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Exploring the Application of Insect Based Drugs in the Treatment of Coronary Heart Disease Based on the Principle of "Networking for Communication"

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Abstract: ***As a common cardiovascular disease, patients with coronary heart disease (CHD) often have chest distress, chest pain, shortness of breath, panic, fatigue, sweating and other symptoms. The basic treatment plan in clinic is to prevent platelet aggregation, regulate lipid and stabilize plaque, and nourish myocardial cells; The theory of "using the network to facilitate communication" was proposed by Ye Tianshi and developed and perfected by Academician Wu Yiling, providing the treatment principle of "communication" for coronary heart disease; Insect drugs can treat CHD from multiple aspects, such as antithrombotic, anti-inflammatory, analgesic, immune regulation, anticoagulant, antioxidant, microcirculation improvement, and protection of vascular endothelial cells; Guided by the "collateral disease theory", this paper discusses the relationship between "collateral for use" and coronary heart disease, insect drugs. From the four aspects of phlegm, blood stasis, wind, and deficiency, it discusses the pathogenesis of phlegm coagulating collaterals, blood stasis, internal movement of collateral wind, and stagnation of collateral deficiency. It establishes the treatment principles of coronary heart disease, which are phlegm resolving, blood stasis dispersing, wind dispelling, and qi flowing. Thus, it discusses the use of eight insect drugs, namely, ground beetle beetle, bombyx batrytica, scorpion, centipede, musk, earthworm, leech, and tabanus.***

Keywords: Theory of collateral diseases, Network for communication purposes, Coronary heart disease, Insect drugs.

1. Introduction

Coronary Heart Disease (CHD) is a condition caused by atherosclerotic plaques in the coronary arteries, which narrow the vessel lumen, leading to ischemia and hypoxia of the corresponding myocardium, resulting in symptoms such as spasm and pain [1]. The 2023 China Cardiovascular Health and Disease Report shows that the prevalence of cardiovascular diseases (CVD) in China has been continuously rising, with an estimated 11.39 million patients with coronary heart disease (CHD) [2]. The formation of CHD plaques is related to lipids, vascular endothelial injury, blood stasis, and hypercoagulable state [3]. Western medical treatment generally adopts coronary stent implantation, as well as lipid-lowering and plaque-stabilizing therapy, and antiplatelet aggregation therapy. However, restenosis after surgery, bleeding symptoms caused by antiplatelet aggregation, and the patient's anxiety and depression cannot be ignored. Traditional Chinese Medicine (TCM), guided by the holistic concept, takes "smoothness" of the heart network as its function, and treats CHD from the perspective of "smoothness" through syndrome differentiation and treatment, which has shown good efficacy with reduced toxicity. In TCM theory, CHD falls under the category of 'Xiongbì' (chest obstruction). The character 'bì' implies blockage or obstruction, which aligns with the pathogenesis of CHD. Both can be understood as pain resulting from obstruction of the heart meridians. Therefore, the principle that 'the collaterals function properly when they are unobstructed' emphasizes the importance of 'unblocking.' Insect-based medicines refer to animal-derived substances in traditional Chinese medicine, and clinical evidence has shown that these medicines have the effect of promoting blood circulation and unblocking collaterals. Professor Zhao Mingjun, based on the theory of 'the collaterals function properly when they are unobstructed,' treats CHD with prescriptions incorporating insect-based medicines, achieving definite therapeutic effects. Pharmacological studies indicate that insect-based medicines can treat CHD from multiple angles, such as anti-thrombosis, anti-inflammatory and analgesic effects, immune regulation, anti-coagulation, antioxidant activity, improvement of microcirculation, and protection of vascular endothelial cells [4].

