Utilization of Polislidae Wasp Venom as Potential New Insect Drugs in the R&D of Wellness Industry

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Abstract: The Polislidae wasp, one species of omnivorous social insects mainly living in the bush or under the leaves. The wasp has a venom sac in its tail, and the venom secreted by a sting can cause a series of body reactions and diseases. Multiple organ failure could be the outcome of wasp sting, if timely treatment or rescue has not been performed. Based on published reports on wasp sting related to medical concerns in recent years, this review summarizes the symptoms caused by wasp sting and corresponding mechanisms of actions. The medical application and relational utilization of the title insect is suggested derived from findings of the systematic review. Furthermore, we herewith sketch the perspectives of R&D on the venom of Polislidae wasp. It is expected to afford comprehensive references and be useful for broader study on the natural components and pharmacological effects of wasp venom.

Keywords: Polislidae wasp, wasp sting, clinical symptoms, insect drug, peptides, wasp venom.

1. INTRODUCTION

The Polislidae wasp is a kind of insects belonging to Polislidae, in Vespoidea, Hymenoptera. These rapid-flying social insects are ferocious predators and widely distributed in the world. Usually, they choose to build nests in the leafy bushes or under the eaves of human habitation. Polislidae wasp is rather aggressive and will attack any vulnerable animals approaching their hives. Untimely treatment after been stung can trigger the syndromes of pain, edema, local damage of the body and even death. The incidence of accidents and injuries caused by wasp stings is relatively high in China, due to the wide distribution of more than 20 species of Polislidae wasps scattered in the country [1,2]. In despite of the harmful results of wasp stings, wasp venom might merit further investigation and development as novel insect drugs according to the positive application of wasp venom's pharmacological effects. However, comprehensive analysis concerning the comparisons among various clinical studies, reports of the pathogenic mechanisms, and the applicable clinical treatments are still missing. The aim of this work is to review the recently published papers regarding wasp venom and stings including many case report, with attempt to provide fundamental information and useful references for further research on venom constituents of Polislidae wasp and its pharmacological effects.

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2. VENOM COMPOSITION AND PHARMACOLOGICAL EFFECTS OF POLISLIDAE WASP

2.1. The Composition of Polislidae Wasp Venom

The wasp venom is a complex mixture of high degrees of physiological and pharmacological activities. Liang *et al*. found that fresh venom from *Polistes olivaceus* exhibited somewhat acidic with a pH value range from 6.0–6.5, which contains hyaluronic acid enzyme, cholinesterase, proteolytic enzymes, DNA enzymes, acid phosphatase, and alkaline phosphatase [3]. Murata *et al*. reported identification of four new peptides from *Polistes rothneyi iwatai* venom, which named *Polistes*-protonectin and *Polistes*-mastoparan-R1, 2, 3. Among them, *Polistes*-protonectin exhibited significant hemolytic activity while *Polistes*-mastoparan-R1, 2, 3 can induce the release of histamine which further led to occurrence of inflammation [4].

2.2. The Pharmacological Effects of Polislidae Wasp Venom

It is well known that melittin, the main component of the bee venom own certain efficacies such as anti-inflammatory, anti-bacterial, anti-tumor, and may also be used on the treatment of rheumatoid arthritis [5,6]. Furthermore, the Vespidae wasp venom peptide were reported to be composed of activated G protein, phosphatidic acid A_2, and many other compounds, which exhibited a variety of biological functions such as to change the intracellular and extracellular concentration of Ca^{2+}, to induce platelet aggregation, and to promote insulin secretion and corticotropin-

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releasing [7]. However, though both Polislidae wasp and Vespidae wasp belong to Vespoidea, the pharmacological studies on Polislidae wasp venom are only at the very preliminary stage of exploration, which are comparable with the investigations upon Vespidae wasp venom.

2.2.1. Hemolytic Effect

Polislidae wasp venom possesses a strong hemolytic activity with the HU_{50} value of 17 μg/mL. Among the venom components, Phospholipase A_2 did not directly act on the cell wall lipids, but rely on the synergy of melittin. Another hemolytic mechanism maybe the Phospholipase A_2 form a complex with the substrate, while the combined-substrate approach to the cell while lying the membrane resulting in hemolysis. However, heparin may to some extent inhibit the hemolytic activity of on the venom of Polislidae wasp [8].

2.2.2. Nerves and Muscle Tension

Crude Polislidae wasp venom can completely block the nerve impulse transmission at the mice phrenic nerve-diaphragmatic muscle joint. The blocking effect is nearly irreversible, and the blocking of the phrenic nerve-diaphragmatic muscle nerve impulses passes prior to the blocking of diaphragmatic muscle contraction. A trace amount of crude Polislidae wasp venom of 1×10^{-4} g/mL can significantly inhibit the myocardial contractility of the ex-vivo heart of toad, while adding atropine may relieve the inhibition [3].

