therapeutic Potential

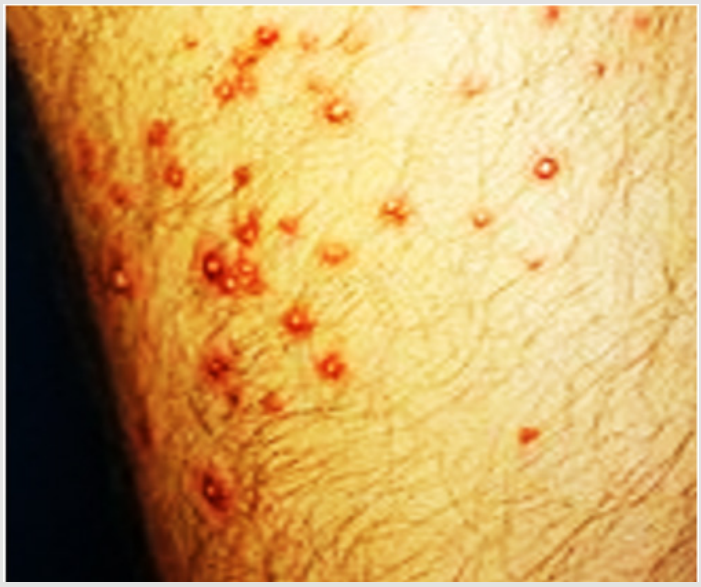
Ant metabolites have anti-cancerous, and various other properties (Al-Tamimi, et al. [50-52]). Many ants such as *Paraponera clavata, Polyrhachis vicina,* and P. *lamellidens* have been reported to show therapeutic potential against cancer, (Dkhil, et al. [53]). The venom of *Pachycondyla senaarensis,* and P. *lamellidens* ants have anti-cancer, and anti-inflammatory potential (Dkhil, et al. 53). Moreover, it also showed anti-neoplastic activity in breast cancer cell lines. Solenopsin and its analogs, from the fire ant (Solenopsis invicta), inhibit phosphatidylinositol-3-kinase, a molecular target for cancer, and has a potential utility as antineoplastic agent (Arbiser, et al. [54]). Further studies on the venom components of S. invicta can help in designing novel anticancer drugs. The venoms of *Tetraponera* spp. contain neurotoxic alkaloids known as tetraponerines, which have attracted interest for their potential cytotoxic and antiproliferative activities. Tetraponerines T5–T8 demonstrated antiproliferative effects against four carcinoma cell lines, with C5 configuration influencing their potency; notably, T7 showed cytotoxic activity against MCF-7 breast cancer cells (Bosque, et al. [55]). Venom-associated compounds from *Odontomachus* monticola have demonstrated antiproliferative activity, while dipeptidyl peptidase inhibits malignant phenotype of prostate cancer cells by blocking basic fibroblast growth factor signaling pathway (Wesley, et al. [56]).

A cytolytic dipeptide isolated from *Tetramorium bicarinatum* was developed as a cancer therapeutic agent (Touchard, et al. [57]). Treatment with hemolymph of C. *compressus* showed anti-hyperglycemic activity in the liver and pancreas of diabetic rats (Krishnan, et al. [58]). Nybomycin, obtained from the endosymbiont Streptomyces of the carpenter ant *Camponotus vagus* Scopoli, also has cytotoxic activity against fibroblasts and lung cancer (Zakalyukina, et al. [59]). Prodigiosin obtained from the endosymbiont Serratia marcescens of *Camponotus floridanus* (Gerber [60]) blocks Wnt/β-catenin-signaling by targeting multiple sites of this cascade which is associated with various types of cancer (Wang, et al. [61]). Experimental studies demonstrate that trained Formica *fusca* workers can discriminate volatile organic compounds (VOC) profiles from human cancer-cell cultures and distinguish urine from tumour-bearing versus tumour-free mice (Costa and De Martinis [62-66]).