2. Theoretical Origin of the 'Network Functions as Its Use' Theory

The Ling Shu · Jingmai Pian states: 'When the meridians are unobstructed, all diseases disappear; when they are blocked, all diseases arise. To live a long life, one must nourish the meridians.' The meridians are the tunnels of the human body, the channels through which qi and blood circulate. When the meridians are smooth, they can distribute refined substances to moisten and nourish the zang-fu organs and resist external pathogens. If the heart meridian is unimpeded and qi and blood circulate smoothly, the healthy qi will be abundant; if the heart meridian is obstructed by internal wind, qi stagnation, or blood stasis, leading to impaired circulation of qi and blood, CHD will occur. The 'Tiaojing Lun' from the 'Suwen' states: 'If the disease is in the pulse, treat it with blood; if the disease is in the blood, treat it with the collaterals.' If the illness arises in the pulse, blood should be used for treatment; if there is an issue with the blood, the collaterals should be regulated. The pulse is the repository of blood, and blood flows within the pulse. If the pulse channel is obstructed, blood circulation becomes impaired, so blood must be regulated to unblock the

pulse. Blood is the function of the pulse; if the blood itself is diseased, such as with phlegm or stasis, the collaterals need to be regulated to restore normal circulation. Ye Tianshi believed that 'long-term illness enters the collaterals' and 'long-term pain enters the collaterals,' thus he proposed that 'the collaterals function when they are unblocked' and established various methods to unblock the collaterals for later generations. Based on his in-depth research and practice on TCM theory of collateral diseases, Academician Wu Yilin proposed that 'collateral vessels are a network structure that maintains life activities and keeps the human internal environment stable.' The collaterals of the heart are prone to stagnation and stasis, easy to enter but difficult to exit, and tend to accumulate into tangible masses. Collateral disease fundamentally stems from blocked collaterals, hence 'the collaterals function when they are unblocked.'

3. The Principle of 'Using the Network to Facilitate Circulation' and CHD

"The Suwen section of the Huangdi Neijing states": 'In cases of heart bi, the pulse is obstructed... When the reverse qi rises, fear occurs.' When the heart's meridians are blocked and heart blood encounters obstruction, it leads to distension below the heart. When the qi and blood distribution in the heart meridians is impaired, and the heart meridians cannot be adequately nourished, symptoms such as restlessness, shortness of breath, and labored breathing occur. The Syndrome Cause and Pulse Treatment records: 'The syndrome of chest bi is also known as stomach bi... This is the syndrome of chest bi.' Improper diet, excessive hunger or satiety, causes spleen and stomach disharmony and turbidity in the middle jiao. CHD often involves deficiency of the collaterals with stagnation, and obstruction of the collaterals by stasis and phlegm-damp. Its fundamental nature is deficiency with secondary excess, resulting from insufficient innate endowment and impaired postnatal organ functions, leading to latent pathogenic factors accumulating internally. Consequently, the heart collaterals become unsmooth, the nutritive and defensive qi circulate improperly, the qi and blood in the heart collaterals are insufficient, their propelling force weakens, causing blood circulation to be impeded. Additionally, when the heart and kidney fail to communicate, insufficient kidney water allows excessive heart fire, which transforms body fluids into phlegm. This phlegm-damp accumulates internally; combined with stasis blood, it lodges in the collaterals, causing obstruction. When the qi and blood of the heart collaterals are blocked, pain occurs, leading to the development of CHD. CHD has a long course and, when the disease persists, it invades the collaterals. If the heart collaterals are damaged, blood circulation becomes weak; when blood stagnates in the vessels, it forms stasis and obstruction. If the spleen collaterals fail to transport, body fluids cannot circulate properly; when fluids linger in the vessels, they transform into dampness and phlegm. If the liver collaterals are not smooth, the function of secretion and excretion is impaired, qi movement is blocked, leading to stagnation of the qi collaterals. This results in more severe pathogenic factors of collateral stasis, blood stasis, dampness, and phlegm. Furthermore, constrained by daily life, diet, and seasonal changes, excessive consumption of qi and injury to yin occur, causing niqi (reversed qi flow), internal wind due to collateral disturbance, and obstruction of heart collaterals, ultimately inducing CHD. CHD also follows the principle that 'collaterals function through unobstructed flow'; thus, it is necessary to unblock where there is obstruction and promote smooth flow where there is stagnation.

