

Hirudin

1. Introduction

Hirudin (hirudin) is a Leech (Leech) and salivary glands have been extracted from a variety of active ingredients in the activity of the most significant and most studied ingredients, which is 65-66 amino acids from the small molecules of protein (peptide). Hirudin have strong inhibitory effect on thrombin is the strongest so far found in the natural specific inhibitor of thrombin. Animal experiments and clinical studies have shown that hirudin can be effective anticoagulant, antithrombotic, and prevent thrombin-catalyzed activation of coagulation factors and platelet reactions and blood stasis phenomenon further. In addition, it also inhibited thrombin-induced fibroblast proliferation, and thrombin stimulation of endothelial cells. Compared with heparin, which not only use less, do not cause bleeding, is not dependent on endogenous cofactor; and heparin have caused the risk of bleeding, disseminated intravascular coagulation in the pathogenesis of antithrombin III are reduced This will limit the efficacy of heparin, using leeches will have good results.

2. Application

Hirudin is a class of promising drugs anticoagulant stasis, it can be used for treatment of various thrombotic diseases, particularly venous thrombosis and disseminated intravascular coagulation therapy; also be used after surgery to prevent arterial thrombosis, prevention solution thrombosis or thrombosis after revascularization; improve blood circulation and blood dialysis in vitro procedure. In micro-surgery because of anastomotic thrombosis often caused by failure of hirudin can be used to promote wound healing. The study also showed that hirudin in cancer therapy can also play a role. It can prevent metastasis of tumor cells, has proved effective in tumors such as fibrosarcoma, osteosarcoma and vascular sarcoma, melanoma and leukemia. Hirudin also with chemotherapy and radiation therapy, as the promotion of tumor blood flow increased efficacy. Animal experiments and clinical studies have shown that intravenous or subcutaneous hirudin had no apparent side effects, whether acute and subacute toxicity tests, blood pressure, heart rate, blood relative, bleeding time and blood chemical constituents were not affected, and no respiratory effects, no allergic reaction, the general non-specific antibodies was found. Semi-lethal dose LD₅₀> 50mg/kg, much greater than the dose used in the treatment (1mg/kg). Especially noteworthy is that hirudin can be administered orally, which bring great convenience to the medication. Hirudin stable, trypsin and chymotrypsin did not destroy its activity, and some of hirudin fragment still inhibited hydrolysis condensate Blood enzymes, which could explain why the oral medicine effects of leech extract the principle remains.

In recent years in China as the main ingredient to hirudin, there are many kinds of proprietary Chinese medicines, such as cerebral blood oral liquid, tablets thrombosis, blood capsule, with its annual output value of tens of millions. New drugs with leeches are constantly studied and introduced. Genetic engineering of recombinant leech-like peptide drugs to replace or hirudin as anticoagulant drug additives stasis, which can be achieved in the near future. As the injection for the treatment of cardiovascular diseases and cancer drugs, the need for further clinical research. Needless to say, recombinant hirudin-like peptide drug development will bring huge social and economic benefits.

3. Hirudin

As an important value for development of hirudin, and the source of leeches is limited, the focus of both domestic and international pharmaceutical industry through genetic engineering, the recombinant hirudin. After 1986, recombinant hirudin in *E. coli* and enzyme expression of the mother, respectively, successfully, in comparison with the natural hirudin, recombinant hirudin in the first 63 amino acids (tyrosine) is not sulfuric acid casein, active slightly lower, and the remaining the same nature. In the treatment of non-toxic dose of intravenous injection side effects. Are some big foreign biotechnology companies have access to

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a wide range of hirudin clinical research. The hirudin-like peptide of the patent, published annually by the amount of at least a dozen more, including hirudin similar peptides in dozens of research papers each year over the total. The end of 1998 recombinant hirudin drugs listed in Germany in 1999, the United Kingdom licensing, countries have registered the United States, Europe, Australia, New Zealand, South Africa 10 countries.

