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Review Article

CENTIPEDE VENOM TOXINS AND ITS BIOMEDICAL AND PHARMACOLOGICAL PROPERTIES

NIDHI YADAV*, RAVI KANT UPADHYAY

Department of Zoology, Deen Dayal Upadhyaya Gorakhpur University, Gorakhpur
Email: rkupadhya@yahoo.com

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ABSTRACT

The present review article explains venoms from various centipede species with their biomedical and pharmacological properties. Centipede venom is a natural source of bioactive proteins, peptides and other small molecules. These use venoms as defense arsenals to paralyze prey. This review paper sketch out important physiological effects like platelet aggregation, anticoagulant, phospholipase A2 and trypsin inhibiting activity. Centipede venom toxins selectively bind Kv2.1 channel and block them. Centipede venom disrupts cardiovascular, respiratory, muscular and nervous systems by targeting the broadly distributed KCNQ channels. It also signifies toxin-voltage-gated integrations and its inhibition. These peptides can be used for developing drugs for treatments as well as bio-insecticides for insect control.

Keywords: Centipedes, Venom glands, Toxins, Peptides, Channel blockers, Biochemical and pharmacological properties

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INTRODUCTION

Centipedes are venom-injecting predator animals belong to phylum: Arthropod; Class: Chilopoda. There are approximately 3500 species of centipedes identified round the globe [1]. These are ancient venomous animals whose first pair of front legs modified into large, poisonous fangs connected to venomous glands. Leg based fangs are used to inject venom which causes severe pain in humans [2]. Such modifications in forficules and venom-bearing limbs do not found in no other arthropods [3]. The venom gland covered by thick cuticle and epidermis, consisting of numerous epithelial secretory units each with its own unique valve-like excretory system [4]. Centipede accidentally bites or stings children, households and fish farmers that is highly painful stings. It causes allergies, severe swelling, chills, fever, weakness, and anaphylactic shock it is unlikely to be fatal (fig. 1).

Centipedes are ecologically important group of soil and leaf litter predators. Centipede exclusively belongs to one order, Scolopendra Morpha [5]. The genus *Scolopendra* represent the best-known genus of centipede worldwide [6, 7]. They possess segmented bodies consisting of 15 to almost 200 segments with one pair of legs per segment. Their venoms contain various components with different biomedical and pharmacological properties. *Scolopendra* attack and predate over small mammals, bats, and amphibians [8]. Chinese redheaded centipede *Scolopendra subspinipes mutilans*, is a venomous centipede found in East Asia and Australasia [9]. The Vietnamese centipede (*Scolopendra subspinipes*) is one of the largest and most aggressive tropical centipedes [7] (table 1).

Centipede venom contains a large number of components with different biochemical and pharmacological properties [10]. Centipede envenomation causes physiological problems such as acute hypertension, myocardial ischemia and infarction, hematuria, hemoglobinuria, rhabdomyolysis, hemorrhage, pruritus, eosinophilic cellulitis, and anaphylaxis reactions in rare cases, death. Its venom also causes pain, paresthesia, lethargy, localized necrosis, headache, dizziness and nausea (fig. 1). Centipede venom also contains 'neurotoxic components that likely combine to cause rapid death. These target voltage-gated sodium and calcium channels as well as potassium channels [11] (table 1). Centipede venoms possess an chemical components which are used as an arsenal for defense, making and killing prey [12]. This article emphasizes various centipede species, its venom, physiological and toxic effects. Centipede venom is therapeutically quite important; its therapeutic uses have been highlighted (table 1).

Source of information

For writing this comprehensive research review on centipede toxins/allergens, various databases were searched. For collection of relevant information specific terms such as medical subject headings (MeSH) and key text words, such as "venom toxins", "biological and pharmaceutical effects", therapeutic uses" published till 2022 were used in MEDLINE. Most especially for retrieving all articles pertaining to the use of centipede venom and its biomedical effects, electronic bibliographic databases were searched and abstracts of published studies with relevant information on the centipede toxins were collected. Furthermore, additional references were included through searching the references cited by the studies done on the present topic. Relevant terms were used individually and in combination to ensure an extensive literature search. For updating the information about a subject and incorporation of recent knowledge, relevant research articles, books, conference proceedings and public health organization survey reports were selected and collated based on the broader objective of the review. This was achieved by searching databases, including SCOPUS, Web of Science, and EMBASE, Pubmed, PMC, Publon, Swissprot, Google searches" From this common methodology, discoveries and findings were identified and summarized in this final review.

