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A Review on Cardiac Myosin Activation: A Novel Contractility-Based Approach In Heart Failure.

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Abstract

Heart failure stands as a continual cardiovascular disorder which worsens with time because the heart cannot provide sufficient blood flow needed for bodily functions and the disease mainly affects people who experience heart failure with reduced ejection fraction (HFrEF). Although guideline-directed medical therapies improve outcomes through neurohormonal pathway modulation they do not restore impaired contractile function while conventional inotropes raise intracellular calcium levels which lead to arrhythmias and increased oxygen needs and negative long-term effects. The therapeutic method of cardiac myosin activation establishes a new treatment option that uses contractility to target the sarcomere by improving actin-myosin interaction which extends systolic ejection time without raising calcium levels or heart rate. The first-in-class cardiac myosin activator omecamtiv mecarbil has shown improved cardiac function and decreased heart failure events through major clinical trials which included patients with severe

systolic dysfunction. The review provides a summary of cardiac myosin structure and function myosin activation rationale and mechanism of action and clinical evidence and future potential as targeted heart failure treatment.

Keywords: Heart failure, cardiac myosin activation, omecamtiv mecarbil, contractility, HFrEF.

Introduction

Heart failure is a long-term medical condition where the heart fails to pump sufficient blood for the body's requirements. The condition affects millions of people throughout the world and serves as a primary reason for hospital admissions which leads to decreased life quality and increased premature mortality.[1] Heart failure patients typically complain of breathlessness and tiredness and swollen legs and decreased capacity to carry out their regular tasks. Heart failure presents a serious public health challenge which continues to grow because medical treatment advances fail to control the increasing problem for patients who suffer from aging and diabetes and hypertension. Heart failure treatment becomes difficult because the disorder consists of multiple heart structural and functional changes which develop throughout its course.[2]

Heart failure treatment faces its most significant challenge through the development of poor cardiac contractility which leads to decreased heart muscle strength. The heart muscle weakness prevents the heart from delivering adequate blood flow throughout the body. Heart failure treatments from the past focused on three main objectives which included decreasing heart workload and maintaining blood pressure and stopping fluid accumulation..[3] The heart treatments extend life expectancy but they fail to enhance the heart's ability to pump blood. Inotropic drugs work as heart contraction enhancers which medical professionals use to treat severe cases yet these drugs raise heart rate and oxygen requirements which lead to negative effects during extended usage.[4]

Conventional inotropic drugs work by increasing calcium levels inside heart cells. Patients experience better heart contractions for a short time, but doctors see an increased danger for people to develop irregular heartbeats and heart tissue damage and higher oxygen needs. This medication can only be used for brief periods because its extended use poses numerous dangers. The medical field now requires safer treatment options, which need to enhance heart muscle contraction, but they must avoid producing dangerous effects. Researchers have therefore started exploring new treatment approaches that target the heart's contractile machinery directly, rather than indirectly altering calcium levels or heart rate.[5]

Researchers developed a new medical method which uses cardiac myosin activation to enhance heart function by studying its effects on molecular heart pumping mechanisms. Myosin serves as a motor protein which heart muscle cells use to create contractions through its binding with actin filaments. In heart failure, this interaction becomes less efficient. Cardiac myosin activators work by increasing the efficiency of this interaction, allowing the heart to contract more effectively. The method improves heart contraction strength and duration while maintaining stable heart rate and oxygen consumption, which makes it a better option than standard treatment methods.[6]

The experimental and clinical studies of omecamtiv mecarbil and other cardiac myosin activators show promising results as new treatment methods. The new drugs treat heart failure by enhancing the fundamental mechanical functions of the diseased heart instead of treating its symptoms. The process of cardiac myosin activation demonstrates its benefits and safety features and its use in clinical practice needs to be understood for upcoming advancements in heart failure treatment. The review provides a straightforward explanation of cardiac myosin activation including its mechanism of action and clinical evidence and potential use as a treatment method for heart failure.[7]

Structure Of Cardiac Myosin

Cardiac myosin serves as the principal motor protein which builds the entire structure of the heart muscle's contraction system. The protein consists of two myosin heavy chains and four myosin light chains as its primary building blocks. Myosin achieves its distinct shape through the formation of a long rope-like structure which results from the two heavy chains twisting around each other. The heart muscle cell contains a heavy chain which develops three distinct parts for its structure: a head region and a neck region and a long tail region.[8]

