MEDICAL AND ECONOMICAL SIGNIFICANCE OF MILLIPEDES

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ABSTRACT

Millipedes as saprophagous epigeic fauna members are involved in the decomposition of organic debris. Diplopod's activity improve circulation of nutrients, elements and accelerate environmental reclamation. Beyond mentioned above Diplopoda can provoke sanitary and epidemiological threats especially during swarming or seasonal migrations activities. Considering following aspects: contact with defensive secretions, pseudo-parasitic activity that imitates helminthiasis or passive transmission of pathogens, we can discuss direct or distant effects on human health. Education and proper prophylactic remain neglected. Variety of substances from millipedes are checked for their medical action: direct body extracts and active chemical components from defensive secretion. Millipedes may serve as source for zoo-pharmacology and zoo-indication development. This issue review shows that both pros and cons of the Diplopod's influences should be considered. Literature was carried out from middle of 20th century article till recent papers. The nowadays literature were found in Google Scholar, PubMed, Medline search base.
Keywords: Millipedes, Diplopoda, secretions, medical importance, antibiotic and antifungal activity.

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INTRODUCTION

Both importance in nature and species diversity rank millipedes just after Insecta and Arachnida [1,2,3]. Diplopoda are the numerous taxon of Myriapoda, that cover approximately 12.000 described species gathered in 145 families and 16 orders [4,5,6,7,8]. Millipedes as epigeic litter dwelling decomposers, produce significant amounts of feces that are distributed through different levels of the soil profile. Excrements enrich the soil with more easily and quickly absorbed compounds [9,10].

Most millipedes display a nocturnal lifestyle, their body color oscillate between shades of brown, beige or black, that help to hide. Other species may exhibit an aposematic bright coloration of the body, or even glow [11,12,13,14]. When stressed, millipedes hide the abdominal sensitive part of the body, head and legs through curling up into a ball or spiral fashion. Escaping by jumping away was also observed [15]. Penicillata entangle predator with thicket of bristles that cover their body [16]. These adaptations were caused by the poor motility that limits escape possibility within the dense litter. Millipedes, in the course of antipredatory and anti parasitic behavior excrete defensive secretions [4,17,18,19]. Tropical millipedes *Rhinocricus* sp. can spray their product for an approximately half of meter distance [20]. Diplopoda, due to the lack of structures and organs for active injection of secretions, belong to the group of poisonous animals [21].

Human habitats are commonly visited by millipedes especially during rainy period. Native and accidentally introduced foreign species should be considered as future synanthropic taxon or pest particularly in case of population gradation within migrating population [22,23].

AIM

The goal of this review was the evaluation of Diplopod's medical influences: threats of human health and future millipedes application prospects.

METHODS

The English- language articles review was extracted from Google Scholar, PubMed, Medline search base. Doctorate thesis bibliography, written by first author of this review, served as source, hence this article includes unique information, native published in polish.

DISCUSSION

DEFENSIVE SECRETIONS

Millipedes when disturbed expel defensive secretions. Representatives of the orders Callipodida Glomerida, Julida, Polydesmida Polyzoniida Spirobolida, Spirostreptida have repugnatorial glands [2,11]. The openings of the defensive glands for the most millipedes are located laterally on both sides, starting from the 5th-6th body segment on the metasomite or at the end of the paranotal projections (Polydesmida). Ozopores are distributed along the body segments dorsally for Pentazonia species [24,25,26]. Members of Chordeumatida, Sphaerotheriida, Polyxenida, Siphoniulida and Glomeridesmida lack repugnatorial glands [27]. Considering the structure of the gland and the composition of the defense secretion, Shear [27] after Eisner et al. [17] had listed three groups of defense glands: Glomerida, Julida and Polydesmida. Ilić et al. [28] complemented the list with fourth type: Coloboghnatha. Physical properties (color and odor), characterize taxon (Fig.1). Composition of defensive secretions can be sophisticated and same group of chemicals appear in different taxa, while others are restricted to specific order or species [25,27].