Venom composition

Centipede venom is natural source of bioactive proteins, peptides and other small molecules. Proteins and peptides possess disulfide bridges with novel pharmacology and three-dimensional structure. Centipede venom peptides target neuronal ion channels and receptors. Their venom toxins induce myotoxic, cardiotoxic, neurotoxic and other toxic effects. The venom components are potent and selective on peripheral targets; envenomation causes diverse physiological complications [12]. Centipede venom, which contains many bioactive and pharmacologically active compounds are important raw materials for Chinese medicine [13]. Centipede venom is used for or used in the preparation of traditional medicine in China and India, Vietnam and South Korea and Japan. The centipede venom diversity of their toxin-like proteins/peptides has large pharmacological importance [4, 14]. These peptides can be used for developing drugs for treatment of microbial diseases [15] as well as bio-insecticides [14]. For general treatment of centipede envenomation ice exposure, hot water immersion and analgesia injection is provided for the treatment of centipede in Taiwan [16].

Physiological effects

Centipede venom comprises a complex mixture of toxins which show both structural and functional diversity. *Scolopendra mojiangica,* and S. *subspinipes mutilans* possess toxin-like molecules which display strong hemolytic and anti-insect activity [13]. Centipede venom imposes

severe pain and other multiple physiological effects such as anticoagulant, platelet aggregating, ion channel inhibition and nerve and muscle cell damage and necrosis [8]. Centipede toxins showed myotoxic, cardiotoxic, and neurotoxic activities. Moreover, severity centipede envenomation increases with the time if treatment is not being made available to the victim, it becomes fatal. Therefore, centipede bite evaluation and management is quite important [17]. Centipede venoms showed following effects.

Neurotoxic

Centipede venom possesses neurotoxins (*S. subspinipes dehaani*) which obstruct structure and function of ion channel. Centipede neurotoxins target brain or the thoracic ganglia affect limb movement [1] (fig. 2). Toxin peptides isolated from *S. subspinipes dehaani* showed diverse physiological effects like platelet aggregating activity; anticoagulant, phospholipase A(2) activity; trypsin inhibiting activity; voltage-gated potassium channel activities; voltage-gated root ganglion neurons inhibition. SsmTx-I also act as a simple inhibitor or channel blocker rather than a gating modifier [9]. It selectively blocks the Kv2.1 current with an IG_{50} value of 41.7 nm. These also showed voltage-gated calcium channel activities [10] (table 1).

Neurotoxins bind directly to G-protein coupled receptors and these indirectly activate endogenous agonists. SsmTX-I possesses intra-molecular disulfide bridge motifs Cys1-Cys3 and Cys2-Cys4 and shows analgesic activity [18]. SsmTx-I significantly blocked voltage-gated K^+ channels in dorsal [9]. Centipedes also possess polyamine-like compounds [19].