Stinging and Venomous Ants: Species, Human Health Risks, and Global Distribution

Approximately 71% of ant species are considered capable of stinging, including medically important genera such as *Solenopsis* (fire ants), *Myrmecia* (bulldog ants), and *Paraponera* (bullet ants). (Schmidt [15]) comprehensively reviewed the chemical composition and pharmacological effects of ant venoms, emphasizing their considerable diversity and biological significance. Most ants can bite, sting, or spray irritant chemicals; however, relatively few species cause clinically significant effects in humans, with severity depending on the ant species and individual susceptibility (Touchard, et al. [57,67,68]). Venoms primarily contain proteins, peptides, and alkaloids, whose components contribute differently to envenomation responses. Clinical effects range from mild, localized reactions at the sting site to severe, potentially fatal anaphylaxis (Chen [37]). Stings from Solenopsis are particularly painful, whereas *Paraponera* is considered to produce among the most painful insect stings (William, et al. [69]). Ants bite or sting when threatened, trapped, or disturbed. Alarm pheromones alert nearby workers, while environmental conditions, bare-handed handling, and proximity to food increase defensive encounters.

Fire Ants: Fire ants *(Solenopsis)* comprise over 200 stinging species. Their venom consists mainly (>95%) of piperidine-derived oily alkaloids (solenopsins), with <1% toxic proteins (Pinto, et al. [70-71]). Stings cause immediate pain and localized burning, followed by urticaria (Fox [71]). Within hours, swelling may develop into a white pustule after 24–36 hours, usually flattening within days (Figure 4) but potentially becoming infected or scarred if scratched (deShazo, et al. [72]). Some individuals develop venom allergies that may progress to anaphylaxis, requiring emergency adrenaline treatment (Lee and Betschel [73-75]). Pustules result from alkaloids, whereas allergic reactions are caused solely by allergenic venom proteins (Javors, et al. [76, 73]).

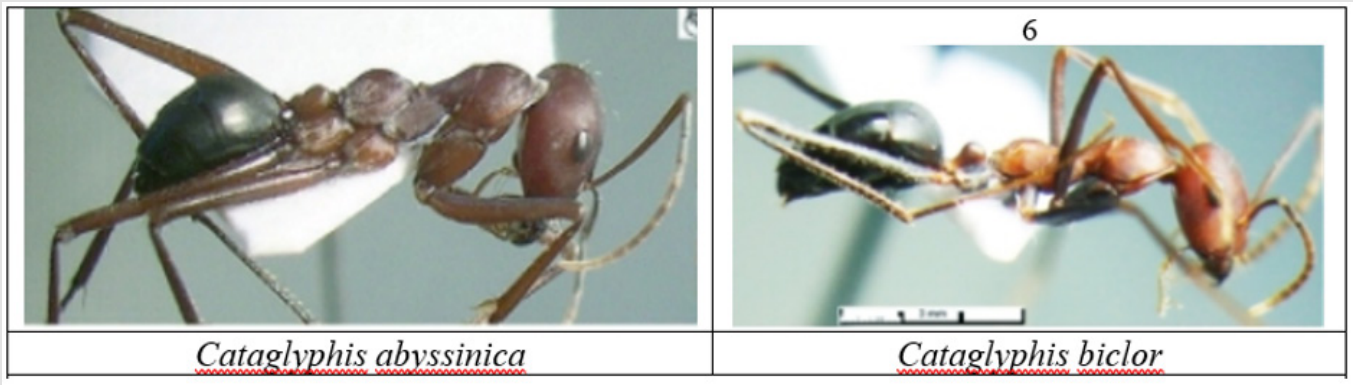


Source: Wikipedia 9/9/2026
Figure 4: Pustules 3 days after fire ant stings.

Pseudo-Fire Ants: Sudan is home to several ant species frequently mistaken for fire ants because of their aggressive behavior and painful, burning stings (Omer and Mahmoud [19]). These ants may clamp onto the skin with their jaws and inject venom, producing intense burning sensations and, in some cases, white pustules. Among them, the Samsum ant (Brachyponera sennaarensis, (Figure 5)) is the most common biting and stinging ant in Sudan. The Brachyponera ruginota is less widely distributed than B, sennaarensis (Omer, et al. [40]).



Figure 5: *Brachyponera sennaarensis.*



Note:

- *Cataglyphis abyssinica*
- *Cataglyphis biclor*

Figure 6: Some *Cataglyphis* genera, Subfamily: Formicinae.