2.2.3. Anti-Tumor Effects

Sun *et al*. found that Polislidae wasp venom exhibit clear cytotoxicity against S180 mouse sarcoma cells, and the cytotoxicity is dose-dependent and time-dependent. 1 mg/mL of the venom may 100% kill the S180 cells in half an hour. The possible mechanism might be the venom inhibiting the cell division thus prevented the tumor cells from replication [9]. Moreover, after treatment of the S180 tumor cells with Polislidae wasp venom before inoculation to mice, the tumorigenic effect of the cells was lost. More interestingly, even a very low concentration (0.01 mg/mL) of venom treatment of tumor cells can significantly prolong the survival date of S180 tumor-bearing mice.

2.3. TOXICITY

The toxicity of Polislidae wasp venom collected from *Polistes olivaceus* upon an insect model, *Periplaneta americana* was measured, and the LD_{50} value is 7.45 μg/g, which is more toxic than the venom collected from *Selenocosmia huwena* (LD_{50} value is 300 μg/g), and the LD_{50} of the venom from *Polistes olivaceus* on mice was 5.54 mg/kg [3], which exhibited less toxic than the poison of *Selenocosmia huwena* (LD_{50} = 1.16 mg/kg) [10], but more toxic than that of the centipede poison (LD_{50} = 22.5 mg/kg) [11]. Schmidt *et al*. also reported the mild LD_{50} values of *Polistes rothneyi* and *P. olivaceus* as 14.5 and 11.2 mg/kg on mice, respectively [12]. Furthermore, they indicated the Polislidae wasp venom exhibited weak damaging potential to blood cells and low influences on phospholipase. Therefore, they indicated that these two venoms merit further pharmacological and medicinal analysis.

3. CLINICAL SYMPTOMS AFTER POLISLIDAE WASP STING AND CORRESPONDING TREATMENTS

3.1. Circulatory System

Zhu analyzed 53 cases of toxicosis caused by Polislidae wasp sting and found that: The sting sites of the patients were redness, pain, heart palpitations. The examination revealed arrhythmia, myocardial enzymes mildly abnormal. Generally treatment of Polislidae wasp sting is local irrigation using 5% sodium bicarbonate solution, iodine alcohol disinfection, and intravenation of methylprednisolone sodium succinate. Most of the patients were recovered in three to five days. For those patient accompanied by occurrence of toxic myocarditis or neurological symptoms, bicarbonate dialysis is needed to perform once every other day, each time for four hours [13]. Another report concerning an Indian patient was the first case of delayed onset of Kounis syndrome following wasp sting, while the patient occurred simultaneously renal and cardiac complications of wasp bite together with the appearance of systemic multiple significant jaundice and pedal edema [14]. After received the treatment of injection of amiodarone and hemodialysis treatment for two months, the patient made full recovery from both the renal and cardiac toxicity.

3.2. Nervous System

3.2.1. Peripheral Nervous System

Bánovčin *et al*. reported the serious local reactions of a 10-years-old patient who was stung by wasp [15], the patient was given antihistamine therapy but found upper limb weakness, difficulty with walking after 28 h,

Polistes rothneyi grahami van de V.

Polistes snelleni Saussure

Polistes hebraeus Fabricius

Polistes gigas (Kirby)

Figure 1: Some examples of common Polistes wasp scattered in Yunnan Province.

and continuous mild headache. After 32 h of stung the right-hand allergic swelling and the right lower extremity paresis, accompanied by fever, but with clear minds. Then sphincter disturbances lead to urinary incontinence while dexamethasone was given intravenously. After 72 h patient head and limbs were improved with the state of motion, mild headache completely disappeared [15]. Another two-years-old female patient was immediately given dexamethasone intravenous treatment after stung by wasp. After 12 h the patient exhibited orbital edema, and gradually extended to the whole body, accompany with the decreased urine output, and difficulty in breathing. Medical examination revealed the blood urea nitrogen, creatinine, creatine phosphokinase levels were increased. Hospitalized ten days, the patient suddenly suffered from serious ptosis and can not open her eyes, neostigmine and other acetylcholine receptor antibodies treatment were negative. Oral pyridostigmine treatment at 7 mg/kg/d giving pyridostigmine for eight weeks finally eliminated the symptoms [16].

