WEP
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Publishing

Transactions on Materials, Biotechnology and Life Sciences
ISSN: 2960-1932, eISSN: 2960-2319 | Volume 7
MISBP 2024

Mechanisms of Action and Current Research Status of New Drugs For Cardiovascular Diseases (Cvds)

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Abstract. Cardiovascular diseases (CVDs) remain one of the leading causes of death and disability worldwide, posing a significant threat to global public health. In recent years, with the advancements in molecular biology and genomics, the development of new drugs for CVDs treatment has made substantial progress, particularly in the fields of anti-inflammatory, anti-fibrosis, and angiogenesis therapies. This thesis investigates the mechanisms of action of these innovative drugs and their clinical applications. Firstly, the critical role of anti-inflammatory drugs in CVDs is analyzed, highlighting how novel anti-inflammatory agents, such as IL-6 inhibitors, modulate immune responses to reduce cardiovascular inflammation. Secondly, anti-fibrotic drugs, such as TGF-β inhibitors, are discussed in detail, focusing on their ability to inhibit fibrosis progression and improve cardiac function by reversing myocardial fibrosis. Additionally, angiogenesis-based drugs, which promote endothelial cell repair and regeneration, are explored for their potential in enhancing microcirculation in the cardiovascular system. The thesis also delves into the prospects of personalized medicine and gene therapy in the development of new CVDs treatments. Emerging technologies, such as multi-target combination therapies, gene editing, and nanomedicine carriers, are expected to bring breakthroughs in the treatment of CVDs. This paper summarizes current research progress and explores future directions, providing theoretical foundations and practical insights for the development of novel drugs for CVDs.

Keywords: Cardiovascular diseases, new drugs, mechanism of action, anti-inflammatory, anti-fibrosis.

1. Introduction

Cardiovascular diseases (CVDs) is a general term for various diseases caused by the abnormal function of the heart and blood vessels, including coronary heart disease, hypertension, heart failure (HF), stroke and so on. As the global population ages and the prevalence of unhealthy lifestyles, such as poor diet, smoking and physical inactivity, the incidence and mortality of CVDs are increasing year by year. According to the World Health Organization (WHO), CVDs has become the number one cause of death worldwide, causing about 17.7 million deaths each year, accounting for more than 31% of all deaths worldwide. In addition, the prevalence of CVDs is also increasing year by year, especially in low - and middle-income countries, where the burden of CVDs is particularly heavy due to insufficient medical resources and lack of prevention and control awareness.

Despite the increasing availability of therapeutic options for CVDs, including drug therapy, interventional therapy and surgery, there are still many challenges and limitations in the efficacy and long-term prognosis of CVDS. First, traditional drugs such as beta-blockers, calcium channel blockers, and anticoagulants can alleviate symptoms and reduce mortality in some patients, but they have limited effect on many complex CVDs, such as HF and reversal of atherosclerosis. Second, many patients respond differently to drugs based on individual differences, and individualized treatment is not yet widely available. In addition, existing therapeutic methods still lack effective targeted interventions for the underlying causes of diseases, such as inflammation, oxidative stress and fibrosis. With the increasing complexity and heterogeneity of CVDs, there is an urgent need to develop new therapeutic strategies to address the shortcomings of traditional therapies. Given the complexity of CVDs and the limitations of current treatments, the development of novel drugs is a key way to address this global health problem. The main purpose of this study is to analyze the need for new drug development by exploring the pathological mechanism of CVDs, focusing on the mechanism of action of new drugs in inflammatory response, fibrosis and angiogenesis. The clinical application prospect of anti-inflammatory drugs, anti-fibrosis drugs and new drugs promoting angiogenesis in the treatment of CVDs was studied in order to provide a new solution for the treatment of CVDs in the future [1].

2. Pathophysiological Mechanism of CVDs

2.1. Molecular Mechanism of Atherosclerosis

Atherosclerosis is a chronic progressive disease with a core mechanism of lipid deposition in the arterial wall, inflammatory response and fibrous tissue hyperplasia. This process usually begins with damage to the endothelium of the blood vessels, causing low-density lipoprotein (LDL) to enter the lower layer of the endothelium, which is subsequently oxidized to form oxidized low-density lipoprotein (Ox-LDL). Ox-LDL is gobbled up by macrophages, forming foam cells that accumulate on the artery wall and gradually develop into atherosclerotic plaques.