Other stinging Sudanese ants belong to 14 Cataglyphis (Figure 6), 24 Crematogaster and 18 Monomorium species. Local populations often colloquially refer to any small, reddish-brown ant that inflicts a burning sting as a "fire ant."

The Bullet Ant: *Paraponera* clavata, commonly known as the bullet ant, is a ponerine ant distributed across humid lowland rainforests of Central and South America. Its sting is rated at the highest level (4) of Schmidt's sting pain index (Schmidt [77]) and produces intense, prolonged pain, accompanied by symptoms such as tremor and local inflammation (Schmidt [77,78]). Its venom contains poneratoxin, a 25-residue neuroactive peptide that modulates voltage-gated sodium channels and disrupts synaptic transmission (Piek, et al. [79,80]). Poneratoxin is a neurotoxic venom peptide that modulates voltage-gated sodium channels, disrupts neural transmission, and shows potential for medical applications (Szolajska, et al. [81]).

Bulldog (Bull ants or Jack Jumper) Ants: The genus Myrmecia comprises 93 species, primarily distributed across Australia and its coastal islands, with one species restricted to New Caledonia, and is renowned for aggressive behaviour and painful stings (Ant Web [82]). *Myrmecia pilosula* venom is highly effective and can cause severe allergic reactions. In Tasmania, approximately 3% of people experience venom allergy, which may result in life-threatening anaphylaxis following stings. Venom immunotherapy (desensitisation) can reduce the risk of severe reactions (Brown, et al. [83,84]).

Harvester Ants: Harvester ants are not a single species but rather a functional group of any of the species or genera of ants that collect seeds. Seed harvesting by some desert ants is an adaptation to the lack of typical ant resources such as prey or honeydew from hemipterans (Beekman [85]). Harvester ants have a rather potent venom. They inject it into their victim via sting by biting down and following up with a rapid sting from their abdomen. This causes 4–8 hours of sharp pain with effects similar to neurotoxicity such as piloerection and localized swelling around the area of the sting (Schmidt [77]). (Omer, et al. [39]) document several species of harvester ants in Sudan across the savanna and semi-arid desert ecosystems. These are *Messor galla, Messor aegyptiacus, Messor angularis, Messor arenarius, Messor barbarus*, and *Messor ruginodis*. Although *Messor* species possess venom containing alkaloids, they are generally considered to pose little threat to humans, and detailed clinical descriptions of their sting-associated pain and local reactions are limited (Uhey and Hofstetter, [86]), compared with Pogonomyrmex and Veromessor harvester ants.

Traditional Entomotherapy Medicinal Uses and Pharmacological Activities of Ants

Ants and their products have a long history of use in traditional medicine across different cultures. Whole ants, larvae, eggs, and venom have been employed to treat a wide range of conditions, including rheumatism, infections, inflammation, pain, and other ailments (Song et al., [87,20,88,89]). Several ant species are traditionally used for gastrointestinal and general health conditions. According to Van Huis [90], *Phedole* sp. is used to treat stomach problems, while whole *Oecophylla* smaragdina ants are consumed as an aphrodisiac. *Oecophylla smaragdina* has also been used by Aboriginal communities in Australia for medicinal purposes. Crushed green tree ants produce a sour, formic-acid-rich water extract traditionally used to treat inflammation and skin infections. The resulting lemon-flavoured drink is also consumed to relieve colds, headaches, and sore throats (Vidhu and Evans [91]). According to Ragunath, et al. [92-93], and the references therein, O. *smaragdina* is traditionally used to treat ≈ 28 diseases including cough, cold, and flu in Africa, Australia, and Southeast Asia (Rastogi, et al. [94, 92, 95]). Aboriginal Australians have also used O. *smaragdina* for headache, and stomach troubles (Islam, et al. [33]). Other Oecophylla preparations have been associated with additional traditional medicinal applications. In Thai culture, O. *smaragdina* has been used for blood detoxification, control of hemorrhage during miscarriage, restoration of the uterus and removal of uterine remnants following childbirth, stimulation of the pulse and heartbeat, and relief of dizziness (Pattarayingsakul, et al. [24]).

