Animal Venom for Medical Usage

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Pharmacopuncture of bee, snake, and toad venoms are being used in Korean medicine institutions. Clinical evidence for the efficacy of these animal venoms has been summarized through a literature search. This research contributes to the development of animal venom-based medicines.

animal venom bee venom snake venom toad venom pharmacopuncture

1. Introduction

Animal venoms, widespread worldwide, are composed of a variety of proteins and peptides that were developed through millions of years of evolution [1][2][3]. They are complex mixtures that vary depending on the venom-producing species [2]. The most known and studied venoms originate from bees, snakes, scorpions, and spiders [1][2].

Venomous animals are a valuable resource for the development of therapeutics [4]. Bee venom therapy is used to treat musculoskeletal diseases (e.g., low back pain, knee osteoarthritis), Parkinson's disease, adhesive capsulitis, and polycystic ovary syndrome [5]; snake venom-based drugs are used to treat hypertension, heart attack, acute coronary syndrome, stroke, pulmonary embolism, and other diseases [6]. While animal venoms are toxic, they can have therapeutic effects [7].

Korean medicine (KM) institutions have been using animal venoms in their pharmacopuncture therapies: animal venoms are injected into acupunctural points using syringes [8]. Pharmacopuncture, also known as herbal acupuncture, is a new form of acupuncture treatment that injects herbal medicine into acupuncture points [9]. In South Korea, pharmacopuncture treatment is one of the most commonly used methods in traditional Korean medicine clinics [10]. Official insurance claims statistics for pharmacopuncture are only available for automobile insurance coverage; it has been reported that approximately 1,555,000 pharmacopuncture sessions were administered to 168,089 patients for related treatments in 2014 [11].

Chinese pharmaceutical companies produce acupunctural medicines approved by the food and drug authorities [12]; these medicinal materials are used in Chinese medicine institutions to treat patients. In South Korea, such medicinal products are made in external herbal dispensaries (EHDs) that employ the level of good manufacturing practice (GMP) required for injections [13]. EHDs are auxiliary facilities of KM institutions that

prepare and supply various types of medicines (e.g., capsules, tablets, powders, pharmacopuncture, and decoction) to KM institutions [14].

2. Discussion

To our knowledge, this study is the first to report on the three animal venom therapies used in KM institutions in South Korea. It covers the current status of the production of pharmacopuncture medicines based on animal venoms, their production processes, and indications. The government played a leading role in this study, which aimed to understand the current status of the production of animal venom pharmacopuncture medicines in EHDs. All of the pharmacopuncture medicines used in KM institutions are being produced in EHDs; this study covered 11 of the 16 EHDs that produced pharmacopuncture medicines (68.8%). Since EHDs prepared these medicines following the prescriptions issued by KM institutions, the production records at EHDs can be considered to represent the current status of the pharmacopuncture medicines used in KM institutions. Therefore, this study provides an overall status of the use of animal venoms for therapeutic applications by KM institutions.

Bee venom products represent the second-largest quantity of pharmacopuncture medicines in South Korea, accounting for 99.06% of the total animal venom-based pharmacopuncture. While bee venom causes neurotoxic symptoms including local paresthesias, headache, dizziness, nausea and vomiting, muscle aches, and rarely, cerebrovascular infarcts [15][16][17][18], recent non-clinical studies demonstrated that bee venom has anti-inflammatory [19], anti-nociceptive [20], and anti-cancer activities [21]. The toxic reactions of bee venom therapy in clinical studies ranged from fatigue [22], erythematous plaques [23], pallor face [24], nausea [24], vomiting [24], and other minor side effects to more serious ones such as limb paralysis [25], dyspnea [25], unconsciousness [26], and death [26]. There have been many clinical and non-clinical studies reporting the side effects and benefits of bee venom therapy. However, due to the possibility of variation in the species of bees and the nutrients they take, the composition of bee venom can differ depending on geography. Therefore, it is necessary to standardize the material, evaluate its toxicity, and examine its benefits.

Snake venom is the 13th most frequently used pharmacopuncture medicine in KM institutions. While snake venoms can be cardiotoxic (e.g., arrhythmias, bradycardia, tachycardia and hypotension) [27], myotoxic (e.g., myalgias, myopathy and rhabdomyolysis) [27], neurotoxic (e.g., ptosis, external ophthalmoplegia, dysphagia, dysphonia and broken neck sign) [28], and nephrotoxic (e.g., ischemia and renal failure) [27], non-clinical studies of snake venom reported effects such as a decrease in blood pressure [29], regulation of blood coagulation [30], and anti-tumor [31] and analgesic activities [31]. The snake-venom-based medicines that have been approved by the Food and Drug Administration (FDA) are administered using tablets (captopril) or intravenous injections (eptifibatide and tirofiban) [32]. Further studies are needed to evaluate the efficacy and toxicity of the routes of administration (e.g., oral, muscle injection, or infusion, etc.).

Toad venom is the least frequently used animal venom in KM institutions (0.27%). While toad venom has toxic effects and causes gastrointestinal, mental, cardiac conduction, and arrhythmic disturbances [33], non-clinical studies have reported anti-inflammatory [34], antiplasmodial activity [35], and antiproliferative effects on cancer cells

[36]. The treatment toxicity is the most important factor limiting its use [37]. Further studies should be carried out to evaluate the benefits and side effects of its use to treat inflammatory diseases.

As is the case with bee stings, animal venom was used as it was, in some cases. However, in most cases, it was used as diluted to an appropriate concentration for clinical purposes. Animal venoms may cause idiosyncratic reactions depending on the individual in addition to their toxic effect [38]. For this reason, it is recommended to have the patient take a certain amount before clinical applications, in order to determine whether the use or administration of such a substance causes adverse effects or not. Also, according to the analysis on the 1,192,667 cases of accidents caused by animal venom over 12 years in Brazil by Chippaux [39], snake bites were linked to the highest fatality rate of 0.43%, followed by bee stings, of which the fatality rate was 0.33%. Since animal venom has toxic effects, it is necessary to refine, dilute, or otherwise process it before clinical use.

This study has several limitations. First, this study was a literature review of the indications and benefits of pharmacopuncture medicines based on animal venoms, without any reviews on the clinical indications in the real world. Further surveys of KM doctors are needed to cover the clinical indications and side effects. Second, a literature review of indications and side effects used only articles published in South Korea, and only articles dealing with injectables were reviewed. International databases will need to be reviewed to evaluate animal venoms factors such as the species, extraction process, and administration routes. Third, this survey was conducted by the government, which measured its accuracy and trustworthiness. However, the validity of the questionnaire was not confirmed.

Despite these limitations, this is the first study reviewing the production volume and current status of animal venom-based pharmacopuncture medicines used in clinical practice in South Korea. Collecting further data is necessary for the standardization of pharmacopuncture medicine and safety of dosages and clinical applications.

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