The head region of cardiac myosin is the most functionally important structural component. It contains the actin-binding site and the ATP-binding site which together function as essential components for both energy usage and force production. This region of the structure exists to transform chemical energy which comes from ATP into mechanical movement. The head region undergoes structural modifications which have a major impact on heart contraction efficiency since it plays an essential role in sustaining normal heart function.[9]

The neck region which people refer to as the lever arm exists next to the head. The region uses two different types of light chains which include the essential light chain and the regulatory light chain. The light chains create stability for the myosin head unit while they assist in increasing movement power during muscle contraction. The neck functions as a hinge mechanism which enables head movement yet preserves correct alignment with actin filaments.[10]

The tail region of cardiac myosin extends in length while its fibrous structure helps to organize muscle tissue throughout the body. Multiple myosin tails come together to form thick filaments which are arranged in a highly ordered pattern within the sarcomere which is the basic contractile unit of heart muscle. The specific structural design transmits force during contraction with maximum efficiency. The heart muscle develops weakened performance because of heart failure when myosin structure experiences any kind of change.[1

Functions of Cardiac Myosin

1. Generation of Contractile Force

Cardiac myosin generates the force which enables heart muscle contractions to occur. Cardiac myosin produces motion when it binds with actin filaments which exist inside heart muscle cells. The myosin head uses ATP energy to execute a pulling motion which brings actin filaments towards the sarcomere center. The muscle fiber contraction process enables the heart to pump blood through the body. A healthy heart exhibits a continuous cycle which operates smoothly to maintain effective blood circulation. Myosin function decrease results in lower contraction force which causes heart failure patients to experience weak heart pumping.[12]

2. Actin–Myosin Cross-Bridge Cycling

The cross-bridge cycle serves as the fundamental mechanism which enables muscle contraction through the actions of cardiac myosin. During this cycle the myosin head attaches to actin and executes a power stroke before detaching to repeat the process. The actin filament moves forward with each cycle which results in muscle shortening. The heart maintains its rhythmic contractions through this process which enables coordinated heartbeats. Contraction efficiency decreases because any disruption in this cycle which decreases total heart capacity.[13]

3. Conversion of Chemical Energy into Mechanical Work

The cardiac myosin functions in two different ways that include its role to convert chemical energy into mechanical energy. Myosin uses ATP as an energy source, breaking it down to fuel movement. The myosin head uses this energy conversion process to create force through its shape changes. The cardiac myosin requires ATP to operate efficiently, which helps produce powerful heart contractions that need minimal energy. The heart muscle of patients with heart failure experiences two problems because their energy conversion process functions at lower efficiency.[14[

4. Regulation of Systolic Ejection

The duration and strength of systolic contraction which occurs when the heart pumps blood out to the body receive regulation through cardiac myosin. The length of time myosin stays bound to actin determines the duration of systolic ejection according to cardiac myosin's control over this process. Heart regulation establishes proper blood flow which occurs during each heartbeat. The heart fails when myosin activity decreases because this effect causes shorter systolic contractions which result in reduced stroke volume and diminished cardiac output.[15]

5. Maintenance of Cardiac Efficiency

The heart achieves its total efficiency through cardiac myosin which generates force without raising heart rate or oxygen usage. The heart can pump more blood because myosin functions efficiently while using less power. Heart failure patients require this disposal system because their body contains limited energy resources. Myosin function-enhancing therapies aim to increase pumping efficiency without creating dangerous effects through elevated calcium levels which result from continuous stimulation.[16]

6. Role in Cardiac Myosin–Targeted Therapy

The direct control of contraction by cardiac myosin makes it an important therapeutic target for heart failure treatment. The use of cardiac myosin activators results in better force production because they boost the interaction between myosin and actin. The targeted method increases strength of heart contractions without any rise in intracellular calcium levels or heart rate increase. Myosin-based treatments provide a safer treatment option which specifically targets patients who have weak heart muscles.[17]

Mechanism of Cardiac Muscle Contraction

The heart uses an organized system of cardiac muscle contraction to achieve effective blood circulation throughout the body. The process requires electrical impulses to transmit signals which activate calcium movement and lead to contractile protein interactions inside heart muscle cells called cardiomyocytes.