2.1.1. Inflammatory response

Inflammation plays an important role in the development and progression of atherosclerosis. After vascular endothelial injury, inflammatory mediators such as cytokines, chemokines and adhesion molecules are activated, prompting immune cells such as monocytes and T cells to gather at the injury site. After entering the artery wall through the endothelium, monocytes differentiate into macrophages and phagocytose Ox-LDL, eventually forming foam cells. At the same time, macrophages and other immune cells release inflammatory factors, such as tumor necrosis factor (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP), further exacerbating the local inflammatory response. This constant inflammation leads to the gradual thickening and fibrosis of the artery wall, and eventually the formation of unstable atherosclerotic plaques that are prone to rupture, leading to the formation of blood clots, which can lead to myocardial infarction or stroke.

2.1.2. Abnormal lipid metabolism

Abnormal lipid metabolism is one of the important pathological mechanisms of atherosclerosis. High levels of low-density lipoprotein cholesterol (LDL-C) are a major risk factor for atherosclerosis, while high-density lipoprotein cholesterol (HDL-C) has an anti-atherosclerotic effect. When LDL-C is deposited and oxidized under the skin of blood vessels, it triggers an inflammatory response and the formation of foam cells, thus accelerating the development of atherosclerotic plaques. HDL-C, on the other hand, is able to transport excess cholesterol from tissues back to the liver through reverse cholesterol transport, reducing the risk of plaque formation. Therefore, regulating lipid metabolism and reducing LDL-C level is the key to preventing atherosclerosis.

2.2. The Pathological Mechanism of Hypertension and Cardiac Hypertrophy

High blood pressure is one of the important risk factors for CVDs, and long-term increases in blood pressure can have profound effects on the heart and blood vessels. Hypertension not only causes mechanical stress of the heart, but also activates a variety of neurohumoral factors, such as the Renin-Angiotensin System (RAS), which accelerates the development of cardiac hypertrophy.

2.2.1. The role of RAS in CVDs

RAS is one of the key systems that regulate blood pressure and blood volume. In hypertensive conditions, renin secretion increases, prompting the conversion of angiotensinogen to Angiotensin I, which is further converted to Angiotensin II (Ang II) under the action of angiotensin-converting enzyme (ACE). Ang II has a strong vasoconstriction effect, which directly leads to the increase of peripheral vascular resistance and blood pressure. In addition, Ang II induces cardiac hypertrophy and fibrosis by acting on cardiomyocytes, which gradually leads to the occurrence of HF. Abnormal activation of RAS not only leads to increased blood pressure, but also exacerbates cardiovascular damage by promoting inflammation, oxidative stress and other pathways.

2.2.2. Relationship between blood pressure and cardiac output

Blood pressure (BP) is the product of cardiac output (CO) and peripheral vascular resistance (SVR). Cardiac output represents the amount of blood pumped by the heart over a given period of time, while peripheral vascular resistance is determined by the resistance and state of the blood vessels. The development of high blood pressure can be explained by increased cardiac output or increased peripheral vascular resistance.

2.3. Vascular Endothelial Dysfunction and Oxidative Stress

The dysfunction of vascular endothelial cells is one of the early signs of CVDs. Under normal circumstances, vascular endothelial cells maintain vasodilation by synthesizing and releasing vasoactive substances such as NO. When endothelial cell function is impaired, the production of NO is reduced, blood vessel constriction is increased, and the risk of atherosclerosis is greatly raised.