The species *Pseudoneoponera* rufipes is traditionally used by gargling ground ants mixed with water to relieve toothache, while consumption of one to two ants per day has been reported for blood-pressure reduction (Siddiqui, et al. [96]). Several *Camponotus* species are also associated with traditional medicinal practices. Adult *Camponotus maculatus* have been used to treat alcoholism (Loko, et al. [97]) and azoospermia (Lacroix, et al. [98]), foot pain and fever (Ouango, et al. 99). Honeypot ants, Camponotus inflatus, are used in traditional medicine by Aboriginal Australians (Islam, et al. [33]). In addition to these traditional applications, (Dong, et al. [44]) investigated honey produced by C. inflatus and reported activity against the bacterium Staphylococcus aureus and the fungi Aspergillus and Cryptococcus. Members of the genus Formica have been reported in traditional medicine for a variety of conditions. Adult Formica sp. are used to treat hepatitis B, sexual impotence, and wounds (Lawal and Banjo [49]), as well as enuresis, jaundice, malaria, memory loss, and ulcers (Loko, et al. [97]). Similarly, *Myrmicaria opaciventris* has been used traditionally to treat enuresis in children aged four to five years in the western regions of Cameroon (Van Huis [46]). The medicinal use of ants also extends to respiratory, cardiovascular, and pain-related conditions. The leaf-cutting ants Atta cephalotes, Atta *serdens* and Atta spp., are traditionally used in Latin America to treat sore throat, stomachache, chest palpitations, and heart disease (Alves and Alves [100]). *Acromyrmex landolti* is an old-style for curing asthma in Brazil (Costa-Neto [101]). Venom from *Dinoponera* ants has demonstrated antinociceptive activity, providing pharmacological evidence relevant to its traditional use for asthma, rheumatism, and back pain in Latin America (Alves and Alves [100]).

Ant-derived compounds have also attracted attention for their antimicrobial, anti-inflammatory, antiproliferative, and other pharmacological activities. Red ants (Tetramorium spp.), used in traditional Chinese medicine, contain the alkaloid N-(2-hydroxyethyl)-benzamide, which demonstrated strong antimicrobial activity against Bacillus subtilis, comparable to that of the positive control (Song, et al. [87]). Chinese black ants, *Polyrhachis* dives, are traditionally used to treat rheumatoid arthritis, osteoarthritis, inflammatory diseases, and disorders associated with the central nervous system (Tang, et al. [88]). Several compounds, including Polyrhadopamines A–E (16–20), troline (21), and compounds 22–30, have been isolated from P. dives and evaluated for anti-inflammatory, antiproliferative, and renoprotective activities (Tang et al., [88,102]). Fire ants have likewise provided bioactive compounds of pharmacological interest. Solenopsin A (8), an alkaloid isolated from Solenopsis invicta and Solenopsis geminata, has been reported to possess antiangiogenic activity. Its proposed mechanism involves selective inhibition of protein kinase B (AKT), a molecular target of interest in cancer research (Arbiser, et al. [54, 103,104]). Ants have also been used in traditional veterinary medicine. The iron ant, Tetraponera rufonigra, is used by local tribes in northeastern India to treat foot-and-mouth disease in cattle. One to two ants are crushed into a powder, mixed with fodder, and administered to cattle up to three times daily (Chakravorty, et al. [20]). Species of Tetraponera are known for potent venom and chemical defenses, which have been associated with antiproliferative activities (Rouchaud and Braekman [105]). Although modern veterinary medicine primarily relies on vaccination and strict biosecurity for con-

trolling foot-and-mouth disease, traditional remedies involving insects and plants continue to be used in remote areas where access to commercial veterinary care may be limited (Seabrooks and Hu [89]).

Ants as A Sources of Pharmaceutical and Biomedically Relevant Compounds

Ants produce diverse chemical secretions involved in defense, communication, and colony protection, including formic acid, hydrocarbons, peptides, proteins, and other bioactive compounds (Hölldobler and Wilson [39]). Their venoms and secretions possess antimicrobial, anti-inflammatory, analgesic, and cytotoxic activities (Tables 1, 2), highlighting their potential as sources of novel therapeutic agents (Agarwal, et al. [18]). Increasing biochemical and pharmacological evidence further supports the medicinal potential of ants and their defense-derived bioactive compounds.