1. Electrical Excitation of Cardiac Muscle

The cardiac muscle contraction process starts when the sinoatrial node generates an electrical impulse which serves as the heart's natural pacemaker. The electrical signal travels through the atria to the atrioventricular node which then sends the signal to the ventricles. The electrical impulse moves through the cell membrane while it penetrates into the cell through transverse (T) tubules.[18]

2. Role of Calcium in Excitation - Contraction Coupling

The cardiomyocyte voltage impulse activation causes the opening of voltage-gated L-type calcium channels which exist on both the cell membrane and T-tubules. The process permits a small amount of calcium to enter the cell from the extracellular space. The sarcoplasmic reticulum contains calcium which undergoes release after the calcium enters the cell through a process called calcium-induced calcium release.[19]

3. Interaction of Actin and Myosin

Calcium ions from the released calcium solution bind to troponin C protein which exists on the actin filament. The binding process creates a structural transformation which moves tropomyosin away from the sites where myosin can bind to actin. Myosin heads can now contact actin because the myosin-binding sites on actin became accessible. This interaction represents the essential process that leads to muscle contraction.[20]

4. Cross-Bridge Cycling and Force Generation

The myosin head begins to pull the actin filament toward the middle of the sarcomere after myosin establishes contact with actin and ATP undergoes hydrolysis to deliver power. The power stroke describes this particular movement. The sarcomere undergoes shortening with each cycle

of attachment followed by pulling and then detaching which results in force generation that drives cardiac muscle contraction.[21]

5. Relaxation Phase of Cardiac Muscle

The process of relaxation starts when SERCA pumps actively transport calcium back into the sarcoplasmic reticulum while sodium–calcium exchangers remove calcium from the cell. The process begins when intracellular calcium levels decrease which leads to calcium leaving troponin while tropomyosin returns to its original position that blocks actin-myosin binding. The mechanism enables the heart muscle to achieve relaxation which results in the heart's capacity to acquire blood.[22]

6. Energy Requirement in Cardiac Contraction

The process of cardiac muscle contraction requires energy to operate. The process needs ATP to support both cross-bridge cycling and the process of calcium reuptake. The mitochondria in cardiomyocytes provide a constant supply of ATP which enables the heart to function continuously.[23]

7. Regulation of Cardiac Contractility

The intracellular calcium concentration and myosin ATPase activity and the initial length of muscle fibers determine the strength of cardiac contraction through the Frank–Starling mechanism. The presence of adrenaline and other neurohormonal factors enables contractility to improve because they increase calcium levels in the body.[24]

Pathophysiology of Heart Failure Related To Contractility

Heart failure occurs when the heart fails to pump blood adequately to fulfill the body's metabolic requirements. The most critical mechanism that drives heart failure exists through reduced ejection fraction (HFrEF) which causes the heart muscle to lose its ability to contract normally.

1. Impaired Myocardial Contractile Function

Heart muscle cells in heart failure lose their capacity to produce force. The heart muscle cells experience structural damage which causes myocardial ischemia and chronic pressure overload and cardiomyopathy to weaken their ability to contract. The myosin heads interact less effectively with actin which results in lower force generation and shorter systolic performance.[25]

2. Abnormal Calcium Handling

Calcium functions as the fundamental element that enables cardiac muscles to contract. The sarcoplasmic reticulum in failing hearts releases less calcium while it fails to properly reabsorb calcium during the heart muscle's relaxation phase. This leads to weak and poorly coordinated contractions. Chronic calcium dysregulation leads to two effects which include delayed relaxation and an increased risk of arrhythmias.[26]

3. Altered Myosin Function and Energy Utilization

Heart failure produces alterations in myosin ATPase activity which results in decreased energy efficiency. The contractile machinery needs greater energy resources but produces lower force output. The body experiences myocardial fatigue because energy needs exceed available energy resources which leads to faster disease development.[27]

4. Reduced Systolic Ejection Time

Ventricular systole experiences both shortened duration and reduced effectiveness because contractility has been impaired. The body experiences poor tissue perfusion and clinical symptoms after the body moves blood through the heart because of shortened ejection time which causes decreased stroke volume and cardiac output.[28]

5. Neurohormonal Compensation and Its Impact

The body uses neurohormonal systems to exist when contractility reaches its lowest point which includes activation of the sympathetic nervous system together with the renin–angiotensin–aldosterone system. The body experiences temporary heart rate and contractility increases through these mechanisms but their continuous operation causes myocardial remodeling together with fibrosis which results in more severe contractile function decline.[29]

6. Ventricular Remodeling and Contractile Dysfunction

Ventricular dilation and myocardial geometric changes result from extended periods of contractile function impairment. Heart remodeling generates mechanical inefficiency because it produces additional wall stress which prevents the heart from achieving proper contractile power.[30]