2.3.1. The role of oxidative stress in arteriosclerosis and HF

Oxidative stress is one of the important pathological processes of atherosclerosis and HF. Oxidative stress refers to a state in which the body produces too much ROS or has insufficient antioxidant system capacity, leading to cell and tissue damage. Excessive ROS not only directly damages vascular endothelial cells, but also accelerates the process of atherosclerosis by promoting lipid oxidation ,such as the formation of Ox-LDL. In addition, oxidative stress activates a variety of inflammatory signaling pathways, such as the NF-κB pathway, further aggravating the inflammatory response of the cardiovascular system. Especially in HF, oxidative stress can induce cardiomyocyte apoptosis and fibrosis, exacerbating cardiac insufficiency.

2.3.2. Free radical and antioxidant defense system

Free radicals, especially ROS, are one of the important factors that cause CVDs. Excessive production of free radicals can damage endothelial cells, smooth muscle cells and heart muscle cells, eventually leading to atherosclerosis and HF. However, the body's antioxidant defense systems, such as superoxide dismutase (SOD), catalase and glutathione peroxidase, are effective at scavenging free radicals and reducing the damage caused by oxidative stress. When the function of the antioxidant system is weakened or the free radical is produced too much, the oxidative stress is intensified, which accelerates the progression of CVDs. Therefore, therapeutic strategies targeting oxidative stress, such as antioxidant supplementation, may have potential clinical application value in the prevention and treatment of CVDs.

3. Research Progress on The Mechanism of Action of New Drugs

3.1. Drugs Based on Angiogenesis and Repair

3.1.1. New drugs promotes vascular endothelial cell repair

An important feature of CVDs is the dysfunction of vascular endothelial cells, which directly affects the normal repair and regeneration process of blood vessels. Vascular endothelial growth factor (VEGF) is an important factor promoting angiogenesis, which can stimulate the proliferation and migration of vascular endothelial cells. VEGF inhibitors prevent pathological angiogenesis by regulating VEGF overactivity and promote the normal repair process of endothelial cells. In addition, NO donor drugs improve vascular endothelial cell function, enhance vasodilation, and reduce vascular resistance by increasing the release of NO.

3.1.2. Results of preclinical and clinical studies

Several preclinical studies have shown that VEGF inhibitors play a significant role in the repair of atherosclerosis and vascular damage. Animal experiments have shown that these drugs can effectively inhibit the formation of unstable plaques and promote the proliferation and regeneration of vascular endothelial cells. In addition, NO donor drugs showed a good effect in improving vascular endothelial function and preventing vascular sclerosis.

Clinical trials have also shown that these new drugs have a good application prospect in improving the prognosis of cardiovascular patients and reducing the incidence of complications. Especially in patients with coronary artery disease, treatment based on VEGF inhibitors and NO donor drugs can reduce myocardial ischemia and reperfusion damage and significantly improve patients' quality of life.

3.2. Mechanism of Action of New Anti-Inflammatory Drugs

3.2.1. New drugs that target the cardiovascular inflammatory response

Inflammatory response is one of the core mechanisms of the pathogenesis and progression of CVDs. Especially in the pathological process of atherosclerosis and myocardial infarction, the release of inflammatory mediators will aggravate the damage of blood vessels and heart tissue. IL-6, a key pro-inflammatory cytokine, plays a central role in the inflammatory response. By binding to its receptor IL-6R, IL-6 activates downstream signaling pathways, such as the JAK/STAT signaling pathway, which initiates inflammation and exacerbates cardiovascular damage [2]. New anti-inflammatory drugs, such as IL-6 inhibitors, can reduce inflammation and damage to the cardiovascular system by blocking IL-6 binding to its receptors and inhibiting signaling.

Molecular mechanism of IL-6 signaling pathway blocking. The key to the IL-6 signaling pathway is the binding of IL-6 to IL-6R. Once this binding is blocked, IL-6 cannot activate the downstream JAK/STAT signaling pathway, thereby inhibiting further release of pro-inflammatory factors and reducing local and systemic inflammatory responses.