4. The Principle of "Using the Network to Facilitate Circulation" and Insect-Based Medicines

Due to their unique biological activity and ability to move freely, insect-based medicines are highly effective in promoting the flow of meridians and activating blood circulation to resolve stasis. Li Shizhen summarized the therapeutic value of insect-based medicines in treating conditions such as apoplexy and CHD in Compendium of Materia Medica, and emphasized their functions of detoxifying and dispersing nodules, as well as promoting meridian flow and relieving pain. The Questions and Answers on Materia Medica records: 'The penetrating and purging effects of animal-based medicines are even more pronounced than those of plant-based medicines.' Insect-based medicines are considered 'substances with flesh and blood,' specializing in eliminating pathogenic factors, unblocking meridians, breaking up blood stasis, and expellingblood stasis, thus directly reaching the root of the disease location. Professor Wu Yiling, in his research on the theory of Luobing (collateral network disease), proposed that insect-based medicines have a unique therapeutic effect of 'pursuing and removing deeply entrenched pathogenic factors of qi and blood', believing that insect-based medicines have the action of searching, clearing, and unblocking, which can deeply penetrate the collateral network to treat diseases such as CHD. Zhang Zhongjing summarized the pathogenesis of CHD as 'Yang deficiency and Yin stringiness', and the 'Shengji Zonglu' (Comprehensive Records of Holy Benevolence) also states: 'The discussion says that chest obstruction disease has a pulse with Yang deficiency and Yin stringiness... due to Yin stringiness, chest obstruction and heart pain occur.' Insect-based medicines are mostly renowned for their ability to unblock collaterals, which aligns perfectly with the pathogenesis of CHD. The principle that 'collaterals function properly when unblocked' guides the use of insect-based medicines in treating CHD.

5. The Role of Insecticide in the Treatment of CHD

Academician Wu Yiling once stated: "Chronic illness, prolonged pain, and long-standing blood stasis enter the collaterals, where phlegm and stagnant blood coalesce. These conditions cannot be effectively treated by herbal medicines that merely disperse or expel pathogens; instead, insect-based collaterals-activating drugs demonstrate unique efficacy." In chronic CHD, wind, qi, phlegm, and stasis intermingle within the body. Insect-based drugs exert even stronger effects in the "activating" pathway. When collaterals are disturbed by wind, insect-based drugs resolve phlegm and clear collaterals. For instance, silkworm pupae and earthworms transform phlegm while clearing collaterals. Scorpions and centipedes dispel wind to regulate collateral vessels; for collateral qi stagnation, musk and Eupolyphaga can be used to promote qi flow and unblock collateral vessels; for collaterals and vessels stasis,

leeches and Gadus can resolve stasis and restore patency. If cardiac collaterals are obstructed, symptoms such as palpitations, chest fullness, and epigastric pain may occur, and insect-derived medicines can nourish the heart collaterals to ensure unimpeded circulation.