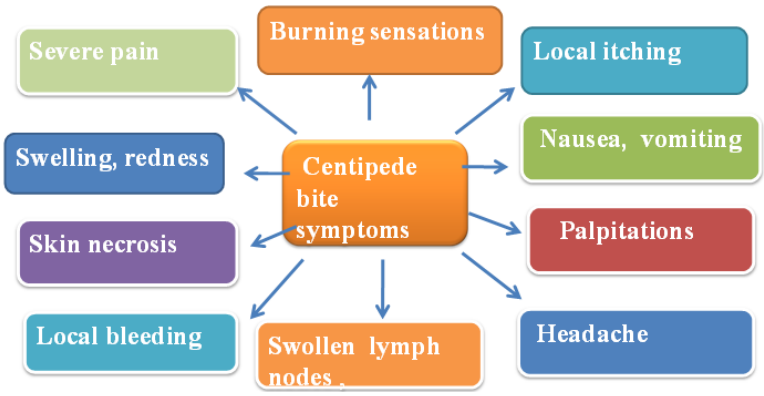

Fig. 1: Symptoms of centipede bite

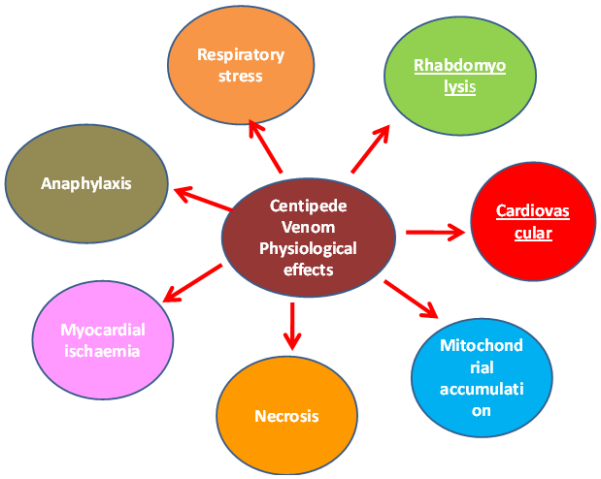

Fig. 2: Physiological effects of centipede venom

Hemolytic activity

Centipede venom causes severe pain, paresthesia and edema, which may develop into superficial necrosis. Centipede venom shows caseinolytic, fibrinogenolytic and gelatinolytic activities. *S. viridicornis* and *O. pradoi* venoms showed hyaluronidase activity. Most of the centipede venoms showed nociception, edema and myotoxicity in mice, but only *S. viridicornis* and *O. pradoi* venoms cause venoms intense direct hemolytic activity on human erythrocyte [20] (fig. 2).

Cytotoxic

The purified proteins/peptides showed different pharmacological properties, like platelet aggregating activity; anticoagulant activity; phospholipase A activity; trypsin inhibiting activity; voltage-gated potassium channel activities; voltage-gated sodium channel activities; voltage-gated calcium channel activities [10]. The centipede peptide toxins effect on ion channels, including Nav, Kv, Cav and the nonselective cation channel polymodal transient receptor potential vanilloid 1 (TRPV1) [21]. *S. viridis* centipede venom possesses a variety of low-molecular-weight peptide toxins which after infliction shows immediate effects on their preys [22]. These target voltage-gated ion channels to interfere with the central system of prey and produce pain or paralysis for efficient hunting (table 1).

Centipede peptide toxins confer chemical, thermal and biological stability. These toxins possess the high potency and specificity and could be used as diagnostic tools and in the treatment of human diseases. SsmTx displays a unique cysteine motif that is completely different from that of other venomous animal toxins [23] (fig. 2).

Muscle damage and necrosis

A different biochemical composition of *S. polymorpha* venom, based on the different effects of four venom fractions on the cells tested, according to statistical evidence. Fractions F6 and F7 caused the

most important alterations. Venom-exposed EDL muscle showed signs of muscle damage including necrosis, loss of fascicular structure as well as mitochondrial accumulations and ragged red fibers (RRF), suggesting impairment in the normal mitochondrial arrangement. Nicotinamide adenine dinucleotide (NADH) and cytochrome oxidase (COX) tests also indicate that respiratory complexes might be affected [24] (fig. 2).

Inflammatory

Centipede envenomation cause local inflammation, intense pain and edema. *Scolopendra viridicornis* centipede envenomation induce leukocyte infiltration mainly neutrophils and monocytes/ macrophages with production of pro-inflammatory mediators. Moreover, *S. viridicornis* venom stimulated the release of IL-6, MCP-1, KC, and IL-1β [25]. Sv venom shows cytotoxic effects and induces morphological changes in RBL-2H3 line. However, lower doses of the venom induced degranulation of both mast cell lines, as well as the secretion of MCP-1, IL-6 and IL-1β [26]. Sv venom exposure, mast cells and histamine are crucial for the establishment of the local inflammatory reaction (table 1) (fig. 2).

Channel inhibitors

Centipede venom possesses low molecular weight toxins which after infliction from pod fangs reach into the blood stream. These selectively bind to the nociceptive transient receptor potential vanilloid 1 (TRPV1) ion channel. This is a polymodal receptor for multiple painful stimuli, to which small peptide toxin RhTx2 from the Chinese red-headed centipede binds and strongly modulates TRPV1 activities [27]. The most abundant toxins expressed in the venom of *S. viridis* belonged to calcium and potassium ion-channel toxins, venom allergens, metalloproteases, and β-pore forming toxins [28].