3.2.2. Mechanism of action and clinical application prospect

IL-6 inhibitors inhibit the progression of atherosclerosis by blocking IL-6 signaling pathway and reducing the infiltration of immune cells such as T cells and macrophages in arterial plaque. Cytokine modulators reduce the intensity of the inflammatory response by regulating the release of other pro-inflammatory cytokines such as TNF-α and IL-1β. Not only have these drugs shown significant anti-inflammatory effects in early trials, but clinical trials have also validated their potential to reduce the rate of cardiovascular events in patients with atherosclerosis. Especially in high-risk patient groups, the use of anti-inflammatory drugs is expected to reduce the incidence of serious cardiovascular events such as myocardial infarction and stroke, and improve the long-term prognosis of patients.

3.3. Mechanism of Action of Antifibrotic Drugs

3.3.1. New drugs for heart fibrosis

Cardiac fibrosis is a common pathological change in many advanced CVDs, usually accompanied by myocardial remodeling and HF. The fibrotic process is primarily driven by the transforming growth factor-β (TGF-β) signaling pathway, which promotes excessive deposition of extracellular matrix such as collagen by activating fibroblasts, resulting in stiff cardiac tissue and decreased contractile function. TGF-β inhibitors, as anti-fibrosis drugs, can reverse the process of cardiac fibrosis by blocking TGF-β signaling, inhibiting the proliferation of fibroblasts and collagen synthesis.

3.3.2. Mechanism of fibrosis reversal and improvement of myocardial function

Antifibrotic drugs slow or reverse the progression of myocardial fibrosis primarily by inhibiting the TGF-β signaling pathway. This class of drugs reduces the deposition of extracellular matrix by preventing the transformation of fibroblasts into active fibroblasts, and to a certain extent promotes the degradation of formed fibrous tissues. In addition, antifibrotic drugs can also protect myocardial function by improving the oxygen supply and metabolism of cardiomyocytes and reducing cardiomyocyte apoptosis. In preclinical studies, TGF-β inhibitors have shown strong anti-fibrotic effects and are expected to be an effective treatment for HF and other fibrosis-associated CVDs in the future. The preliminary results of clinical studies also show that these drugs have good application prospects in reducing cardiac load and improving cardiac function.

4. Innovative Drug Research

4.1. New Drugs Based on Targeted Therapies

Research and development of RNA-targeting drugs, such as siRNA and mRNA vaccines. In recent years, RNA-based targeted therapies have made remarkable progress in several disease areas, especially in the treatment of CVDs, where RNA interference (RNAi) technology and the development of mRNA vaccines have shown great potential. RNA interference technology selectively inhibits the expression of pathogenic genes through siRNA, and can effectively interfere with specific signaling pathways related to CVDs. For example, siRNA drugs that target the low-density lipoprotein receptor (LDLR) and PCSK9 genes have shown promising results in clinical studies of lowering cholesterol levels in the blood. This class of drugs can reduce the degradation of LDLR by silencing the expression of PCSK9 gene, thereby increasing the clearance of LDL-C and reducing the risk of atherosclerosis [3]. The range of applications of mRNA vaccines is also expanding, especially for the prevention and treatment of CVDs. mRNA vaccines encode specific antigens or therapeutic proteins that are translated into cells to produce target proteins that activate the immune system or repair damaged tissue. In chronic inflammatory diseases such as atherosclerosis, mRNA-based therapeutic vaccines have shown potential to regulate inflammatory responses. In general, RNA-based targeted therapy technology provides efficient and precise intervention means by regulating gene expression, and is expected to become a new direction for future CVDs therapy.

4.2. Cell Therapy and Regenerative Medicine Drugs

Application and prospect of stem cell therapy in cardiovascular repair. Cell therapy and regenerative medicine have shown broad prospects in the field of cardiovascular repair. Serious cardiovascular events such as myocardial infarction can lead to irreversible damage and death of cardiomyocytes, leading to cardiac insufficiency. While traditional treatments are not effective at repairing damaged heart muscle tissue, stem cell therapy offers a potential means of repair. Stem cells, especially bone marrow-derived mesenchymal stem cells (MSC) and induced pluripotent stem cells (iPSCs), can differentiate into cardiomyocytes, vascular endothelial cells and other cardiovascular cell types, thereby promoting the recovery of cardiac function. In animal models and early clinical trials, stem cell therapy has demonstrated its potential for myocardial regeneration and improved heart function. These cells can promote the formation of new blood vessels and reduce myocardial fibrosis by secreting growth promoting factors and anti-inflammatory factors [4].