Table 1: Non-proteinaceous bioactive compounds found in ants and their properties (adapted and modified from (Agarwal, et al. [18]).

Compound	Property
Phenolics	Used in food and cosmetics as an additive (to prevent rancidity), antioxidant, with anti-inflammatory and anti-microbial activity
	Anti-malarial, anti-inflammatory property, neurotoxic activity
	Anti-inflammatory, antioxidant, anti-proliferative, and anti-bacterial property
Pyrazines	Antioxidant, anti-fungal, anti-inflammatory, inhibit bacterial biofilm formation
Acidic compounds	Antioxidant, anti-bacterial, anti-viral, and hypocholesterolemic activities
Alkaloids	Anti-microbial property
	Anti-angiogenic, anti-cancerous activity
	UV-resistance; anti-microbial and anti-cancerous property
Esters	Anti-arthritic property
Alkylamines	Anti-microbial activity
Long chain fatty alcohols	
Polyketide lactones	Anti-arthritic property

Table 2: Proteinaceous bioactive compounds found in ants and their properties (adapted and modified from (Agarwal, et al. [18]).

Proteinaceous Bioactive Compounds	Reported Biological Activity/Function
U1-PSDTX-Pt1 subunit LS1	Anti-inflammatory
U1-PSDTX-Pt1 subunit LS2	
U-poneritoxin(01)-Dq6a	Anti-trypanosomal activity
Phospholipase A1	Immunomodulatory/immunological activity
M-poneritoxin-Ng1a	Antimicrobial and insecticidal
U1-myrmicitoxin-Mr1a	
U-myrmeciitoxin(01)-Mg3a	Antimicrobial activity
U-myrmeciitoxin(01)-Mg4b	
U-poneritoxin(01)-Om1a	
M-poneritoxin-Da4b	
U1-poneritoxin-Da3b	
M-ectatotoxin-Eb2b	
Delta-paraponeritoxin-Pc1a	
M-myrmicitoxin(01)-Tb1a	
U1-poneritoxin-Dq5a	Neurotoxic activity
Omega/M-ectatotoxin-Et1a subunit A	
U1-poneritoxin-Ae1a	
U1-ectatotoxin-Eb1a subunit A	
U1-ectatotoxin-Eb1a subunit B	
U1-poneritoxin-Na1a	Anti-microbial, hemolytic activity, and insecticidal
U1-poneritoxin-Ni1a	
M-myrmeciitoxin-Mb2a	Anti-microbial and histamine-releasing activity
M-myrmeciitoxin-Mb1a	
M-myrmeciitoxin-Mp1	Cytotoxic, hemolytic, and anti-microbial activity

Non-proteinaceous bioactive compounds

1) An array of structurally diverse non-proteinaceous bioactive compounds was identified in ant secretions (Table 1), encompassing phenolics, pyrazines, acidic compounds, alkaloids, esters, alkylamines, long-chain fatty alcohols, and polyketide lactones, which may contribute to the biological activities of

ant secretions through distinct and often structure-dependent molecular mechanisms.

2) Phenolic compounds exhibit diverse bioactivities attributable to their capacity for hydrogen/electron donation, redox modulation, and interactions with cellular signaling pathways (Stevens, et al. [106]). Reported antioxidant, anti-inflammatory, antimicrobial, antiproliferative, and antimalarial effects in ants are structure- and concentration-dependent (Hoenigsberger et al. 2019 and 2020).

3) The diverse biological activities of Pyrazines are related to their nitrogen-containing heterocyclic structures and molecular interactions with cellular targets (Hou, et al. [107]).

4) Acidic compounds may exhibit antioxidant and antimicrobial effects through redox modulation and interference with microbial growth. Reported antiviral and hypocholesterolemic activities are compound-specific (Hoenigsberger et al. 2019 and 2020).

5) Alkaloids exhibit diverse pharmacological activities through interactions with microbial membranes, enzymes, nucleic acids, and cellular signaling pathways (Lima, et al. [108,109]).

6) Certain esters exhibit anti-arthritic activity through modulation of inflammatory and oxidative pathways. However, esterification alters physicochemical properties and bioavailability (Balak [110]).