3.2.2. Central Nervous System

Yang and Li reported one case of a 62-year-old patient was stung by Polislidae wasp and suffered from left limb weakness, unable to lift his left shoulder and left leg, and accompanied by left lower extremity pitting edema. B-ultrasound showed the presence of small amount of effusion in bilateral pleural and peritoneal. Head magnetic resonance imaging scan indicated that the right frontal and parietal cerebral infarction with a small amount of bleeding. The patient was diagnosed as hemorrhagic infarction and acute renal failure. The treatment was adopted to improve cerebral circulation, giving anti-infection, protecting liver functionality, and hemodialysis treatment. But the symptoms did not improving significantly and consciousness was lethargy liking after 2 weeks treatment [17]. Another symptoms of a clinical lacunar infarction patient arose from

Polislidae wasp sting was similar, electrocardiogram showed appearance of sinus rhythm, left ventricular surface of high voltage, the head CT showed the left internal capsule hind legs to see punctate hypodense lesions with a fuzzy boundary. The patient was orally taken "Yin Dang Xin Nao Tong" capsules and nifedipine after admission, giving defibrase brain protein hydrolyzate and pantoprazole to intravenous infusion, and using "Bu Yang Huan Wu Decoction" as complementary treatment. Three days later the patient was improved and discharged [18]. Crawley *et al*. reported that wasp stings patients displayed cerebral edema, encephalitis, cerebral infarction [19] while Sachdev *et al*. described that other symptoms appeared generally after stung for 30–96 h [20].

3.3. Digestive System

Tan and Wei reported a 1.5-year-old patient stung by the Polislidae wasp and induced toxic hepatitis symptom. The patient appeared local congestion and necrosis at the stung site. Next day symptom such as body skin and sclera stained yellow, dark yellow urine, decreased urine output, liver enlargement were appeared, no fever or vomiting. Clinical examination revealed total bilirubin was high, but hepatitis B and hepatitis C virus were negative, heart, lungs and nervous system was normal. After hepatoprotective, antiviral therapy treatment the patient's jaundice significantly reduced, together with liver narrow, and the rest of the index close to normal [21]. Qiu *et al*. recorded two male cases of wasp-sting-induced multiple organ dysfunction and acute pancreatitis. The patients' systemic multiple were stung, and successively symptom such as nausea, vomiting, oliguria, mild skin stained yellow were appeared, while lung breathe sounds and heart are normal. B-ultrasound showed that the gallbladder wall edema, liver and pancreas grow up in the patients. Give regular fasting, water deprivation, lifted spasm, analgesia, acid suppression, inhibition of pancreatic secretion, while rehydration to correct electrolyte and acid-base balance disorders. After treatment the acute pancreatitis symptoms was eliminated, and serum amylase returned to normal [22].

3.4. Urinary System

Cheng reported a case of acute renal failure arose from wasp sting happened to a 6-year-old patient. Edema appeared in a large area in the head, face and limbs of the patient, accompanied by the situation of lethargy, breathe difficultly, dark brown urine, percussion pain at the bilateral renal area. Routine urinalysis found Pro++, BLD++, BIL+, URO+. Immediate treatments such as peritoneal dialysis, blood dialysis, anti-inflammatory, and liver-protecting therapy were performed. The symptoms will eliminate after one month while the biochemical indices become normal [23]. D'Cruz described another patient was stung by wasp and associated with type 1 renal tubular acidosis [24]. After 9 h of stung, sudden onset weakness was happened, but no vomiting, rash and other symptoms could be seen. Intravenous chlorpheniramine and hydrocortisone treatment were given. Ammonium chloride test suggested the diagnosis of type I (distal) RTA. Furthermore, the metabolic acidosis was indicated by arterial blood gas analysis. Giving of potassium chloride and sodium bicarbonate therapy led to the attenuation of the symptoms [24]. Zhang and Chen recorded a 31-year-old male case being stung by Polislidae wasp which demonstrated oliguria and gross hematuria [25]. Biochemical check found that the patient' serum K^+ was significantly higher than normal, but blood pressure and heart rate were normal, no pathological murmur could be traced. ECG showed sinus rhythm, T-wave tip. After diuresis, hemodialysis treatments for one week the serum indicators and ECG T-wave returned to normal [25].