List of organic components include: quinazolinone alkaloids (glomerine, homoglomerine) (Glomerida); heterocyclic molecules substituted with nitrogen (for Polyzoniida); terpenes (pinen and limonene) (for Polyzoniida, Siphonophorida); benzoquinones, hydroquinones and their derivatives (for Julida, Spirobolida, Spirostreptida); phenols (for Callipodida, Julida, Polydesmida) [29-37]. Cyanogenic compound such as mandelonitrile; benzoyl cyanide are noted for all millipedes but few [38, 39]. Well documented in the literature, and thus extremely diverse in terms of chemical composition of defense substances, is the Juliformia superorder [19,27,37,40,41].

Fig. 1. *Blaniulus guttulatus* (Fabricius, 1798). Blind Julida member, discharging the characteristic pigmented defensive secretion. Photo Monika Jung.

MEDICAL IMPORTANCE, SHORT AND LONG TERM EFFECTS ALTERNATIONS

Reports on the threat of human health associated with defensive secretions concern on the possibility of local dermal and systemic malfunction or toxicosis [42,43]. Blackening erythematous lesions but also paresthesia was described by Neto et al. [44] on emergency room case report of 23-year-old female in Bangu, Rio de Janeiro. Odors emitted by the millipede *Oxidus gracilis* (C.L.Koch, 1847) (Polydesmida) cause headaches after prolonged exposure [45]. Julida; *Cylindroiulus caeruleocinctus* (Wood, 1864), *Cylindroiulus latestriatus* (Curtis, 1845), *Choneiulus palmatus* (Němec, 1895), *Ommatoiulus sabulosus* (Linnaeus 1758), *Leptoiulus proximus* (Němec, 1896) secrete para-benzoquinone known for their genotoxic effects. Methyl-1,4 benzoquinone present in the secretions of the Brazilian Spirobolida species *Rhinocricus padbergi* Verhof, 1938 and *Floridobolus penneri* Causey, 1957 leads to carcinogenesis [20, 32]. Benzoquinones ejected by tropical species when reach ocular area leads to lacrimation, periorbital oedema, conjunctivitis, keratitis followed by corneal ulceration. The oily and adhesive secretion, causes contact erythema and blisters [46].

The most common event is accidental rupture of a millipede hidden in clothing, footwear or leaf litter and provoke lesions; erythematous, purpuric, cyanotic [44,47]. Painful, burning sensation, dermatitis and necrosis of the limb and proximities appear and clinical picture depends upon chemical composition of the secretion and the time of exposure [42,48].

Prolonged contact with the skin and accompanying mucous membranes provoke recovery difficulties of the tissue with possible gangrene progression. Pathogenesis includes: superficial dermal injury, burns of the skin followed by blisters with discoloration that undergoes secondary infection. Browning, blackening and unusual skin abbreviations mask inflammation that can persists even for a few months [46,47,49-51].

MEDICAL ISSUES AND DISEASES RELATED

Incidental ingestion of millipedes leads to noninvasive colonization of human alimentary tract. Numerous *Nopoiulus kochii* (Gervais, 1847) were seen in excrement and vomited material [52]. Mowlavi et al. [53] reported *Brachyiulus lusitanus* Verhoeff, 1898 being free living inhabitant of gastrointestinal tract. According to Kiełczewski [54] *Polydesmus complanatus* (Linnaeus, 1761) and *Julus terrestris* Linnaeus, 1758 provoked ailments similar to helminthosis. Stojałowska [55] after Brumpt [56] and Pawłowski [57] have listed *Cylindroiulus teutonicus* Pocock, 1900 *Julus terrestris* Linnaeus, 1758. and *P. complanatus* as pseudoparasites. Unpalatable taste is being masked by fruits and vegetables occasionally inhabited by foraging millipedes *Blaniulus guttulatus* (Fabricius, 1798). There is a possibility of oral administration of millipede's eggs or immature stages from drinking water [55].

Epidemiological issue is proposed also for tapeworm transmission. Vakarenko and Kornyushin [58] described larval cysticercoid: *Sobolevitaenia verulamii* (Cestoda, Cyclophyllidea), carried by *Glomeris connexa* C. L. Koch, 1847 (Glomerida). Adult tapeworm is bird's (Turdinae) dwelling parasite. Dipolpoda: *Fontaria virginensis* (Gray, 1832) (Polydesmida) and *Julus* sp. serve as intermediate hosts for larvae of the flat worm *Hymenolepis diminuta* (Cestoda, Cyclophyllidea). Humans may be the definitive host for this species, not to the mention the possibility of auto-invasion hence multiple infections [59,60].