A major toxin component [Ssm Spooky Toxin (SsTx)] in centipede venom inhibits the sales channel in conspecifics but not in heterospecifics to cause short-term, recoverable, and nonlethal envenomation. This same toxin causes fatal heterospecific envenomation, for example, by switching its target to the Shaker channels in heterospecifics without inhibiting the Shaker channel of conspecific *S. subspinipes* individuals. These findings suggest that the venom components exhibit intricate coevolution with their targets in both heterospecifics and conspecifics, which enables a single toxin to develop graded intraspecific and interspecific antagonistic interactions [29] (table 1) (fig. 2).

Ssm Spooky Toxin (SsTx) isolated from red-headed centipede is a potent blockage of the expressed KCNQ channels to simultaneously and efficiently disrupt cardiovascular, respiratory, muscular, and nervous systems. SsTx is a basic 53 residues compound that is main killer arsenal in centipedes' defense and predation. It inhibits KV1.3 channel, Both SsTx and its mutant SsTx_R12A inhibit cytokines production in T cells without affecting the level of KV1.3 expression [30]. SsTx blocks KCNQ potassium channels to exert the lethal toxicity [11]. Centipedes' venom has evolved to simultaneously disrupt cardiovascular, respiratory, muscular, and nervous systems by targeting the broadly distributed KCNQ channels, thus providing a therapeutic strategy for centipede envenomation [11]. Venom toxinSsTx blocks KCNQ potassium channels and impose lethal toxic effects and kill in its prey [31] (table 1) (fig. 2).

Therapeutic uses

Centipedes are venomous terrestrial predators; its venoms are complex cocktails of water, salts, small bioactive molecules, peptides, enzymes and larger proteins, with peptides usually comprising the majority of toxins [32]. Centipede venom is used in traditional medicine in China for the treatment of many disorders, such as stroke-induced hemiplegia, epilepsy, apoplexy, whooping cough, tetanus, burns, tuberculosis, as well as myocutaneous disease [33]. Centipede venom is also used for the treatment of cardiovascular diseases for in Korea, China, and other Far Eastern Asian countries [34, 35]. Centipede venoms are highly complex chemical arsenals that are rich in dissolved-constrained peptides. Centipede venoms peptides target neuronal ion channels and receptors [4] (table 1).

The venom of centipedes could be an excellent source of peptides for developing drugs for treatments as well as bio-insecticides for agrochemical applications [14]. Its peptides, enzymes, exhibit a large array of anticancer and anti-pathogenic activities [36]. Voltage-gated sodium channel NaV 1.7 serves as an attractive target for chronic pain treatment. These could be used to make analgesic. SP-TOX, selectivity and potency of Ssm6a upon NaV 1.7 It decrease inflammatory pain in a rat model [37]. Centipede venoms are complex mixtures of biochemically and pharmacologically active components such as peptides and proteins [38]. These include ion channel modulators, antimicrobial peptides, different enzymes, enzyme inhibitors, anticancer peptides, antithrombotic peptides, as well as anticoagulants and centipede extracts [34, 35]. These possess novel pharmacology and three-dimensional structure and could be more useful for therapeutic purposes [4, 34, 35].

Centipede venom is a rich and complex natural source of bioactive proteins, peptides and other small molecules that aid in predation or defense. The venom can induce myotoxic, cardiotoxic, neurotoxic and other toxic effects. It also shows myocardial ischemia and infarction, hematuria, hemoglobinuria, rhabdomyolysis, hemorrhage, pruritus, eosinophilic cellulitis, as well as anaphylaxis. More prevalent are symptoms including pain, paresthesia, lethargy, localized necrosis, headache, dizziness and nausea. The constituents target different cellular processes and pathways which in turn trigger a cascade of physiological reactions in the victim [12].

Allergic activity

Major centipede allergen Sco m 5 from *Scolopendra subspinipes mutilans* major centipede allergen Sco m 5 from *Scolopendra subspinipes mutilans.* Sera positive for Sco m 5 IgE-binding was cross-reactive against venom from the wasp Vespa mundane. The use of Sco m 5 to identify centipede-allergic individuals could be important, given the high potential allergenicity of Sco m 5 among the general Chinese population, along with the likely possibility of cross-reactivity against wasp venom among centipede-allergic patients [39] (table 1).