4.3. Nano Drug Carrier and Intelligent Drug System

Nanodrug carriers and smart drug systems have made remarkable progress in the treatment of CVDs in recent years. Traditional drug therapy has some problems such as large dose, wide distribution and poor targeting, which lead to limited curative effect and significant side effects. Nanomedicine carrier technology can accurately deliver drugs to the lesion site through nanoparticles, significantly improving the therapeutic effect and safety of drugs. Nano drug carriers can achieve targeting by modifying surface molecules, so that drugs can preferentially enter damaged cardiovascular tissues and reduce the impact on normal tissues.

In the treatment of CVDs, nanomedicine carriers are not only capable of carrying traditional small molecule drugs, but also can be used to deliver gene drugs, siRNA or protein drugs. The smart drug system can release drugs at the point of lesion, thereby reducing systemic side effects and providing a new idea for personalized treatment of CVDs.

In summary, emerging technologies such as RNA-targeting drugs, cell therapy, and nanomedicine carriers provide a variety of cutting-edge and efficient means for the treatment of CVDs. These technologies not only improve treatment outcomes, but also reduce side effects, laying the foundation for personalized, precise treatment.

5. Current Status and Challenges of Clinical Trials of New Drugs

5.1. Design of Clinical Trials of New Drugs for Cvds

Early stages of drug screening: Phase I and Phase II clinical trial design and optimization. The development of new drugs for CVDs typically goes through a rigorous clinical trial phase, consisting primarily of Phase I, II, and III trials. The primary goal of Phase I clinical trials is to evaluate the safety, tolerability, and pharmacokinetic profile of new drugs in healthy volunteers. In this phase, new drugs usually start at a low dose and gradually increase the dose to determine the maximum tolerated dose (MTD) and potential side effects. Phase II clinical trials focus on evaluating the efficacy of new drugs and determining the optimal therapeutic dose. This phase usually involves a small number of patients and aims to initially evaluate the efficacy of the drug in the target patient population through randomized, double-blind or placebo-controlled trials. Phase II trials of new CVDs drugs need to be specifically designed to observe the effects of the drug on key cardiovascular indicators such as blood pressure, cardiac function parameters, and markers of inflammation. At the same time, this phase also needs to optimize key parameters such as administration route and dose interval to ensure that the drug can demonstrate the best efficacy and safety in Phase III large-scale trials.

5.2. Bottleneck and Challenge of New Drug Research and Development

Safety, efficacy, and limitations of long-term follow-up data. Despite significant progress in the development of new drugs for CVDs in recent years, there are still multiple challenges in the research and development process. First, safety has always been one of the core challenges of new drug development. The complexity of the cardiovascular system makes many new drugs may show good efficacy in early clinical trials, but in large-scale trials or long-term use, there may be unpredictable side effects. Second, effectiveness assessment is also challenging. Many new CVDs drugs show short-term improvements on specific measures, such as lowering blood pressure or reducing atherosclerotic plaque, but their effect on long-term cardiovascular events is unclear. Phase III clinical trials typically require years of follow-up in large groups of patients to assess the effectiveness of a new drug in preventing endpoint events such as myocardial infarction and stroke. This kind of long-term follow-up is not only costly, but also difficult to ensure patient compliance.

6. Future Development Direction and Prospect

6.1. Multi-target Combination Therapy

The combined treatment scheme of CVD is regulated by multiple ways. The etiology of CVDs is complex and usually involves a variety of pathological mechanisms. A single drug can only target a specific pathological process, and it is difficult to fully control the progress of the disease. Therefore, multi-target combination therapy has become an important strategy for the treatment of CVDs. By combining a variety of drugs with different mechanisms of action, CVDs can be regulated in multiple ways to achieve comprehensive control of disease progression. In multi-target combination therapy, common strategies include the combination of anti-inflammatory drugs with antifibrotic drugs to simultaneously inhibit the inflammatory response and the cardiac fibrosis process [5]. Multi-target combination therapy can not only improve the treatment effect, but also reduce the incidence of adverse reactions by reducing the dose of each drug. Future studies should further optimize the drug combination regimen and validate its long-term efficacy and safety through large-scale clinical trials [6].