Arthropods as vectors extend microorganisms passively or actively. The possible transmission of infectious diseases is being considered and relevant in case of swarm population gradation of migrating millipedes. Reports of passive transmission bacteria to humans by millipedes goes as follows: *C. caeruleocinctus* transfer: *Klebsiella ozaenae*, *Citrobacter freundii*, *Serratia marcescens* and *Pantoea agglomerans*, *Raoultella planticola*, *Salmonella arizonae, Xanthomonas maltophila*. *O. sabulosus* transmits: *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Enterobacter sakazakii*, *Citrobacter freundii*, *Pantoea agglomerans*, *Hafnia alvei* and *Raoultella planticola* [20,61-66].

APPLICATIONS FOR MILLIPEDE'S SECRETIONS IN MEDICINE AND ZOO PHARMACOLOGY

Chemical secretions of millipedes, are well documented in the literature for their repellent or sedative and toxic properties [27,67,68]. Arachnids and vertebrates consuming millipedes *Glomeris marginata* (Villers, 1789) were poisoned by glomerin and homoglomerin [69]. Para-cresol is defensive allomone that deter ants [70, 71]. Mosquitoes *Aedes aegypti* fed less frequently during laboratory trial for blood samples with benzoquinones from *Orthoporus dorsovittatus* (Verhoeff, 1938) [67]. The long time effect of benzoquinones as preventive method against lone star tick, *Amblyomma americanum* was checked in laboratory tests by Carroll et al. [68].

Primates use millipedes directly to control blood-feeding arthropods. Rubbing living millipedes on the fur was observed for wedge capped capuchin monkey *Cebus olivaceous* [72]. Mixing defensive secretion with onion, garlic was noted by Weldon et al. [73] for capuchin monkey *Cebus apella* and by Zito et al. [74] in case of black lemur *Eulemur macaco* and owl monkeys *Aotus* spp.

Millipedes are usually spit out or vomited due to their repulsive smell and taste [75]. However secretion-resistant vertebrate enrich their diet with millipedes, with no symptoms of poisoning, predatory controls the population of millipedes in turn [55,73,76]. Diplopoda might be edible after some preparation and are used for their anti-pathogenic properties. A decoction from *Tachypodoiulus niger* (Leach, 1814) is used by the inhabitants of Mizoram in India against tuberculosis [77]. The Bobo tribe folks of Burkina Faso consume millipedes to improve the caloric content of the meal but also due the potential antimalarial effect [78]. As an element of prophylaxis against intestinal parasites the Red-fronted lemurs *Eulemur rufifrons*, eat millipedes after squeezing and preliminary chewing of arthropods which liberates defensive secretions [79]. Prey rolling behavior was noted for Coati *Nasua* spp. [73]. Representatives of the tropical batrachofauna choose millipedes to supplement their diet with valuable poisonous substances accumulated in body in order to deter predators. Alkaloids found in dermal glands of poisonous frogs were derived from ingested ants and millipedes [80,81]. Spiropyrrolizidine oximes found in the skin of *Dendrobates pumilio* living in Panama, are derived from chemical secretions from consumed millipedes *Rhinotus purpureus* (Pocock, 1894) and beetles [81-82]. Arthropoda are source of compounds of pharmacological properties, this therapeutic effect is used both in folk and conventional medicine [40,83,84]. Research are being carried out on the pharmacological use of batrachotoxin e.g. epibatidine alkaloid from skin glands of poisonous dendrobatidae *Epipedobates tricolor* [80]. Chemical is known as mediator of non-opioid receptors thus no addictive, analgesics but toxic in low doses. Nowadays investigations are being concerned on synthetic analogs with safe and selective therapeutic effect [85]. There are research on Glomeridae and Julidae secretion as antioxidant and suppressor of nerve degeneration factor [86-87].