Anticancer activity

Scolopendrasin VII isolated from the Centipede, *Scolopendra subspinipes mutilans* induce necrosis was mediated by specific interaction with phosphatidylserine. It makes pores in membrane of cancer cells [40]. It stimulates macrophages and neutrophil activity. This is inhibited by the formyl peptide receptor 1 (FPR1) antagonist cyclosporine H [41]. A novel antimicrobial peptide acting via formyl peptide receptor 2 shows therapeutic effects against rheumatoid arthritis In oriental medicine, centipede *Scolopendra subspinipe smutilans* has long been used as a remedy for rheumatoid arthritis (RA), a well-known chronic autoimmune disorder [42]. Scolopendrasin X strongly stimulates mouse neutrophils, results in intracellular increase of calcium ions, and chemotactic migration through pertussis toxin-sensitive G-protein and phospholipase C pathway, and increased superoxide anion production in neutrophils. Another toxin peptide isolated from *Scolopendra subspinipe smutilans* peptide scolopin 1 (AMP-scolopin 1) showed broad-spectrum activities against bacteria, fungi, and tumor cells. Similar activity is reported in recombinant scolopin1 and synthetic scolopin 1 [43] (table 1).

Analgesic activity

SsmTX-I specifically blocks Kv2.1 ion channel and showed analgesic potential. SsmTX-I contains intramolecular disulfide bridge that possess motifs specially having Cys1-Cys3 and Cys2-Cys4 [18]. Animal venom peptides have proven to have potential as new types of analgesic medicine (table 1).

Arthritis

Scolopendra spp. venom is used treat arthritis in Korean traditional medicine [35].

Table 1: Showing important centipede species, its venom toxins and physiological effects

Species	Common name	Toxin/Venom	Disease/Symptoms	Physiological effect	References
Scolopendra subspinipes mutilans	Chinese red-headed centipede,	Ssm Spooky Toxin	Severe pain acute hypertension, myocardial ischemia and, in rare cases, death.	Blocking potassium transport in and out of cells. Breathing problems	[9]
Scolopendrasubspinipesdehaani	Thai centipede	Cocktail of toxins Spooky Toxin (SsTx)	Acute hypertension, myocardial ischemia and, in rare cases, death	Disrupts the victim's cardiovascular, respiratory, muscular and nervous systems	[9]
S. gigantean	Amazonian giant centipede	5-hydroxytryptamine, histamine, lipids, polysaccharides, and various enzymes such as proteinases and esterases.	Intense local pain, oedema, local hyperthermia, and blood clots at punctures.	Myocardial ischaemia, hypotension, myocardial toxic effects and anaphylaxis.	[11]
S. heros	Giant desert centipede	5-hydroxytryptamine, histamine, lipids, polysaccharides, and various enzymes such as proteinases and esterases.	Rhabdomyolysis, Tenderness, tingling, and numbness around the bite	Localized pain swelling and redness bleeding itchiness or burning numbness, swelling of the lymph nodes	[11]
Scolopendra cataracta	Laos waterfall centipede	serotonin, haemolytic phospholi pasea cardiotoxic protein, and a cytolysin	Pain, erythema and edema.	Disrupts the victim's cardiovascular, respiratory, muscular and nervous systems	[12]
Scolopendra cingulate	Megarian banded centipede	Serotonin, haemolytic phospholip ase, a cardiotoxic protein, and a cytolysin.	Affect heart muscle, hemoglobin in the urine damaged skeletal muscle tissue	Rhabdomyolysis and muscular damage	[12]
Scolopendra galapagoensis	Peruvian giant centipede	Serotonin, haemolytic, phospholi pase, a cardiotoxic protein, and a cytolysin	Severe pain and localized, swelling, inflammation and allergy	Puncture cell membrane and cause cell death	[12]
Scolopendra subspinipesmutil ans,	Chinese red-headed centipede,	SsmTX-I blocks Kv2.1 ion channel	Analgesic potential	Analgesic	[18]
S. viridicornis and O. pradoi	Amazonian giant centipede	Nociception, edema and myotoxicity	Hyaluronidase activity	Intense direct hemolytic activity on human erythrocyte	[20]
S. viridis centipede	Southeasstern centipede	venom possesses a variety of low-molecular-weight peptide toxins	Infliction shows immediate effects on their preys	Puncture cell membrane and cause cell death	[22]
Scolopendra morsitans	Tanzanian blue ring leg	Release of serotonin causes severe pain response	Affects nervous systems of invertebrates, and autonomic nervous system of vertebrates, to rapidly paralyze	Cytotoxic activity against human erythrocytes	
S. polymorpha	Tiger Centipede	5-hydroxytryptamine, histamine, lipids, polysaccharides, and various enzymes such as proteinases and esterases.	Heart attack, urine in blood, damage of skeletal muscle tissue excessive bleeding skin infections	Muscle damage, necrosis (cell/tissue death), loss of fascicular structure, and ragged red fibers, a type of diseased mitochondrial accumulation.	]24]
Scolopendra viridicornis	Amazonian giant centipede	release of IL-6, MCP-1, KC, and IL-1β	strong insecticidal activity	Cause local inflammation, intense pain and edema	[25]
Scolopendra subspinipes mutilans	AMPs	Centipede venoms contain toxins which serve as AMPs and were found active against several bacteria	Antimicrobial	Puncture cell membrane and cause cell death	[33]