Rationale For Cardiac Myosin Activation In Heart Failure

Heart failure with reduced ejection fraction HFrEF primarily affects patients through its negative impact on their systolic contractility which results in decreased cardiac output and insufficient tissue perfusion. The persistent symptoms and frequent hospitalizations together with the advancing disease process continue to affect patients despite healthcare providers making extensive progress through guideline-directed medical therapy GDMT. The majority of heart failure medications available today create their effects by altering neurohormonal pathways instead of directly enhancing myocardial contractility.[31]

Traditional positive inotropic agents which include β-adrenergic agonists and phosphodiesterase inhibitors function to enhance myocardial contractility by increasing cytosolic calcium concentrations and cyclic adenosine monophosphate (cAMP) levels. The agents provide short-term hemodynamic benefits but their extended use results in heightened arrhythmia rates and myocardial ischemic events and increased oxygen consumption and greater death risk which prevents their use in extended medical treatment.

The process of cardiac myosin activation creates a new way to achieve targeted therapeutic results through its unique mechanistic operation. Myosin activators work directly on cardiac sarcomeres to boost actin–myosin cross-bridge formation which results in longer systolic ejection time without raising intracellular calcium levels or heart rate. The body achieves better cardiac efficiency which leads to improved stroke volume results while reducing both proarrhythmic and ischemic dangers.[32]

Therefore, cardiac myosin activation represents a safer, contractility-based therapeutic strategy that complements existing heart failure therapies and holds promise for improving outcomes in patients with advanced systolic dysfunction.

Cardiac Myosin As A Therapeutic Target

The force-generating motor protein cardiac myosin enables heart muscle contraction through its function of producing mechanical power from ATP chemical energy through its binding with actin filaments. Scientists have developed a new treatment method that uses cardiac myosin because they discovered that heart failure patients need improved strength to overcome their main medical issue.

1. Role of Cardiac Myosin in Contractility

Cardiac myosin plays a direct role in systolic contraction by forming cross-bridges with actin. The strength and efficiency of contraction depend on myosin heads that link with actin because their connection duration determines their interactive power. Heart failure leads to decreased myosin activity which results in insufficient and defective cardiac pumping.[33]

2. Limitations of Traditional Inotropic Therapies

Conventional inotropes, such as beta-agonists and phosphodiesterase inhibitors, increase contractility by raising intracellular calcium levels. The medications work effectively for a brief period but they lead to increased oxygen consumption in the heart muscle and develop into arrhythmias which result in death after extended use. This highlights the need for safer, more targeted therapies.[34]

3. Rationale for Targeting Cardiac Myosin

The process of cardiac myosin activation leads to better heart muscle contractility results which occur without any rise in intracellular calcium levels. The agents produce their effects by establishing direct myosin–actin connections which lead to increased systolic ejection time and force production while the body maintains its normal calcium levels. This makes cardiac myosin an attractive therapeutic target.[35]

4. Selectivity and Safety Advantages

Cardiac myosin activators work specifically on cardiac muscle while leaving skeletal and smooth muscle functions intact. The drug's ability to target specific areas enables doctors to treat patients with heart failure because it minimizes side effects and keeps the drug safe for extended use.

5. Impact on Cardiac Efficiency

The process of cardiac myosin activation enables more efficient energy production which leads to higher stroke volume and cardiac output, while the body maintains its normal energy usage and oxygen requirements. The contractility of the heart works efficiently through this process which provides essential support to patients who experience severe systolic dysfunction.

Mechanism of Action of Cardiac Myosin Activators

Cardiac myosin activators represent a new drug category which strengthens cardiac muscle contractions through their direct interaction with the cardiac myosin protein. The agents function as medical treatments which increase contractile strength without causing the heart to beat faster or producing more calcium within the cells.

1. Direct Binding to Cardiac Myosin

The cardiac myosin activators specifically target the catalytic domain of cardiac myosin. The myosin head behavior during the contractile cycle changes because of this binding interaction. The drugs help myosin maintain its force-producing state which enables myosin to better bind with actin filaments.[36]

2. Enhancement of Actin–Myosin Cross-Bridge Formation

The cardiac myosin activators first establish a bond which leads to an increase in myosin heads that successfully execute cross-bridge formation with actin. This mechanism results in enhanced force production throughout the sarcomere. The increased cross-bridge availability strengthens systolic contraction without changing calcium concentration inside the cell.[37]

3. Prolongation of Systolic Ejection Time

The use of cardiac myosin activators causes myosin to remain attached to actin for extended periods. The heart maintains its pumping capacity during each heartbeat because of extended systolic ejection times. The body experiences increased stroke volume and cardiac output because of this mechanism which operates without any heart rate changes.[38]

