Part I
Natural Small-Molecule Drugs for the Prevention and Treatment of Cardiovascular Diseases

Overview

All functions and states of the human body are dependent on the functioning of the cardiovascular system, and this is the system most commonly affected by disease. More importantly, cardiovascular disease not only affects the functional status of the body but is also a direct threat to life. Therefore, cardiovascular disease is a disease of particular concern to the population.

Because of the great harm caused by cardiovascular diseases, people have paid special attention to finding drugs for the treatment of these diseases. Both traditional Chinese medicine—which has been used for thousands of years—and modern Western medicine have realized the importance of cardiovascular diseases, and the drugs used for the treatment of cardiovascular disease are therefore also of great concern.

As early as 2000 years ago, in the "伤寒论: On Cold Damage, Translation & Commentaries by Zhang, Zhongjing" the theory of "promoting blood circulation and remove blood stasis" served as an important basis for the treatment of cardiovascular disease in traditional Chinese medicine. "Avicenna Medical Code" and its forerunners have focused on cardiovascular disease, also beginning many years ago. Accordingly, the prevention and treatment of cardiovascular disease with drugs has received considerable attention from medical experts.

The development of modern medicine, especially chemistry and related techniques, has enabled the discovery of compounds with pharmacological effects in plants, animals, and other natural materials. Some of these compounds have been developed as drugs for the treatment of cardiovascular diseases. These natural small-molecule drugs used for the prevention and treatment of cardiovascular diseases represent some of the earliest natural drugs found in plants. From the early cardiac glycosides used for the treatment of heart failure, many drugs have been developed and used clinically for the treatment of a variety of cardiovascular diseases. The discovery of drugs for the treatment of cardiovascular diseases has not

only led to progress in the research of natural medicines, but has also increased the understanding of cardiovascular pathology.

Heart failure is a disease with very high mortality. The use of cardiac glycosides has saved the lives of many heart failure patients and has also promoted the study of the pharmacological mechanisms of cardiac drugs. Since the time that cardiac glycosides were first used, a number of natural products with potent actions on the heart have been found, and related compounds with modified structures have been developed; these compounds have been employed for the treatment of heart failure. Among them are many natural small-molecule compounds; for example, digoxin, divaside, digitoxin, and lanatoside. The widespread use of cardiac glycosides has also promoted the clinical study of heart failure. However, the obvious drawbacks of natural cardiac glycosides are their significant toxicity and narrow therapeutic window. The general effective dose is close to the toxic dose, and the clinical application of cardiac glycosides is risky and difficult. For this reason, scientists around the world have conducted lengthy and extensive research on these drugs, but so far have not found ideal cardiac glycosides.

Long-term studies of cardiac glycosides have demonstrated that these natural drugs not only have potent effects on myocardial contractility, but also cause changes in the heart rate. Through studies of the mechanism of glycoside effects on the heart rate, the understanding of the electrophysiological function of cardiac drugs was improved and the study of antiarrhythmic drugs was promoted. Consequently, natural antiarrhythmic drugs such as quinidine and tetrandrine have also been used.

Many natural products that affect cardiovascular function, especially those products that modify chronic pathological changes in the cardiovascular system, have been used clinically, such as the drugs used for the treatment of myocardial ischemia, thrombosis, and other cardiovascular conditions. Natural small-molecule drugs, such as ligustrazine, tanshinone IIA, cyclovirobuxinum D, puerarin, daidzein, ferulic acid, and rutin, have played an important role in the treatment of cardiovascular diseases.

In the study of antihypertensive drugs, the discovery and clinical application of reserpine, ajmaline, and other small-molecule compounds have promoted understanding of both the pathogenesis of hypertension and the mechanism whereby drugs lower blood pressure.

Natural small-molecule drugs used for metabolic regulation, such as metformin, have become important for the treatment of diabetes, and are widely used clinically. The discovery and application of lovastatin has opened up a new area in the development and application of lipid-lowering drugs. The dicoumarin drugs, which have a powerful anticoagulant effect, are important for the prevention of coagulation and thrombosis.

Another important natural small-molecule drug for the treatment of cardiovascular diseases is anisodamine, which improves the microcirculation and is used for the treatment of infection with toxic shock; this drug has saved millions of lives.

These natural small-molecule drugs used in the prevention and treatment of cardiovascular diseases are obtained from different plants worldwide, most of them

being isolated from traditional Chinese medicines that have been used for their effects in "activating blood circulation to dissipate blood stasis". The application of these drugs also promotes an understanding of the theories of traditional Chinese medicine.

Many drugs that are now used clinically for the prevention and treatment of cardiovascular diseases represent notable achievements of modern medical science. The breakthroughs made in the development of these drugs are closely related to the development and application of natural medicine; this is particularly seen in modern research investigations of natural medicines used for the prevention and treatment of cardiovascular disease—these investigations provide us with valuable experience and knowledge. Reviewing the history of the development and clinical application of these drugs will promote the development of new drugs.