7) Ants Alkylamines may exhibit antimicrobial effects through membrane and cellular interactions. Their activity depends on chain length, substitution, and charge, necessitating compound-specific evaluation (Kabara, et al. [111,112]).

8) Long-chain fatty alcohols possess physicochemical properties enabling interactions with biological membranes and may exhibit antimicrobial or anti-inflammatory effects. However, these activities depend on chain length, concentration, and structure (Kabara, et al. [111])

9) The anti-arthritic activity of polyketide lactones may arise from modulation of inflammatory pathways and mediators.

Proteinaceous compounds identified in ant venom: The reported literature demonstrates that proteinaceous bioactive compounds (PBCs) present in ant venoms exhibit a diverse range of biological activities, including anti-inflammatory, anti-trypanosomal, immunomodulatory, antibacterial, antimicrobial, insecticidal, neurotoxic, cytotoxic, hemolytic, and histamine-releasing effects, highlighting their considerable pharmacological and biotechnological potential (Table 2). The table show that:

1) (Pan and Hink [113]) isolate two PBC compounds with anti-inflammatory activity from the tropical ant, Pseudomyrmex triplarinus.

2) U-poneritoxin(01)-Dq6a extracted from the venom of the predatory giant ant Dinoponera quadriceps by (Torres, et al. [114]) proved to be Anti-trypanosomal.

3) The fire ant sting proved to exhibit immunotherapy function (Hoffman, et al. [115]). The venom of Solenopsis invicta is an effective source of immunotherapy as it is rich in phospholipase A1. Its venom is a mixture of allergens, toxins, and components required by the ant for its protection from its own venom (dos Santos, et al. [70]). The venom of S. invicta inhibits Pseudomonas fluorescens (de Carvalhoet al., 2019).

4) New antibacterial and insecticidal peptides from the venom of the ant Pachycondyla goeldii was detected by (Orivel, et al. [116]) and from the venom from the ruby ant Myrmica rubra by (Heep, et al. [117]).

5) Eight PBC with antimicrobial activities were recovered from several ant species including D, quadriceps by (Torres, et al. [114]); of the giant ant Dinoponera quadriceps (Cologna, et al. [118]); Odontomachus monticola (Kazuma, et al. [119]); the giant red bull ant, Myrmecia gulosa (Robinson, et al. [120]).

6) Neurotoxic activity was detected in the venom of ants by (Aili et al., [55,114,57]).

7) From the jumper ant Myrmecia pilosula the peptide M-myrmeciitoxin-Mp1 with cytotoxic, hemolytic, and antimicrobial activity was described by (Wu, et al. [121]). Similarly, the Australian ant genus Myrmecia, M-myrmeciitoxin-Mb2a and M-myrmeciitoxin-Mb1a show antimicrobial and histamine-releasing capacity (Inagaki, et al. [122]). Similarly,

8) Anti-microbial, hemolytic activity, and insecticidal activities of U1-poneritoxin-Na1a and U1-poneritoxin-Ni1a were reported from the venom of ants by (Aili, et al. [55]).

Ants as Mechanical Carriers of Pathogenic Bacteria and Fungi

Ants are not typically biological vectors but can mechanically carry pathogens on their bodies and appendages. While scavenging contaminated areas such as trash, sewage, and decaying matter, they acquire bacteria and fungi, subsequently transferring these to food and hospitals.

Pathogenic Bacteria: The Pharaoh ant, Monomorium *pharaonis*, has been reported to harbor pathogenic bacteria, including Pseudomonas aeruginosa, S. aureus, Klebsiella spp., Salmonella spp., and Escherichia spp., with P. aeruginosa being the most frequently isolated pathogen (Lutinski, et al. [123]). According to (Alharbi, et al. [124]) bacterial isolates associated with M. *pharaonis aincluding* Shigella *sonnei*, Acinetobacter *lwoffii,* Serratia marcescens, Salmonella *choleraesuis*, Proteus mirabilis, Pseudomonas *luteola*, Hafnia alvei, and Klebsiella *ozaenae*. Monomorium destructor carry a similarly diverse array of pathogenic bacteria posing a major public-health challenge