5.1 Phlegm Obstructing the Collaterals, Resolving Phlegm to Clear and Unblock the Collaterals

The Treatise on the Origins and Symptoms of Various Diseases (Volume 20) states: "Phlegm arises from blood and vessel obstruction, where retained fluids fail to dissipate, thus forming phlegm." When blood stasis and fluid retention occur, the body cannot resolve them spontaneously, leading to phlegm formation. The Medical Canon explains: "Thickened fluids transform into phlegm or fluid retention, which, if prolonged, seep into the vessels, clouding the blood." Blood can also convert into fluids; their incompatibility generates phlegm and stasis. The spleen is the source of phlegm production. When the spleen and stomach fail to function properly, phlegm-dampness accumulates internally, obstructing qi and blood circulation and causing heart collaterals to block. The lungs are the gathering place of phlegm. When lung qi is imbalanced, fluid distribution becomes disordered, leading to internal water-dampness accumulation, which in turn generates phlegm-turbidity. Phlegm coagulation disrupts qi and blood flow, resulting in fatigue and sweating. Excessive phlegm-dampness obstructing the spleen and stomach causes nausea and vomiting. CHD is closely associated with disordered distribution of body fluids, internal generation of phlegm-dampness, and impaired circulation of qi and blood. It involves the functions of visceral organs such as the heart, lungs, and spleen. The interplay of phlegm and blood stasis obstructs the meridians, leading to impaired heart meridian flow and the onset of CHD. The heart collaterals are blocked by phlegm and blood stasis, resulting in impaired dispersion of lung qi and failure of body fluids to distribute. Phlegm-turbidity internally generates and ascends to the chest, obstructing the heart meridian, manifesting as symptoms such as chest tightness, heart pain, and shortness of breath. The Yi Bian: Five Urinary Disorders and Differentiation of Body Fluids states: "There are qi-transformed body fluids and dietary body fluids. The stomach is the sea of body fluids, hence phlegm accumulates there." Phlegm coagulates in the heart meridian, causing congestion of the heart collaterals. Impaired flow leads to pain, resulting in CHD and the manifestation of chest pain. Phlegm obstructs the meridian pathways, disrupting the ascending and descending functions of qi. Consequently, the dispersion of heart qi and lung qi becomes abnormal, leading to chest tightness and shortness of breath. Phlegm coagulation impairs the circulation of qi and blood, causing fatigue and sweating. Excessive phlegm-dampness obstructing the spleen and stomach leads to nausea and vomiting.

Eupolyphaga can expel phlegm, resolve stagnation, unblock collaterals, and treat injuries. It is salty, cold in nature, and slightly toxic. The Leigong Paofa Zhi Xing Jie states: "Eupolyphaga is specifically indicated for blood disorders, particularly for blood stasis and congestion." Its efficacy lies in the collaterals, where it functions to remove obstruction, phlegm-dampness, and stagnant blood. Guishuhua [5] and teams discovered that Eupolyphaga sinensis (commonly known as Chinese stink bug) exhibits therapeutic effects in ameliorating the inflammatory microenvironment of coronary arteries and repairing endothelial damage. Experimental studies demonstrated that E. sinensis significantly improves the gut microbiota structure in rats, increasing the relative abundance of Lactobacillus and Clostridium species. Gamma-aminobutyric acid (GABA) may serve as a key metabolite underlying its lipid-lowering effects, while Lactobacillus and Clostridium species are likely pivotal microbial components in this mechanism. [6]. Research by Wang Shaoping's team [7] discovered that the active peptide DP17 from the ground beetle may improve gut microbiota balance in hyperlipidemia animals by inhibiting lipid absorption receptors in the intestinal mucosa, thereby promoting rapid lipid excretion. The silkworm (Mulberry silkworm, Bombyx mori) has the function of promoting blood circulation and unblocking collaterals. As recorded in Ben Cao Qiu Zhen: "Silkworm is used to treat wind-related diseases in silkworms. It treats wind and phlegm, disperses nodules, and regulates meridians, as it is said to act through qi interaction and willpower." Professor Li Shimao pointed out that silkworm can enter the blood vessels and the collaterals of the heart, hence it is commonly used to treat palpitations and chest pain caused by phlegm stagnation in the collaterals [8].1-DNJ in silkworm pupae significantly downregulates the N-glycosylation level of cardiac proteins in diabetic mice. The intervention effect of 1-DNJ on N-glycosaminoglycan α-1, 6-fucosylation is pronounced, indicating that 1-DNJ alleviates diabetic cardiomyopathy-associated fibrosis by inhibiting the formation of N-acetylglucosamine and reducing its release [9]. Wang Shanshan's research team [10] previously discovered that silkworm extract could prolong rabbit blood clotting time. They further found that the mechanism by which silkworm extract improves ischemia - reperfusion - induced neurological damage in rats may be related to its anticoagulant effects and promotion of cerebral microvascular endothelial cell proliferation. Based on this, it is reasonable to consider that silkworm extract may also have beneficial effects on myocardial ischemia. For CHD with phlegm-accumulating and collaterals obstructing syndrome, the combined use of Eupolyphaga sinensis and silkworm extract synergistically promotes phlegm resolution, thereby clearing and unblocking collaterals.