3.5. Immune System

Qu *et al*. recorded an anaphylactic shock case arose by Polislidae wasp sting. The 21-years-old male patient was stung at the head and immediately felt the symptoms of wound swelling, pain, blurred vision, palpitation, chest tightness, dizziness, sweating and fainting [26]. Medical analysis indicated his heart and liver function was normal. Giving epinephrine and promethazine intramuscular injection, intravenous infusion of dexamethasone, breath oxygen, the patient gradually awake and blood pressure returned to normal one hour latter [26]. Cai *et al*. described a case of immune hemolytic anemia resulting from Polislidae wasp sting. The 54-year-old male patient found oliguria and edema soon after been stung, and dark brown urine appeared at the 3rd day and less than 100 mL/day, accompanied by frequent nausea, vomiting, stool black, yellow sclera, lung breath sounds rough, whole abdominal tenderness, and percussion pain in kidney area. Examination revealed that the concentrations of hemoglobin, white blood cell count, and platelet counts were all lower than normal, reticulocytes 16.9%, while no red blood cell fragments was found. Routine urine examination found that direct

anti-human globulin is +++, and indirect anti-human globulin is negative. The immunoglobulin in the normal range. Giving dexamethasone intravenous infusion once a day, while oral administration of sodium bicarbonate to alkalization of urine, use anisodus choline and prostaglandin E_1 to improve microcirculation, together with the hepatoprotective and anti-infectious therapy. Following reexaminations found that the direct anti-human globulin decreased from +++ to ++ in 92 d, while to normal after 5 months [27].

3.6. Other Injuries

3.6.1. Corneal Injury

Li *et al*. mentioned a 28-year-old female case of corneal injury by Polislidae wasp sting. The patient was stung at left eye and immediately feel itching, blurred vision, photophobia, tearing, decreased visual acuity. After 4 d, the patient was found injured eye corneal edema, opacification, the real layer of gray muddy, normal anterior chamber depth, room observant and pupil shoen, light reflex is sensitive, eyes as clear diagnosis of keratitis. After intravenous antibiotics, oral administration of vitamin C, local subconjunctival injection of tobramycin, using tarivid eye drops water combination therapy the prognosis is better [28]. Moreover, Li *et al*. reported another 15-year-old female case being stung by for one month, they found the anterior chamber depth of the patient is middle, aqueous unclear, the pupil extremely dilated, less round, lens turbid white, the rest of the eye invisible. This case lack of timely treatment was finally diagnosed as secondary glaucoma and traumatic cataract [29].

3.6.2. Multiple Organ Dysfunction Syndromes (MODS)

Fan and Zhou analyzed 12 cases suffered from Polislidae wasp sting. After been stung the patients exhibited skin irritation, local wound purulent secretions, difficulty breathing, unconsciousness, oliguria, gross hematuria and melena. Checking liver function, renal function, myocardial enzymes and electrolytes disclosed that all these indices of patients were abnormal. All of the 12 cases were found accompanied with acute renal failure and MODS [30]. Furthermore, Yang analyzed 14 cases of Polislidae wasp sting patients and compared the different efficacies of the treatments. The author summarized the effective therapy is timely treatment hemodialysis once a day to correct the acidosis and electrolyte imbalance, intravenous infusion methylprednisolone of 1 or 2 times per day, intravenous infusion alprostadil, give glutathione reductase and omeprazole once per day. For infection patient used third generation of cephalosporin antibiotics in the anti-inflammatory treatment [31]. MODS is difficult to deal with, while clinicians should provide timely and symptomatic treatment base on the patient's body condition and symptoms appeared. The four death cases in these two literature died of respiratory failure and ventricular arrhythmias caused by pump failure.

3.6.3. The Effect of Tumorigenic

Yang and Si mentioned a patient suffered from Polislidae wasp stung at the right earlobe four years ago, after being stung, the lump gradually grew up, anti-infective therapy failed to exhibit efficacy. The lump owns smooth surface and tough, no tenderness, no adhesion to the surface of the skin, patient can open mouth unlimited, no special exception, around the lump is not palpable lymph nodes. It is diagnosed the right parotid gland adenoma, while the pathological diagnosis indicated the presence of right parotid gland schwannoma with cystic degeneration. Surgical treatment easily removed this tumor [32]. This research was to some extent in agreement with other previously published work which found that the Polislidae wasp toxin induced pseudolymphoma by Sandbank *et al*. [33].

3.6.4. Limb Compartment Syndrome

Normally, the compartment syndrome of the hand is usually the result of trauma or burns happened to an uncommon entity in children. However, Sawyer *et al*. described the first case of a 5-year-old boy who developed a compartment syndrome of the hand after a single wasp sting that required emergent fasciotomy. After treatment, the patient healed uneventfully while at 5-month follow-up had full use of his hand, full range of motion, and normal 2-point discrimination in all the fingers [34].

4. WASP BITES AND MECHANISM OF ACTION

4.1. The Advantages and Disadvantages of the Polislidae Wasp

China is carrying out large-scale defarming-and-reafforestation project. With the progress of returning farmland to forest and ecological environment gradually improved, the events of wasp sting happened more frequently [2]. In city, firefighters often take actions in response to the residents' request to destroy the invading wasps. However, to protect the biodiversity in

China and to keep the ecological balance, more nestles of wasps have been moved to the mountains or in the fields, while these wasp species demonstrated excellent predators to control pests. For example, feeding wasp in cotton fields suffered from serious pest in Hunan, and Jiangsu provinces of central China led to successfully bio-control of the pests [35].