(Ifeoma [125]). The Ghost Ant (T. *melanocephalum*) and the Crazy Ant (P. longicornis) are problematic in hospitals, they move between sterile zones and waste areas, carrying opportunistic pathogens like Staphylococcus spp., Serratia spp., and Klebsiella spp., (Rodriguez, et al. [126]). Fire ants (Solenopsis invicta and Solenopsis spp.) can carry pathogens, including Salmonella, E. coli, and Clostridium. Their stings break human skin introducing these bacteria (Ifeoma, [125]). Paratrechina spp. and Monomorium floricola ants were found most frequently in São Paulo, Brazil. the hospital. Ants had a high capacity for carrying bacteria such as Bacillus spp., Listeria spp., Pseudomonas aeruginosa, Klebsiella spp., Streptococcus spp. and S. aureus (Máximo, et al. [127]). Pavement Ants (Tetramorium caespitum) nest in cracks near pavements, sidewalks, and trash piles, their bodies routinely pick up coliforms and soil-borne pathogens before they invade indoor pantries (Ifeoma [125]). Odorous House Ants (Tapinoma sessile) crawl through sewage lines, pipes, and garbage, and can pick up E. coli, Salmonella spp., S. aureus, Klebsiella pneumoniae (Ifeoma [125]).

1) Contamination of Food.

The Argentine Ant (Linepithema humile) carry foodborne pathogens like Escherichia coli and Salmonella spp., (Wetterer, et al. [128]). Ants Technomyrmex difficilis and Solenopsis geminata are often found in domestic kitchens of Mauritius harboring Bacillus spp., E. coli, Salmonella spp., and Listeria monocytogenes (Simothy, et al. [129]). (Guarda, et al. [130]) found that kitchens and canteens in schools are dominated by Monomorium floricola, M. pharaonic, Pogonomyrmex naegelii, Dorymyrmex brunneus, Solenopsis saevissima, Brachymyrmex sp., Pheidole sp., and Pubiventris sp., harboring Staphylococcus aureus and E. coli. They stated that the presence of ants in school kitchens and canteens may pose a risk of food contamination.

2) Contamination of Hospitals.

Ant species such as: *Linepithema humile*, Tapinoma *melanocephalum, Brachymyrmex* sp., *Paratrechina* longicornis, Monomorium pharaonis, Solenopsis saevissima, Tetramorium bicarinatum and Wasmmania auropunctata are mechanical carrier of Bacillus sp., E. coli, Enterobacter sp., Enterococcus sp., Klebisiella sp., Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus capitis, Staphylococcus haemolyticus, Staphylococcus cohii and Staphylococcus saprophyticus; Pseudomonas aeruginosa of the hospital (Máximo et al. [127,131-133, 125]). Paratrechina longicornis is a vector of pathogens in Iranian hospitals (Shahi, et al. [134]). Out of 59 ant species in Brazilian hospitals, Tapinoma melanocephalum, P. longicornis and Solenopsis saevissima were the most common (de Castroa, et al. [131]). Klebisiella pneumoniae is highly dangerous to newborns and individuals undergoingintensive treatment, especially the strain producing carbapenemases (Miranda, et al. [135]). It is important to highlight that the 12 different isolated etiological agents were found associated to M. pharaonis with this ant considered as the most contaminated. Studies in Indonesia found four strains of microorganisms associated only to M. pharaonis (Lestari, et al. [13]) and elevated levels of contamination were associated with T. melanocephalum with 60 species of bacteria (Teixeira, et al. [137]).

3) Fungi Isolated from Ants in Hospital Environments

Ants found inside hospitals can carry pathogenic fungi on their external surfaces (Table 3). Aspergillus flavus collected from *Camponotus* vittatus. *Cyphomyrmex rimosus* and Pheidole megacephala is an opportunistic fungi pathogen (Aquino, et al., [138]). Similarly, is the fungus *Purpureocillium lilacinum* from Tapinoma *melanocephalum* from and *Paratrechina* longicornis (Aquino, et al. [138]). According to (Pantoja, et al. [139]) over 75% of the ants from two public hospitals in Fortaleza, Ceará. carried pathogenic fungi, with Tapinoma *melanocephalum* and Pheidole spp., were the principal carriers. (Aquino, et al. [138]) from a public hospital in Itabuna, northeastern Brazil found 42 ant species yielded 47 fungal strains, with Aspergillus, *Purpureocillium*, and Fusarium being the predominant genera. Ants in hospital environments such as T. *melanocephalum*, P. longicornis, P. megacephala, S. *saevissima* and C. vittatus, T. *simillimum*, established fungal/pathogen carriage and mechanical transmission of A. flavus, F. *solani*, P. *lilacinum* and Rhizopus spp. However, carriage alone is not direct proof of ant-mediated transmission or causation of hospital-associated infection.