Antimicrobial activity

Centipedes possess novel peptides which show strong antimicrobial activity against various pathogens. These peptides (AMPs) also play important role in Ecdysis process of centipede *Scolopendra subspinipes subspinipes* [44]. These also show broad-spectrum antibacterial activity and [45]. Centipede venoms contain toxins which serve as AMPs and were found active against several bacteria [33]. One of the most important cellular events in arthropods is the melting of the cuticle (Ecdysis). The centipede *Scolopendra subspinipe smutilans* is an environmentally beneficial and medically important arthropod species. The centipede *Scolopendra subspinipe smutilans* is a medically important arthropod species. Although this species are increasingly applied as a reliable source of new antimicrobial peptides, the transcriptome of this species is a prerequisite for more rational selection of antimicrobial peptides [46]. Antifungal activity is reported in antimicrobial peptide, scolopendin 1, derived from centipede *Scolopendra subspinipe smutilans* [47, 48]. Scolopendin 2 (AGLQFPVGRIGRLLRK) is also isolated from same species, it is a cationic antimicrobial peptide isolated from centipede. This, scolopendrasin II bound to the surface of bacteria through a specific interaction with lipoteichoic acid and a lipopolysaccharide, which was one of the bacterial cell-wall components. It shows broad-spectrum antimicrobial effects by forming pores in the cell membrane of pathogens [49] Scolopendrasin II may be useful for developing peptide antibiotics [50] (table 1).

It also Scolopendin 1 exerted an antimicrobial activity without inducing haemolysis of human erythrocytes [47]. These antimicrobial peptidesalso evoke an innate immune response [48] the antimicrobial peptide scolopendrasin VII, derived from

Scolopendra subspinipe smutilans stimulates macrophages, resulting in chemotactic migration via FPR1 signaling, and the peptide. *Scolopendra subspinipe smutilans* stimulates macrophage chemotaxis via formyl peptide receptor 1. It is also used to treat rheumatoid arthritis (RA), a well-known chronic autoimmune disorder [42].

An Anticancer Activity of the Antimicrobial Peptide Scolopendrasin VII Derived from the Centipede, *Scolopendra subspinipe smutilans* induce necrosis that are mediated by specific interaction with Phosphatidylserine, which is enriched in the membrane of cancer cells. [40]. Scolopendrasin X strongly stimulated mouse neutrophils, resulting in intracellular calcium increase, chemotactic migration through pertussis toxin-sensitive G-protein and phospholipase C pathway, and increased superoxide anion production in neutrophils [51]. AMPs from centipede venoms are promising biologically active molecules (candidates) which work against bacteria, protozoans, fungi and viruses [52].

Antimicrobial peptide scalloping 1 (AMP-scalloping 1) is a small cationic peptide identified from centipede venoms of *Scolopendra subspinipe smutilans*. It has broad-spectrum activities against bacteria, fungi, and tumor cells, which may possibly be used as an antimicrobial agent. The recombinant scolopin1 had similar antimicrobial properties to the synthetic scalloping 1 [43].