4. Improvement in Contractile Efficiency

The agents improve ATP usage efficiency which cardiac myosin uses for energy. The system produces additional mechanical work from each

ATP spent which results in higher myocardial efficiency. The method proves crucial because energy depletion creates major challenges in heart failure situations.[39]

5. Calcium-Independent Inotropic Effect

Cardiac myosin activators differ from traditional inotropes because they maintain intracellular calcium levels at normal rates. The body avoids calcium overload which results in arrhythmias and heart muscle damage. The drugs offer better long-term safety because they operate through a mechanism that does not depend on calcium.[40]

6. Reduction in Myocardial Oxygen Demand

The cardiac myosin activators increase heart contractility without causing increased heart rate or calcium movement which leads to increased myocardial oxygen consumption. The treatment decreases ischemia risk which is especially beneficial for patients who have existing coronary artery disease.[41]

7. Hemodynamic Effects at the Ventricular Level

Cardiac myosin activators enable increased stroke volume and decreased ventricular wall stress while they enhance left ventricular ejection fraction at the ventricular level. The changes lead to better cardiac function which helps heart failure patients experience relief from their symptoms.

8. Effects on Ventricular Remodeling

The contractility improvement and decreased wall stress lead to better heart function which helps stop or reverse negative changes in ventricular shape. The structural advantage will produce long-term clinical benefits which will help treat heart failure progression.[42]

Pharmacological Agents Targeting Cardiac Myosin

Researchers established a new therapeutic technique which uses cardiac myosin as its target to achieve direct control over myocardial function through their action at the sarcomere. The drugs which target cardiac myosin function differently from existing cardiovascular medications because they directly control the process of actin and myosin interaction to boost heart function while reducing unwanted side effects. The agents use two main categories which depend on their impact to either enhance or reduce cardiac myosin function which controls heart muscle movement.[43]

1. Cardiac Myosin Activators

Cardiac myosin activators enhance systolic function by increasing the number and duration of actin–myosin cross-bridges during cardiac contraction. The substances distinguish themselves from standard inotropic agents because they do not raise intracellular calcium levels or increase oxygen needs of the heart muscle.

Omecamtiv Mecarbil

Omecamtiv mecarbil functions as the first existing medical solution which selectively activates cardiac myosin to treat heart failure with reduced ejection fraction (HFrEF) condition. The drug operates by attaching to the catalytic domain of cardiac myosin to maintain the protein in its force-producing condition. The system achieves higher cardiac efficiency through improved stroke volume and extended systolic ejection time without adding extra heart rate or intracellular calcium levels. Clinical studies including COSMIC-HF and GALACTIC-HF have tested the therapy's ability to decrease heart failure incidents which especially benefit patients suffering from severe systolic dysfunction.[44]

Danicamtiv (MYK-491)

Danicamtiv represents a new type of cardiac myosin activator which researchers currently study in clinical trials. The drug demonstrates superior half-life and better drug distribution characteristics when compared to omecamtiv mecarbil. The results from early-stage studies show that the treatment enhances contractility while the body tolerates it well which may help treat chronic heart failure.[45]

2. Cardiac Myosin Inhibitors

Cardiac myosin inhibitors effectively diminish excessive heart muscle contractions which medical professionals apply to treat conditions that involve heightened muscle contractions such as hypertrophic cardiomyopathy (HCM).

Mavacamten

Mavacamten functions as a selective cardiac myosin inhibitor which medical professionals use to treat patients with obstructive hypertrophic cardiomyopathy. The treatment decreases excessive actin–myosin cross-bridge formation which results in reduced left ventricular outflow tract obstruction and enhanced diastolic function. The treatment demonstrates success as a heart failure drug while it does not treat heart failure with reduced ejection fraction because it proves that cardiac myosin functions as an effective target for clinical drug development.[46]

Aficamten

Aficamten serves as an investigational cardiac myosin inhibitor which demonstrates a shorter duration of action and predictable drug effects. The drug undergoes clinical trials to assess its effectiveness against hypertrophic cardiomyopathy while it potentially offers better dosing control in comparison to mavacamten.[47]

Drug	Class	Indication	Key Effect
Omecamtiv Mecarbil	Myosin Activator	HFrEF	↑ Systolic ejection time
Danicamtiv	Myosin Activator	HFrEF (investigational)	↑ Contractility
Mavacamten	Myosin Inhibitor	Obstructive HCM	↓ Hypercontractility
Aficamten	Myosin Inhibitor	HCM (investigational)	Controlled myosin inhibition

Clinical Evidence And Major Trials

Research studies for cardiac myosin activators have established their safety and their effectiveness and their function as treatments for heart failure. The initial evidence originates from research studies about omecamtiv mecarbil which represents the first drug in its category as a cardiac myosin activator. The clinical trials investigated how the drug impacted cardiac function and clinical results and patient tolerability who experienced heart failure with reduced ejection fraction (HFrEF).