Table 3: Medically relevant fungi associated with ants collected in hospital environments.

Ant Species	Fungal Taxon	Medical Relevance	Reference
Tapinoma melanocephalum	*Aspergillus flavus*	Cause invasive aspergillosis	(Pantoja, *et al*. [139])
	Fusarium solani	Invasive and localized human infections	(Aquino, *et al*. [138])
	Cladosporium cladosporioides	Primarily environmental	
Tetramorium simillimum	*Aspergillus flavus*	Opportunistic pathogen	
Paratrechina longicornis	*Cladosporium cladosporioides*	Environmental mold	
	Rhizopus sp.	Can cause invasive mucormycosis	
Tapinoma melanocephalum	*Mucor* sp.		
Solenopsis saevissima	*Cunninghamella echinulata*		
Pheidole megacephala	*Purpureocillium lilacinum*	Uncommon human pathogen	
Tapinoma melanocephalum	*Candida* spp.	Some species cause bloodstream infections	(Pantoja, *et al*. [139])
Pheidole spp.	*Rhodotorula mucilaginosa*	Immunocompromised patients	

Future perspectives

(Piqueret, et al. [140]) stated that ants learn fast and do not forget: associative olfactory learning, memory and extinction. (Piqueret, et al. [141]) examined the potential of invertebrates in detecting disease via olfaction. These qualifies certain ant species (e. g. Formica *fusca, Lasius niger, Camponotus* spp., and *Linepithema* spp.). through leaning to detect changes in biological matrices including urine *odours* and potentially sweat. In this context, trained ant workers can discriminate diseases-associated urinary VOC profiles through a three-group comparison design (Table 4). This design would help distinguish condition-associated VOC patterns from both normal physiological variation and VOC alterations that may occur across different disease states. Important prerequisites associated with this is collection of material in chemically inert glass containers. Randomize sample identification so that tests are blinded to clinical status. Ant colony preparation require maintaining several target queens under controlled laboratory conditions. For a meaningful interpretation, the experiment should avoid treating individual observations from the same patient or colony as independent. A suitable hierarchical model would be a generalized linear mixed-effects model, where random effects account for repeated measurements associated with individual ants, colonies and patients.

Table 4: Experimental groups and their roles in assessing ant responses to disease-associated volatile organic compounds (VOCs).

Group	Purpose
Patients with the condition of interest.	Assess whether ants respond to VOC patterns associated with the condition.
Healthy controls.	Establish baseline VOC profiles and behavioural responses in individuals without the condition.
VOC from different disease states.	Determine whether observed ant responses are specific to the condition of interest or reflect VOC changes associated more generally with disease.

Conclusions

Ants possess diverse nutritional, nutraceutical, and medicinal applications, with traditional uses addressing gastrointestinal, respiratory, reproductive, inflammatory, infectious, cardiovascular, neurological, and veterinary disorders. Increasing pharmacological research on ant-derived venoms, alkaloids, honey, and other bioactive compounds supports investigation of their therapeutic potential. Advances in metabolomics, genomics, and proteomics have facilitated the identification of bioactive molecules and potential drug targets. Future research on ant extracts and their microbial symbionts may enable environmentally sustainable therapeutic development.

Author Contributions

ZN Mahmoud, MA Mohamed and AK Omer: formatting, verification of scientific names, ants as food, finalization of the draft; SZ Mahmoud pharmaceutical concepts; SZ Mahmoud and NZ Mahmoud ants in traditional and modern medicine. Each contributor reviewed and edited his part.

Ethics

Approval and consent to participate, human and animal rights, consent for publication, availability of data and materials are not applicable. This research did not receive any kind of grant. The authors declare no conflict of interest, financial or otherwise.

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