5.2 Internal Movement of Collaterals, Dispelling Wind to Achieve Spontaneous Regulation of Collaterals

Wind-induced disorders refer to the invasion of pathogenic wind. Wind is the primary cause of various diseases, characterized by its mobility and variability, with a light and rising nature that wanders unpredictably. When the body's vital qi is deficient, pathogenic wind internally generates, obstructing the meridians and impeding the flow of qi and blood. If it invades the heart meridian, it leads to stasis in the heart collaterals, resulting in chest pain. The Yellow Emperor's Inner Canon states: 'Wind is the origin of all diseases.' CHD may develop from prolonged illness, constitutional weakness, or deficiency of vital qi; or from emotional stagnation leading to chronic depression. External pathogenic heat-toxins or liver qi stagnation transforming into fire may internally generate heat-toxins that induce wind. Qi deficiency and blood weakness allow wind pathogens to

invade internally. When collaterals become agitated, the pathogenic wind—being a yang pathogen—often manifests in critical states. Spasms of the heart collaterals occur when wind arises, creating a mixture of deficiency and excess that generates turbid qi, rendering the body unable to resist, ultimately leading to CHD. Therefore, prompt expulsion of wind pathogens and dredging of collaterals are essential. Collateral disease represents pathological changes in collaterals, serving as the core mechanism of the disease and its root cause. Collaterals may remain stable or abnormal: stable ones ensure unimpeded flow, while abnormal ones trigger disease onset. Once disease emerges, pathological collaterals manifest, and once formed, collateral disease becomes established.

Insect-derived medications, due to their migratory and invasive properties, can directly target the affected area. Therefore, they are often employed to calm wind, relieve spasms, relax tendons, and unblock collaterals, thereby treating the internal movement of collaterals in CHD. The whole scorpion possesses the effect of dispelling wind and unblocking collaterals. As stated in Ben Cao Zheng Yi: "Scorpions are venomous insects with a pungent taste. Their ability to treat wind is attributed to their migratory and invasive nature... This can temporarily suppress the symptoms." The therapeutic principle of whole scorpion in treating wind is likely due to its migratory and invasive properties, which align with the clinical manifestation of CHD, where "wind is characterized by its tendency to move rapidly and change frequently." Syb-prII-1 is a β-type scorpion neurotoxin isolated from the venom of BmK scorpion, which significantly alleviates pain behavior in rats. Naseem et al. described a novel scorpion toxin, Cm 28, which blocks KV1.2 and KV1.3 channels and inhibits T-cell activation. These properties may be utilized for the development of novel therapies for neuroinflammatory and autoimmune diseases [11]. Leptucin, a substance from the venom of the scorpion, demonstrated 95% analgesic activity at a dose of 0.48 mg/kg in the hot plate test, and histopathological evaluation revealed no hepatotoxicity, nephrotoxicity, or cardiotoxicity [12]. The centipede (Scolopendra) possesses the properties of dispelling wind and relieving spasms, as well as unblocking meridians and alleviating pain. As recorded in Medical Records of Chinese and Western Medicine: "It has a slightly pungent taste and a mildly warm nature. Its penetrating power is the most rapid, penetrating internally to the viscera and externally to the meridians, capable of opening any area where qi and blood are stagnant." As an insect with an exceptionally numerous number of segments, the centipede exhibits the fastest penetrating power, demonstrating excellent meridian-activating effects within the human body. The extract AMP-scolopin 2 from the centipede exhibits broad-spectrum antibacterial activity and demonstrates hemolytic effects on human and rabbit red blood cells [13]. The antibacterial peptide identified as Pinipesin in the molting extract of Centipede (Tenebrio molitor) was characterized by mass spectrometry. Pinipesin demonstrated effective antibacterial activity against various microorganisms and exhibited low hemolytic effects on human erythrocytes at high concentrations, likely exerting its effects intracellularly by interfering with protein synthesis [14]. Zhang Xichun referred to the whole scorpion as the 'five medicinal ingredients of centipede,' indicating that centipede exhibits stronger efficacy than the whole scorpion. Gong Lihong's team investigated the anti-inflammatory and immunosuppressive effects of Wenban Decoction, which incorporates both the whole scorpion and centipede, in inhibiting the progression of atherosclerosis [15-17]. The combination of Scorpion and Centipede exhibits potent pharmacological properties, with its wind-dispelling action directly targeting the pathological site. The elimination of internal wind leads to spontaneous regulation of collateral vessels. Professor Wang Xian's team proposed the theory of "internal movement of collateral wind," which fundamentally attributes the pathogenesis to heat-toxicity generating wind and collateral deficiency inducing wind [18, 19].