6.2. Application of Artificial Intelligence (AI) and Big Data in New Drug Research and Development

The application of AI and big data technologies in the development of new drugs in CVDs provides powerful tools for drug development and clinical decision making. AI-assisted drug design can accelerate the process of drug screening and optimization by analyzing vast amounts of biological and chemical data. Traditional drug research and development often takes a lot of time and resources, but AI technology can quickly identify potential drug targets through machine learning algorithms, predict the interaction between drugs and proteins, and simulate the metabolic pathway of drugs in the body, thus significantly shortening the new drug research and development cycle. In terms of individualized analysis of patient data, AI and big data technology can help doctors develop personalized treatment plans based on a patient's genomic information, medical history, lifestyle and other factors. Through the analysis of large-scale patient data, AI can identify the response patterns of different patient groups to specific drugs, predict drug efficacy, and optimize treatment plans. In addition, AI technology can also monitor patients' condition changes in real time, and help doctors adjust treatment plans in time to prevent cardiovascular complications by integrating physiological monitoring data, imaging data and electronic medical record information [7].

6.3. Potential Applications of Gene Therapy

With the development of CRISPR/Cas9 and other gene editing tools, gene therapy has a broader application prospect in CVDs [8]. In CVDs, the application of gene therapy mainly focuses on two aspects: preventive gene editing and therapeutic gene replacement. Preventive gene editing can prevent the occurrence and development of diseases by repairing disease-causing genes related to atherosclerosis and hypercholesterolemia. For patients who already have the disease, gene replacement therapy can restore normal physiological function by introducing functional genes into the body to replace the disabled genes [9]. Although gene therapy has shown great potential in preclinical studies, its widespread application still faces many challenges, including the safety of gene editing, the effectiveness of targeted delivery, and immune rejection. Therefore, future research should further improve the gene editing technology, optimize the gene delivery system, and ensure the safety and effectiveness of its clinical application through long-term follow-up studies. In general, cutting-edge technologies such as multi-target combination therapy, AI and big data, and gene therapy provide a multi-dimensional innovation direction for new drug research and development of CVDs. As these technologies continue to advance, the treatment prospects for CVDs will become even brighter [10].

7. Conclusion

The research and development of new drugs for CVDs have progressed significantly over the past few decades. The in-depth study of various pathological mechanisms of CVDs provides theoretical basis and target selection for the development of new drugs. There are many new drugs that not only improve patients' short-term symptoms but also show potential for long-term prevention.

Innovative drugs offer new hope for the treatment of CVDs. Through multi-target combination therapy, the drug can not only reduce the progression of CVD but also significantly reduce side effects and provide a more comprehensive treatment plan. Rapid advances in cutting-edge technologies such as RNA interference, mRNA vaccines, and gene editing have also enabled us to more precisely target the genetic and molecular basis of CVDs, enabling personalized therapy. In addition, AI and big data technologies provide efficient tools for drug discovery, accelerating drug screening, optimizing clinical trial design, and tailoring treatments to patients through individualized analysis.

Despite significant progress in the development of new drugs for CVDs, future research still needs to address some key questions. First of all, the research of multi-target combination therapy should be further strengthened to optimize drug combinations and develop more effective combination therapy programs by exploring the interactions of different drugs. Second, safety and long-term efficacy remain core issues in the development of new drugs, especially in cutting-edge technologies such as gene therapy and cell therapy, which need to ensure their long-term safety. In addition, current drug delivery efficiency still has some limitations, especially drug delivery systems targeting specific CVD areas need to be further improved. Technologies such as nano-drug carriers and intelligent drug systems should be more widely used and developed in the future to improve the targeting of drugs and reduce systemic side effects. Finally, the combination of genomics and big data technologies will further advance the development of personalized therapy by analyzing the genomic data of large numbers of patients to provide more precise treatment strategies.

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