Insecticidal

Centipedes use the toxins as poisonous arsenals for prey capture and defense against predators. These possess insecticidal neuropeptides similar to polyamine-like compounds. These can be sued to make bioinsecticide to control insect pests. *Scolopendra subspinipe smutilans* crude venom showed strong insecticidal activity [13].

Proteome and transcriptome analysis

Centipede venom is evolved from ancient toxin peptide reconstruction and amino shifting and positioning and refinement. These are cocktail of diverse toxic like peptides with compositional evolution [5] but few of them are functionally characterized [14]. Centipede venom toxins might evolve under strong negative selection [53]. By using extraction transcriptomic analysis of *S. subspinipes* and *S. subspinipes mutilans* revealed many toxin-like proteins/peptides were found expressed outside the venom gland and involved in gene recruitment processes [54]. A large diversity of centipede toxin-like proteins in *Scolopendra subspinipe smutilans* nine hundred twenty-three and 6,736 peptides, which were separately isolated from the venom and torso tissues [54]. From red bark centipedes (*Scolopocryptops sexspinosus* venom adamalysin-like metalloproteases were isolated. By using transcriptomic studies 1468 nontoxin transcripts identified in the transcriptome [55]. *Cryptopsi heringi* centipede belongs to *Cryptops* genus it synthesize and secrete novel putative toxin Cryptoxin-1. Its recombinant form promote edema in mice footpads with massive neutrophils infiltration [56].

Mode of action

Centipede venoms are complex mixtures of biochemically and pharmacologically active components such as peptides and proteins. Scolopendrasin X strongly stimulated mouse neutrophils, resulting in intracellular calcium increase, chemotactic migration through pertussis toxin-sensitive G-protein and phospholipase C pathway, and increased superoxide anion production in neutrophils. Target receptor for scolopendrasin X, formyl peptide receptor (FPR)2 mediated scolopendrasin X-induced neutrophil activation. Moreover, scolopendrasin X significantly blocked inflammatory cytokine production induced by lipopolysaccharide in mouse neutrophils [51]. Ssm Spooky Toxin (SsTx) isolated from red-headed centipedes is a potent blockage of the expressed KCNQ channels to simultaneously and efficiently disrupt cardiovascular, respiratory, muscular, and nervous systems. Centipede venom also possesses neurotoxins (*S. subspinipes dehaani),* ion channel acting components and venom allergens. SsmTX-I specific blocker of Kv2.1 ion channel. A major toxin component [Ssm Spooky Toxin (SsTx)] in centipede venom inhibits the Shal channel in conspecifics but not in heterospecifics to cause short-term, recoverable, and nonlethal envenomation. Based on receptor binding and quick action on cell membrane and ion channels toxin peptide could become source of cancer therapeutics [57, 58] and microbial diseases [59]. Centipedes possess diverse natural toxins with multiple biological activities and are of high pharmacological use [119]. Most of them are used in self-defense molecules and for predation [120, 121].

CONCLUSION

Centipedes inflict venom in humans by using fangs or venom glands found in their first pair of limbs. From various researches it has been explored out that centipede venoms contain so many toxins-like proteins/peptides and other components with different biochemical and pharmacological properties. Most of centipede toxins are anticoagulants, ion channel inhibitors, neurotoxins and hemotoxins. These toxins cause myocardial ischemia and infarction, hematuria, hemoglobinuria, rhabdomyolysis, hemorrhage, pruritus, eosinophilic cellulitis, and anaphylaxis reactions. Centipede venom causes pain, paresthesia, lethargy, localized necrosis, headache, dizziness and nausea. Centipede bites in human are not uncommon and can cause acute hypertension, myocardial ischemia and, in rare cases, death. Centipede venom also possesses neurotoxins ion channel acting components and venom allergens. These could be used for generation of new types analgesic medicine and bio-insecticides. It has broad-spectrum activities against bacteria, fungi, and tumor cells, which may possibly be used as an antimicrobial agent. Centipede venoms can be used to make bio-insecticides or anti-parasitic drugs. All possible solutions regarding pharmacology, toxin discovery and characterization, toxin structures, clinical aspects, and potential applications can be easily achieved.

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AUTHORS CONTRIBUTIONS

Ravi Kant Upadhyay and Nidhi Yadav were responsible for conception, experiments, writing and revising the manuscript.

CONFLICT OF INTERESTS

Declared none

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