5.3 Deficiency and Stagnation of Collaterals, Free Flow of Qi with Unobstructed Collaterals

Excessive invasion by the six exogenous pathogenic factors, excessive emotional disturbances, overindulgence in food and drink, and improper balance between work and rest can all lead to deficiency and stagnation of collaterals qi, depletion of kidney essence, and rootlessness of innate qi generation. Compounded by internal pathogenic factors or external pathogen invasion, coupled with dietary indiscretion, damage to the spleen and stomach, and deficiency of acquired qi sources, these factors ultimately result in deficiency of heart collaterals qi. The branches of heart collaterals extend horizontally, branch into layers, distribute longitudinally and laterally, with narrow collaterals and sluggish qi-blood circulation. Thus, heart collaterals qi is prone to stagnation, and qi-deficient collaterals are also susceptible to qi stagnation—this is the principle of "qi deficiency retention" as described by Ye Tianshi. The deficiency and stagnation of collaterals impair the function of qi transformation, leading to disharmony of collaterals, blood, body fluids, fluids, and essence, thereby generating pathogenic toxins such as blood stasis, phlegm-turbidity, and heat-toxins. Qi deficiency results in sluggish blood circulation and collaterals stagnation. Qi governs blood, and blood nourishes qi; when qi flows, blood flows; when qi stagnates, blood stasis occurs. The Yellow Emperor's Inner Canon states: 'The heart governs the blood vessels,' and further notes: 'All blood belongs to the heart.' The qi of the heart collaterals is essential for blood circulation. When the qi of the heart collaterals is deficient, it fails to propel blood flow, leading to impaired circulation and stasis of blood in the collaterals, resulting in the syndrome of deficiency and stagnation of the heart collaterals. Qi deficiency leads to blood stasis, and stasis gives rise to various diseases. Deficiency and stagnation of the heart collaterals manifest as the syndrome of chest obstruction. Therefore, replenishing the qi of the heart collaterals is the key to treating deficiency and stagnation of the heart collaterals.

Musk possesses a pungent and aromatic quality that opens the orifices, dispels darkness, and unblocks collaterals. As recorded in Medical Records of Chinese and Western Medicine, musk is described as "slightly pungent in taste and mildly warm in nature, with the most rapid penetrating power to reach internal organs and external collaterals, capable of opening all areas where qi and blood congeal." Through network pharmacology studies, it has been discovered that muscone, a component of musk, promotes myocardial glycolysis and inhibits NLRP3 pathway activation, thereby