We genetically engineered recombinant hirudin made a lot of systematic research, has a solid technical foundation. We are from the domestic culture of medical leech hirudin was cloned cDNA was sequenced, and synthesized the E. coli preferred codons hirudin gene was constructed secretory E. coli expression vector, the optimal expression condition, were highly expressed, the product of direct secretion to run things, greatly simplifying the downstream project. We based the characteristics of hirudin was designed for mass production of low-cost separation and purification of new technology, no high performance liquid chromatography or reversed phase chromatography, only purified by three steps, namely, the products were electrophoretically pure. We present the expression of hirudin, the purity and rate reached international advanced level.

4. Technology prospects

Cardiovascular diseases and cancer are major public health problem of two kinds of diseases, disease prevention and control of drugs in these two categories is the focus of new drug development. Leech in expelling blood, stasis, pass through, such as the effect of Xiaopi China for thousands of years Chinese medicine has been proven by practice, recombinant hirudin anticoagulation Suppository and the tumor with chemotherapy and radiotherapy on the clinical role for foreign demonstrated . Injection injection are higher, and currently used in clinical anti-deep vein thrombosis. As oral agents can be achieved in the short term economic and social benefits. The recombinant hirudin-like peptide drugs to replace leech or as the addition of proprietary components, is estimated at 100 million yuan at least get the economic benefits. With the expansion of clinical trials, it can be used for more prevention and treatment of diseases, the development of a bright future

The Unique killer for heart and brain disease.

The Natural biological products hirudin peptide protein tablets, for hypertension, arteriosclerosis, high blood cholesterol, high blood viscosity, high blood sugar, stroke (cerebral thrombosis), coronary heart disease, fatty liver, diabetes, varicose veins, obesity, prostate disease, kidney disease, backache leg pain, etc. with blood circulation disorders of the disease have significant effects, taking 50 minutes later, "a drop of blood monitor" or microscopic observation, red blood cell aggregation (like candied fruit as closely linked to) the phenomenon of elimination, carrying oxygen and transporting carbon dioxide greatly increased the capacity; taking more than 20 days after the body such as the excessive lipid index may return to normal, so that patients get rid of "high blood pressure, high cholesterol, high blood viscosity, high blood sugar, high urine sugar," "five high" threats, fast effective than ever before in any other type of drugs.

The effect of hirudin peptide protein tablets

√ regulate blood fat √ eliminate fatty liver √ Prevention of Stroke √ activate the body's own thrombolytic function, to avoid a return of blood clots √ dissolve blood clots directly √ elimination of atherosclerosis
√ control of diabetes and complications

Scientific research shows that: This is extracted from the leech acid peptide within the protein ---- hirudin, is found in the world so far the strongest known natural material and anti-thrombin substance, which has strong anticoagulant, dissolved suppositories and other lipid-lowering effect, used to treat a variety of clinical thrombotic disease, elimination of blood vessel blockage, so that depolymerization of blood cells, thrombus dissipation, for exudate absorption and capillary blood re-pass, thus improving the microcirculation. Is the control of

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human cardiovascular disease effects natural medicine, and clinical use of domestic current hospital anticoagulant, anti-thrombosis drug, compared with full security, full absorption rate, absorption speed and the effect is good.

Leeches for medical treatment, at home and abroad have a long history, beginning in mind in our country, "Shen Nong Ben Cao Jing", future generations of medical monographs, such as Li Shi Zhen's "Compendium of Materia Medica" and all modern version of "Chinese Pharmacopoeia" are recorded.

Modern medical research shows that the body contains a variety of medicinal leech components, such as hirudin, heparin, anti-thrombotic factors, among which leech salivary gland secretion of hirudin is an acidic polypeptide, is the most powerful known natural thrombin inhibitors, very small amount of hirudin can inhibit the activity of thrombin in the blood, and has reduced the role of blood viscosity; In addition, hirudin also with the expansion of blood vessels, easing blood vessel smooth muscle spasm and promote the function of absorbing exudate, vein graft can remain open after surgery.