MILLIPEDE'S SECRETIONS AND THEIR IMPACT ON HEALTH CARE

Diplopoda dwell ruderal places, heaps and spots of decomposition with composting materia [88-93]. Suspected function of secretions is support of survival in environments inhabited by variety of organisms including pathogens [94]. There are reports on Diplopod's antifungal and antibacterial characteristic detected for hemolymph or body extract [95-97].

Fungicidal and bactericidal activity of 1-octen-3-ol, from *Niponia nodulosa* Verhoeff, 1931 (Polydesmida) secretion was described by Omura et al [98]. Laboratory trials reveal inhibitory effect of *Pachyiulus hungaricus* (Karsch, 1881) (Julida) secretion on variety bacteria; *Aeromonas hydrophila*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Xanthomonas arboricola*, *Listeria monocytogenes*, *Staphyllococcus aureus* and *Bacillus subtilis* and fungi; *Asprgillus flavus*, *Aspergillus niger*, *Fusarium subglutinans*, *Fusarium semitectum*, *Fusarium equiseti* and *Gliocladium roseum* [87,99]. In vitro trials over *Megaphyllum unilineatum* (C. L. Koch, 1838) (Julida) defensive secretion reveal fungicidal action on *Fusarium* sp. [87]

Both p-cresol and phenol which are present in Julida secretions, effectively inhibit the development of fungal spores and mycelia. Phenol (carbolic acid) was formerly used for disinfection in health facilities. Phenolic derivatives form cave predator *Apfelbeckia insculpta* (C.L. Koch,1867) (Callipodida) play antifungal and antibacterial activity [27, 100].

Benzoquinones and derivatives secreted by Julida, Spirobolida, and Spirostreptida exhibit toxicity against fungi, and bacteria and nematodes [83,87,99,101]. Antibiotic action against Gram-positive bacteria (including methicillin-resistant S. aureus) was descried by Glukhova et al. [102]. In vitro research carried by teams; Stanković et al. [99], Pesewu et al. [101] proved that millipede extract (benzoquinones) were destructive for methicillin resistant *S. aureus* strain. Development of *S. aureus* was inhibited after organic acid and alkaloid defensive secretion compounds of *Tachypodoiulus* sp. [103].

Defensive secretion as mixture of benzoquinonoids from of *Rhinocricus* sp. possess fungicidal properties and bactericidal activity for both Gram positive, negative pathogens including *S. aureus* [104]. Diplopoda should be considered as a source of multi complexes molecular systems of potential toxicity on pathogenic microorganisms.

Medical issue are also disorders regarded to human progressive industrial activity and environmental contamination. Trace element toxicosis which are achieved in low doses [105-107]. Millipedes can survive in contaminated area. The cooperation of edaphic organisms enable the creation of favorable conditions and habitats for development of pioneer species population, facilitating the process of secondary succession [88,108,111]. Environmental monitoring is based on zoo indicators and millipedes serve for habitat evaluation. Pedobionts succession and sarcophagus activity increase decomposition processes, therefore Diplopoda may help with reclamation of polluted area [88,108,109,111-120].

CONCLUSIONS

Diplopoda are frequently seen in human habitats and considering as a nuisance during swarming behavior and massive migrations. Although the most toxic secretions were described for tropical taxa and more severe clinical cases are noted from equatorial regions, native and alien species shifts their geographic distribution. Children are the most exposed group as result of their natural vigor and curiosity along with poor education of prophylaxis. Directly exposed to defensive section and the most frequently injured are bare body extremities or face and eyes. To identify chemicals and asses the threat the millipede sample should be delivered. Although most symptoms pass after a few days, dermal discoloration changes may persist and wounded skin is a root for secondary infection. There is a risk of passive transport of pathogenic bacteria to human settlements. Occupationally exposed are field and forestry workers, common inhabitants at leisure and work places. Education means of preventive measure and risk factors assessment are being neglected.

Millipedes are potential source for pharmacology development e.g. drug improvement. This progressive field of science is a great promise due to a growing demand and new applications being discovered. Diplopoda are crucial for proper microelement turn over hence play role in secondary succession and monitoring of environment reclamation. Ecotoxicology may help with prognosis of domestic area pollution and influence on health condition of inhabitants. Proper millipede's population control and prophylaxis measures could limit threats both direct and indirect for human health which escalate especially in synanthropization context.

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

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