4.2. Timely Processing of Polislidae Wasp Bites

According to previously published research [2, 13-34], the dangers of wasp bites to human bodies demonstrated in various aspects. The local reaction exhibited as swelling and pain by wasp sting, whilst the influence to body exhibited mainly as arrhythmia, liver dysfunction, kidney dysfunction, anaphylactic shock, neuromuscular and movement disorders. Furthermore, we also noticed that the injured degrees of toxic reaction and allergic reaction are also quite different after getting stung of the victims because of their various physical status and different constitutions. Therefore, the patients being bitten should promptly go to hospital, while focusing on examination of functionalities of liver, renal, myocardial enzymes, and check of blood, etc. Especially, to those patients who are stung in a large area must subjected to protective treatments upon their heart, liver and kidney, to avoid the occurrences of a toxic reaction, organ damage, or MOSD caused by wasp venom entering into human body due to the delayed treatment.

4.3. Pharmacological Mechanisms of Polislidae Wasp Bites Applicable to the Development of Insect Drugs

Though Polislidae wasp sting is somewhat dangerous and sometimes fetal, for the local residents in southwestern China especially in Yunnan province, Polislidae wasp has nevertheless been used historically as an alternative drug on treatment of rheumatic diseases [36]. Moreover, modern medical studies also have found that though bee venom also affects nervous system, cardiovascular system, respiratory system, endocrine system, immune function, inflammation, and other pathological processes, small doses of bee venom (such as bee sting) exhibited satisfactory effects on the treatment for certain diseases such as tumor, viral-infectious disease, heart disease, and HIV etc. [37]. However, because of a wasp sting may cause a series illnesses and appeared more serious symptoms than a bee sting, therefore a thorough understanding upon the pathogenic mechanism of the wasp venom is critical to future utilizing wasp venom for pharmacological interests. Based on the above reports, the pathogenic mechanisms of Polislidae wasp sting might be categorized as follows according to the above-mentioned clinical cases.

4.3.1. Mechanism of Inducing Heart Damage

The wasp venom can cause myocarditis, arrhythmia and other heart damage, but the exact mechanism is unknown. These may be initiated by melittin's inhibiting of mitochondrial and synaptic Na^+-K^+-ATP enzyme activity [38]. A report indicated that acute myocardial infarction caused by wasp sting may due to the wasp venom leading anaphylactic shock, which successively induced inadequate perfusion of coronary artery [39].

4.3.2. Mechanism of Inducing Brain Damage

The wasp venom can dilate blood vessels, thus having significant antihypertensive effect. After the blood pressure substantially declined, brain insufficiency might happened which will lead to cerebral infarction. A myasthenia gravis symptoms after wasp stung was reported [40], which was supposed to be initiated by venom allergens or toxic effects interfering with the synthesis and release of acetylcholine, thus resulting in the neuromuscular transmission disorders.

4.3.3. Mechanism of Inducing Liver Damage

The mechanism of wasp venom's causing liver damage might attributable to melittin and its metabolites which inducing a large number of inflammatory mediators to form antigen-antibody complex, and to deposit in sinusoids surface of liver cells to damage them. It can also activate T cells, inducing CTL responses and antibody-dependent T cell mediated cytotoxicity, thus resulting in a large number of liver cell necrosis [41].

4.3.4. Mechanism of Inducing Renal Damage

The most significant influence of wasp venom on the kidney is composed of the following aspects [42]: (1) hyaluronidase and proteolytic enzymes existed in the venom have cytolytic effect, which can cause dissolution of the tissue cells and lead to renal tubular degeneration and necrosis; (2) the phospholipase A_2 in the venom may act on the smooth muscle of blood capillaries, decreasing the tension of the capillaries, leading to a drop in blood pressure and a decrease of renal blood flow perfusion; (3) histamine, serotonin and the released endogenous histamine by allergic response after wasp stings all make telangiectasia, and make the permeability enhanced, while tissue

hyperemia, edema, exudation, and the decrease of effective circulating blood volume resulted in renal ischemia; (4) the venom possesses strong hemolytic activity, which can make lysis of erythrocytes, inducing haemoglobin to block the renal tubules, thus cause an acute renal tubular necrosis.