ameliorating myocardial ischemia-reperfusion injury [20]. qRT-PCR experiments demonstrated that muskone alleviates cardiac injury by reducing the secretion of pro-inflammatory cytokines and promoting the secretion of anti-inflammatory cytokines. Western blot analysis revealed that muskone exerts cardioprotective effects by inhibiting the phosphorylation of key proteins in the STAT3, MAPK, and TGF-β/SMAD signaling pathways. This indicates that muskone can partially mitigate Ang II-induced cardiac hypertrophy by suppressing the STAT3, MAPK, and TGF-β/SMAD signaling pathways [21]. Among Chinese patent medicines primarily containing musk, such as Shexiang Baoxin Pills, Compound Musk and Astragalus Dripping Pills, and Musk Tongxin Dripping Pills, numerous clinical and experimental studies have demonstrated that musk possesses antioxidant stress effects, enhances non-specific immune function, and inhibits tumor growth [22]. The earthworm possesses the efficacy of promoting blood circulation. Studies have found that arginine and glycine in earthworm can dilate blood vessels, inhibit platelet aggregation, defend CVD, and antagonize endotoxin-induced myocardial damage [23, 24]. The team led by Li Weixia discovered that the amino acids contained therein are closely related to lipid metabolism, cell growth, migration and adhesion, immune inflammation, and antithrombotic effects [25]. DPf3 from C. wilhelmina exhibits excellent direct hydrolytic activity against fibrin, fibrinogen, and blood clots, along with mild prothrombin activation activity, and has been identified as possessing antithrombotic properties. Additionally, DPf3 significantly prolongs the activated partial thromboplastin time (APTT) and reduces fibrinogen levels, indicating that DPf3 exerts its antithrombotic effects through endogenous and/or common pathways, as well as the third coagulation phase [26].DLBS1033, a water-soluble kallikrein-like component isolated from P. fuciformis, exerts its effects of reducing blood viscosity and inhibiting platelet aggregation by increasing cyclic adenosine monophosphate (cAMP) levels and suppressing calcium ion transport [27]. Wingkinase also exhibits the effect of inhibiting inflammatory factor expression [28]. Wei Haixia demonstrated significant therapeutic efficacy of worm kinase capsules in treating CHD patients, which can improve hypercoagulable state and prevent coronary thrombosis [24]. The deficiency and stagnation of qi, combined with turbid and turbid substances, are treated by using musk and earthworm to promote the circulation of collaterals, while the flow of qi is nourished to ensure the smoothness of collaterals.

5.4 Stagnation of Collaterals, Dispersing Stasis to Restore Collateral Patency

When Qi flows freely, blood circulates smoothly; when Qi is obstructed, blood stagnates and becomes stasis. Stasis obstructing the heart collaterals often manifests as stabbing chest pain and a dark purple tongue and pulse. Inadequate Qi circulation disrupts the normal distribution of fluids, while stagnant blood impedes fluid metabolism, leading to phlegm-turbidity and water retention. As stated in the Suwen: Treatise on Arthralgia, “The pulse is the abode of blood; obstruction causes heart pain.” Stasis caused by impaired nutrient circulation inevitably compromises pulse patency, and impaired pulse pathways with obstruction of the heart meridian inevitably result in heart pain. The Suwen: Zhi Zhen Yao Da Lun states: “All pains, pruritus, and sores originate from the heart.” When the nutritive and defensive qi stagnate, blood and qi become obstructed, and the meridians are blocked, the heart governs the blood vessels. In such cases, the stagnation of blood and qi leads to CHD. Treatment involves regulating qi and blood, and unblocking the nutritive and defensive qi, thereby alleviating chest pain. Blood stasis is a tangible pathogen; once formed, it inevitably impedes the flow of qi, causing qi stagnation. This is the principle that “blood stasis must be accompanied by qi stagnation.” Qi stagnation further disrupts blood circulation, creating a vicious cycle of blood stasis and qi stagnation. Once blood stasis forms, whether within or outside the vessels, it can disrupt local or systemic blood flow. When the collaterals are obstructed by blood stasis, the stasis is dispersed, and the collaterals become unobstructed.