Use of hirudin treat cardiovascular, thrombosis, rheumatism, hypertension, myocardial infarction, rheumatoid arthritis, stroke, abdominal pain, amenorrhea, postpartum lochia endless, liver, lymphatic system, angina, eye disease, unknown tumor and cervical lymph node of nuclear and other diseases.

In addition, hirudin is also rich in protein and amino acids, used to develop a variety of health food, in the elderly and prevention of high blood lipids, hypertension, liver disease, cardiovascular and cerebrovascular disease and cerebral thrombosis, etc. have remarkable results. Preparation of antifreeze can cream, skin cream, hair growth cream or other creams and other beauty make-up on Blood Products

Treatment of liver cirrhosis with Leech

Leech in the treatment of digestive diseases is widely used, there are consumers for stasis syndrome and liver cirrhosis, but also the spleen and stomach function and help to improve transport of the spleen. Liu Si had used the leech to treat of hepatitis with jaundice, Chinese Medicine of the patients, if who is stasis and effective, and to treat the stasis with yellow should first choose the leech.

Liver cirrhosis is one of the illnesses of digestive diseases. In the TCM way to treat the disease, from the point to remove the stasis. Wang Si to set thierself the Sonsumer Pill (Leech 75 grams ,Zhe Chong, pao Shanjia each 100 grams, 50 grams of rhubarb) mainly treated 40 cases of patients with liver cirrhosis. Patients each time consumers Pill 5 grams, daily doses of 2 to 3 times, taking a course of 2 months and, based on ultrasound to check liver function and recovery of the liver. As a result, the group of 40 patients, 11 patients with symptoms disappeared completely retracting the liver to normal liver function has returned to normal. were followed up for three years, no recurrence; 13 patients with symptoms, liver retraction to normal, normal liver function, to basic recovery. 12 patients improved, and only 4 cases with chronic nephritis and thrombocytopenia in patients with no significant improvement

Knowledge of the hirudin

Hirudin content in the leech's body little, but the magic and only a few micrograms of the blood will not be solidified.

Hirudin, also known as "polypeptide protein", in the role of human health care is increasing. Hirudin in clinical practice can ease the spasm arteries, reduce blood clotting, dilate blood vessels, increase blood circulation, promote exudate absorption capabilities. Therefore has been widely used for high blood pressure, high blood sugar, high blood viscosity, high blood lipids, high cholesterol and myocardial infarction difficult by the disease. Hirudin is also widely used in biochemistry. In addition, the leech body contains a variety of medicinal ingredients, caused the elimination of postoperative complications, to prevent premature coagulation of blood has an important role.

Hirudin (peptide protein) is a small protein, because small molecules into the blood soon after taking the drug, not only effective, role very quickly, very

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patient with severe cardiovascular adaptation.

The benefits of farming leech

1. Direct benefits:

The current market price of the dry leech 400 RMB / kg, while the average yield of dry leech is 50KG (based on the experience in a culture), like this:400X50 =20,000 RMB / mu(667M2) / year.

2. Indirect benefits:

Has been the main raw material of leech new drug for cardiovascular disease,suchas"Tong Xin Luo Capsule", "brain new capsule," "pulse blood capsules" and "Shuxuetong injection" and more than 30 enterprises from the national development and to be listed and a huge indirect benefits, with the extraction and use of hirudin, more effectively enhance the value of medicinal leeches.

3. Social benefits:

Leech breeding technology promotion will be effective in easing the global compact formula because the problem of wild resources to meet the needs of the rapid development of Chinese medicine industry. At the same time adjusting the agricultural structure in some areas, the protection of wild resources and maintain ecological balance. Especially as a special breeding industry the local economy, improve the income of local farmers is of great significance. On the other hand, drugs can effectively treat and cure time early cardiovascular disease patients, the protection rate of the population and longer life, but also a social.

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