4.3.5. Mechanism of Influencing on Immunization

Wasp venom may cause allergic which belongs to a type I allergy. At the first time of wasp sting the body produces IgE. When repeated sting occurs, the venom, act as a allergen, will enter the sensitized body to combine mast cells and IgE of basophils cell membrane to release histamine, eosinophil chemotaxis chemotactic factor media cause smooth muscle spasm, vascular dilatation, increased microvascular permeability, and tissue edema [43]. Sometimes, there will be a delayed type allergy, which is considered as an immune-mediated type III allergic reactions and activation reaction upon immune complex deposition and complement system [44]. The reason of wasp venom's causing autoimmune hemolytic may be laid to that the causative agent acting on red blood cells to change the allergenicity of the membrane, to stimulate the formation of antibody, thus resulting in anti-erythrocyte antibody. In addition, patient's immune mechanisms might also have been destroyed and lost its recognizing function, leading to the production of the autoantibodies and their combination with the erythrocyte membrane antigen [45].

5. CONCLUSION AND FUTURE PERSPECTIVE

5.1. Future Perspectives of Polislidae Wasp Venom Utilization And R&D

The Polislidae wasp venom toxicity is serious harm of human, but using biologically active substances existing in the venom to treat human diseases will make this natural resource extremely valuable. However, the systematic investigations on chemical composition and pharmacological activities are rather lacking during the past decades, which urged our interest of further detailed research. Yunnan Province has rich resources of Polislidae wasp with altogether 19 species [46], which may ensure the source origin of Polislidae wasp venom.

Though preliminary chemical check indicated the most popular substances of the venom are peptidic [12], thorough components check of the Polislidae wasp venom is essential to fully reveal its bioactive substances. Inspired by the findings of preliminary investigations on the pharmacological effects and toxicity of wasp venom [3, 8-12] as well as reported clinical symptoms after Polislidae wasp stings [13-34], in-depth comprehensive pharmacological studies should be carried out with techniques including bioassay-guided extracts and pertinent bioactivity evaluation [47-54]. The to-be-determined pharmacological effects of Polislidae wasp venom include but are not limited to those towards neuronal systems, cardiovascular and blood circulation systems, antibacterial and antifungal activities, anti-viral infections, anti-tumor effect, and therapeutic effects on autoimmune diseases, rheumatism, and rheumatoid.

In addition, Polislidae wasp venom may dissolve muscle tissues, this natural venom or purified peptides from the venom merits further investigations and development to be the material base for the new inventions of health products on the treatment and control of obesity and the management of beauty and wellness. To fulfill its R&D, experiments against leptin receptor, ciliary neurotrophic factor, cannabinoid receptors, neuropeptide Y5 receptor, β3-adrenergic receptor, and fatty acid transport protein 4 should therefore be carefully performed.

5.2. Conclusion

Above all, in people's impression, Polislidae wasp belongs to pests of risky for human beings. But the double-sided nature of things enlightens us that we should make full use of this God-given resource, to overcome prejudices on it, and to optimally exploit the other nature of its beneficial to human health. This requires the joint efforts of worldwide scientists including entomologists, biochemists, pharmacologists, toxicologists, pharmacists, and so forth.

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REFERENCES

[1] Li TS. Economic Insect Fauna of China (Volume 30, Vespoidea). Beijing. Science Press 1985; 58-74.

[2] Xiang HQ, Lai GF, Shen LR. Progress of hazards and governance in sting wasps. Zhejiang J Prev Med 2004; 16: 60-1.

[3] Liang SP, Wang Z, Huang JJ, Zhong X. Biological characterization of crude venom from the wasp (*Polistes olivaceus*). Acta Sci Nat Univ Norm Hunan 1994; 17: 49-54. DOI: CNKI:ISSN:10002537.0.1994-03-010

[4] Murata K, Shinada T, Ohfune Y, *et al*. Novel biologically active peptides from the venom of *Polistes rothneyi iwatai*. Biol Pharm Bull 2006; 29: 2493-7. http://dx.doi.org/10.1248/bpb.29.2493

[5] Wang SF, Yang BM, Li LB, Li H. Review and prospect for study on pharmacological action of melittin. Tianjin Pharmacy 2003; 15: 53-7. DOI: CNKI:SUN:TJYA.0.2003-04-028

[6] Zhao YH, Liu AS, Li RQ, *et al*. Progress in biological mechanism of melittin. Acta Entomol Sin 2007; 50: 737-44. DOI: CNKI:SUN:KCXB.0.2007-07-014

[7] He QY, Yu XD. A general survey of the study of mastoparan (MP) from wasp venom. J Chongqing Normal Univ (Nat Sci Edition) 2007; 24: 76-80. DOI: CNKI:ISSN:1672-6693.0.2007-01-020

[8] Li YH, Hu FL, Liu YH. Bee venom allergen phospholipase A_2. Chem of Life 2001; 21: 299-302.