Hirudo, with the efficacy of breaking blood stasis and promoting menstruation, expelling blood stasis and resolving stagnation. It is salty, bitter, and neutral in nature, with slight toxicity. The Tangye Bencao records: “Hirudo, bitter in nature, promotes blood circulation, and salty in nature, inhibits blood.” The main active component of Hirudo, hirudin, exhibits thrombin-inhibiting effects, which can significantly improve microcirculation, prevent platelet aggregation, and exert lipid-regulating and hemostatic effects [29]. In vitro and in vivo animal experiments demonstrated that pretreatment with leech extract conferred survival benefits in spontaneously hypertensive rats and significantly reduced angiotensin II-induced cardiac hypertrophy and fibrosis. Compared to the control group, leech extract treatment attenuated angiotensin II-stimulated markers of cardiac hypertrophy, and the translational expression of stress-related mitogen-activated protein kinase was also inhibited. In vivo, leech extract treatment markedly improved the cardiac hypertrophy phenotype in hypertensive rats [30]. A novel potent anticoagulant protein, CRA, has been identified in medicinal leeches. This protein directly inhibits thrombin and, based on indirect evidence, can be confirmed to act on other proteases in the coagulation cascade [31]. Quyu Xiaoban Capsule, with hirudo as its primary component, not only improves platelet function but also enhances lipid profile indicators [32]. The insect Mengchong has a bitter and slightly salty taste, a cool nature, and is toxic. It enters the liver meridian and possesses the effects of dispelling blood stasis, breaking up accumulations, and promoting blood circulation to regulate menstruation. Mengchong can enhance immune function and promote tumor cell apoptosis [33]. The experimental extract of Aedes aegypti belongs to the flavonoid class. Pharmacological studies have demonstrated that the polymeric polysaccharides from Aedes aegypti proteins can prevent thrombosis by significantly inhibiting the processes of platelet adhesion, aggregation, activation, and release induced by arachidonic acid (AA) and thrombin [34]. Dangdang Decoction, primarily composed of leech and hornet, has demonstrated certain therapeutic effects in modern clinical and animal experiments, including improving microcirculatory disorders, regulating hemorheology and hemodynamics, enhancing insulin resistance, and inhibiting inflammatory responses [35].Academician Wu Yiling proposed that the pathological site of CHD lies in the collaterals of the heart, advocating the therapeutic approach of ‘unblocking collaterals and removing stasis’ for CHD, which

has achieved tangible clinical efficacy.

6. Summary and Outlook

Insect-derived medicines predominantly exhibit collaterals-activating properties. Based on the collaterals theory's principle that' collaterals function through unblocking, 'their therapeutic potential and efficacy in treating CHD have garnered significant academic attention. The application of insect-derived medicines in CHD treatment directly targets the pathogenesis. Due to their distinct properties, flavors, and meridian tropism, these medicines demonstrate unique characteristics. This article discusses eight insect-derived medicines: earthworm, silkworm, Scorpius, Centipeda, Musk, Earthworm, Hirudo, and Drosophila. By leveraging their functions of resolving phlegm, dispersing stasis, dispelling wind, and regulating qi, combined with the CHD treatment principle of 'collaterals function through unblocking,' the advantages of insect-derived medicines are highlighted. However, further in-depth research is still required to elucidate the specific mechanisms and targets of insect-derived drugs in the treatment of CHD, thereby revealing their underlying mechanisms. Furthermore, critical issues in the field of herbal formulations, such as the principles of compatibility for entomogenous drugs, optimal combination patterns, and their mechanisms of action, require further in-depth research. Concurrently, given the inherent toxicity of entomogenous drugs, studies aimed at reducing toxicity and enhancing efficacy also hold significant practical importance. Therefore, to comprehensively elucidate the complex relationships among network disease, CHD, and entomological drugs, future research requires accumulating more clinical and basic study data. This will deepen our understanding of the pathogenesis of CHD, optimize treatment regimens for entomological drugs, and explore their potential therapeutic targets, thereby providing more precise and effective traditional Chinese medicine interventions for CHD patients.

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