[9] Sun TM, Fu Y, Liang W, *et al*. Experimental study of the killing effect of wasp venom on the tumor cell. Chin Arch Trad Chin Med 2003; 21: 681.

[10] Liang SP, Qin YB, Zhang DY, *et al*. Biological characterization of spider (*Selenocosmia huwena*) crude venom. Zoolog Res 1993; 14: 60-5. DOI: cnki:ISSN:0254-5853.0.1993-01-011

[11] Wang Y, Chen YQ, Han YD, *et al*. The biological activity of the centipede venom (*Scolopendra subspinips mutilans* Koch). Chin Sci Bull 1985; 30: 218-20.

[12] Schmidt, JO, Lee, T-S, Chao, J-T. Pharmacological activities of *Polistes rothneyi graham* and *P. olicvaceus* (Hymenoptera: Vespoidea) venoms, a preliminary report. Chin J Entomol 1993; 13: 259-63.

[13] Zhu CY. Clinical analysis on 53 cases of toxicosis caused by wasp sting. Mod Diagn Treat 2008; 19: 247-8.

[14] Jairam A, Kumar RSV, Ghosh AK, *et al*. Delayed Kounis syndrome and acute renal failure after wasp sting. Intern J Cardiol 2010; 138: e12-14. http://dx.doi.org/10.1016/j.ijcard.2008.06.004

[15] Bánovčin P, Havlíčeková Z, Jeseňák M, *et al*. Severe quadriparesis caused by wasp sting. Turkish J Pediat 2009; 51: 485-8.

[16] Mondal N, Krishnamurthy S. Narayanan P, Srinivasan S. Bilateral ptosis in a child following massive attack by a swarm of wasps. J Child Neurol 2011; 26: 1322-4. http://dx.doi.org/10.1177/0883073811405051

[17] Yang XA, Li GQ. A case report of brain damage caused by wasp stings. Chongqing Med 2009, 38: 2456-7.

[18] Ren H. One case of lacunar infarction by wasp stings. Guangming J Chin Med 2009; 24: 2185.

[19] Crawley F, Schon F, Brown MM. Cerebral infarction: A rare complication of wasp sting. J Neurol Neurosurg Psychi 1999; 66: 550-1. http://dx.doi.org/10.1136/jnnp.66.4.550

[20] Sachdev A, Mahapatra M, D'Cruz S, *et al*. Wasp sting induced neurological manifestations. Neurol India 2002; 50: 319-21. http://www.neurologyindia.com/text.asp?2002/50/3/319/1413

[21] Qin JP, Wei LG. A case of toxic hepatitis by wasp sting. Chin J Hepatol 2000; 8: 189.

[22] Qiu HY, Zuo C, Liu F, *et al*. Two cases of multiple organ dysfunction and acute pancreatitis by wasp sting. Med J West China, 2008; 20: 450-1.

[23] Cheng XH. One case of children acute renal failure induced by wasp sting and its care. Today Nurse, 2002; 1: 38-9.

[24] D'Cruz S, Chauhan S, Singh R, Sachdev A, Lehl S. Wasp sting associated with type 1 renal tubular acidosis. Nephrol Dial Transplant 2008; 23: 1754-5. http://dx.doi.org/10.1093/ndt/gfm855

[25] Zhang Q, Chen J. One case of hyperkalemia huge and T-wave induced by wasp stings. Jiangsu J Prac Electrocardiol 2001; 10: 268-9.

[26] Qu R, Hu HY, Xiao GC. A case report of wasp sting-induced anaphylactic shock. Intern J Emerg Crit Care Med 2004; 1: 449.

[27] Cai SF, Zhang L, Gao L. A case of immune hemolytic anemia resulting from wasp sting. ACTA Acad Med Militaris Tertiae 2003; 25: 732,735.

[28] Li J, Wei X, Li B. A case report by wasp stings on corneal. Jilin Med J 2007; 28: 1086.

[29] Li WF, Han YJ, Zhang MH, Chen JL. A case report of multiple lesions on the eye cause by wasp sting. Chin J Ocul Trauma Occupat Eye Dis 2006; 28: 568.

[30] Fan CH, Zhou LX. Clinical analysis of wasp sting induced multiple organ dysfunction syndrome. Med Innov China 2009; 6: 26-7.

[31] Yang X-B. Clinical analysis of 14 cases by wasp stings induced multiple organ failure. Chongqing Med 2010; 39: 3000-1.

[32] Yang LJ, Si XH. A case report of parotid schwannoma caused by wasp sting. J Clin Stomatol 2008; 24: 99-100.

[33] Sandbank M, Barr-Nea L, Ishay J. Pseudolymphoma of skin induced by oriental hornet (*Vespa orientalis*) venom ultrastructural study. Arch Dermatol Res 1978; 262: 135-41. http://dx.doi.org/10.1007/BF00455382

[34] Sawyer, JR, Kellum EL, Creek AT, Wood GW. Acute compartment syndrome of the hand after a wasp sting: a case report. J Pediat Orthop B 2010; 19: 82-5. http://dx.doi.org/10.1097/BPB.0b013e32832d83f7

[35] Jiang SJ. The protection and utilization of wasps. Special Econ Anim Plant 2006; 3: 8-9.

[36] Guo Y, Gao P, Zhao Y. Scientific breeding technology to ensure the sustainable utility of the vespidae insects resources. J Anhui Agricul Sci 2012; 40: 10906-8.

[37] Guo FB. Modern pharmacological studies of venom. Apicult Sci Technol 2003; 2: 29-30.

[38] Yang S, Zhang XM, Jiang MH. Inhibitory effect of melittin of Na^+, K^+ ATPase from guinea pig myocardial mitochondria. Acta Pharmacol Sin 2001; 22(3): 279-82. DOI: CNKI:SUN:ZGLL.0.2001-03-014

[39] Levine HD. Acute myocardial infarction following wasp sting: report of two cases and critical survey of the literature. Amer Heart J 1976; 91: 365-74. http://dx.doi.org/10.1016/S0002-8703(76)80222-0

[40] Brumlik J. Myasthenia gravis associated with wasp sting. J Amer Med Assoc 1976; 235: 2120-1. http://dx.doi.org/10.1001/jama.1976.03260450032026

[41] Shi TD, Ren H, Luo Z. Bee venom acupuncture induced acute liver failure: a case report. ACTA Acad Med Militaris Tertiae 2006; 28: 183.

[42] Zhu XH, Song XS. Blood purification (HP/HD) treatment of acute toxic nephropathy induced by severe wasp sting. Mod Med & Health 2005; 21: 189-90.

[43] Yan J, He Z, Chen HH. Three cases of wasp sting-induced anaphylactic shock. Chin J Misdiagn 2006; 6: 790.

[44] Ghosh, JB, Roy M, Bala AK. Delayed onset interstitial nephritis following multiple wasp stings. Indian J Nephrol 2009; 19: 71-3. http://dx.doi.org/10.4103/0971-4065.53326

[45] Zhang JH. Modern Blood Disease Therapeutics. Beijing. People's Military Medical Publisher 1997; 266-7.

[46] Dong D, Wang Y. Studies on the vertical distribution of Vespoidea and analysis of the Fauna in Yunnan Province, China. Zoolog Res 1992; 13: 83-7. DOI: CNKI:SUN:DWXY.0.1992-04-009

[47] Yang LX, Huang KX, Li HB, *et al*. Design, synthesis and examination of neuron protective properties of alkenylated and amidated dehydro-silybin derivatives. J Med Chem 2009; 52: 7732-52. http://dx.doi.org/10.1021/jm900735p

[48] Jiang X, Ao L, Zhou C, *et al*. Design, synthesis, and evaluation of two series of Territrem B analogues Chem Biodiv 2005; 2: 557-67.

[49] Li H, Zhou C, Pan Y, *et al*. Evaluation of antiviral activity of compounds isolated from *Ranunculus sieboldii* and *Ranunculus sceleratus*. Planta Med 2005; 71: 1128-33. http://dx.doi.org/10.1055/s-2005-873169

[50] Li H, Zhou C, Zhou L, *et al*. *In vitro* antiviral activity of three enantiomeric sesquiterpene lactones from *Senecio* species against Hepatitis B virus. Antiviral Chem & Chemother 2005; 16: 277-82.

[51] Wang XY, He ZC, Song LR, *et al*. Chemotherapeutic effects of bioassay-guided extracts of the American Cockroach, *Periplaneta americana*. Integr Cancer Ther 2011; 103: NP12-23. http://dx.doi.org/10.1177/1534735411413467

[52] Ding HX, Lu W, Zhou CX, *et al*. Synthesis and cytotoxicity evaluation of some isoquinoline derivatives related to 1-arylnaphthalene lignans. Chin Chem Lett 2005; 16: 1279-82.

[53] Zhang XQ, Peng L, Peng F. Research advance of medicinal insects in treatment of gastric carcinoma. Med Recapitulate 2011; 17: 1318-20. DOI: CNKI:SUN:YXZS.0.2011-09-016

[54] Chen J, Peng F. Research advance of anti-hepatoma medicinal insects. Med Recapitulate 2010; 16: 2823-5. DOI: CNKI:SUN:YXZS.0.2010-18-036

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