1. Early Phase Clinical Trials (Phase I and II Studies)

The first clinical studies evaluated omecamtiv mecarbil for safety and tolerability and pharmacokinetics through testing in both healthy volunteers and heart failure patients. The clinical trials showed that the medication produced higher systolic ejection times and higher stroke volumes through increasing dosage. The observed benefits resulted without noticeable heart rate increases or myocardial oxygen consumption increases. The Phase II trials demonstrated better left ventricular function and smaller ventricular volumes which proved that direct myosin activation can improve heart function without causing safety issues.[48]

2. ATOMIC-HF Trial

The ATOMIC-HF (Acute Treatment with Omecamtiv Mecarbil to Increase Contractility in Acute Heart Failure) trial evaluated intravenous omecamtiv mecarbil in patients hospitalized with acute heart failure. Researchers studied how effectively patients could breathe better after treatment for their primary medical condition which involved dyspnea. Higher-dose cohorts displayed better symptom improvement results although they did not achieve the study's main goal across all dosing groups. The medication demonstrated good safety for emergency use because no major arrhythmia or ischemic event raised safety concerns during the study.[49]

3. COSMIC-HF Trial

The COSMIC-HF (Chronic Oral Study of Myosin Activation to Increase Contractility in Heart Failure) trial assessed the effects of oral omecamtiv mecarbil in patients with chronic HFrEF. The study showed that patients experienced major enhancements in their heart function because their systolic ejection time and stroke volume increased while their left ventricular end-systolic and end-diastolic volumes decreased. The results showed that chronic myosin activation leads to positive changes in heart structure. The trial also confirmed that the drug operates through a calcium-independent mechanism while maintaining an acceptable safety level.[50]

4. GALACTIC-HF Trial

The GALACTIC-HF (Global Approach to Lowering Adverse Cardiac Outcomes Through Improving Contractility in Heart Failure) trial tested omecamtiv mecarbil against cardiovascular death and heart failure events in its phase III trial with patients who had symptomatic HFrEF. The study found that heart failure-related events decreased at a modest level which reached statistical significance among patients who had extremely low ejection fraction levels. The trial showed that myosin activation which improves contractility provides substantial clinical advantages when used with standard treatment methods.[51]

5. Safety Outcomes Across Clinical Trials

Omecamtiv mecarbil showed positive safety results throughout major trials. The study found no significant heart rate increase which also applied to blood pressure and serious arrhythmia cases. Some patients showed mild increases in cardiac biomarkers which demonstrated the need for dose monitoring. The safety data demonstrate that cardiac myosin activators can be used safely for extended periods when administered through controlled dosing methods.[52]

Future Perspectives And Ongoing Research

Cardiac myosin activation represents a promising shift toward mechanism-based treatment of heart failure, and ongoing research continues to refine its clinical role. Future studies will determine which patient group will benefit most from myosin activators, focusing especially on individuals with advanced heart failure and severely reduced ejection fraction.

The development of next-generation cardiac myosin activators which include danicamtiv will achieve three goals through its research work. The drugs provide better treatment results because their safety features are more effective than the first-generation drugs which include omecamtiv mecarbil.[53,54]

Researchers currently investigate the effectiveness of combination treatment methods which use cardiac myosin activators together with SGLT-2 inhibitors and ARNIs and standard medical treatments. The research study investigates how pharmacokinetic-based dosing combined with biomarker-based patient selection will enhance patient treatment results. Researchers will study how cardiac myosin activation affects acute decompensated heart failure and early stage disease and special patient groups who have renal impairment. Molecular cardiology and sarcomere biology research developments will increase treatment options because they enable personalized management of heart failure through cardiac myosin activation.[55]

Conclusion

The development of cardiac myosin activation treatment for heart failure establishes its value because this method treats the heart disease that causes reduced ejection fraction through its direct effect on heart muscle contraction problems. The system functions differently from traditional inotropic agents because cardiac myosin activators work to improve systolic performance without needing calcium as their active control mechanism. The clinical evidence supports

omecamtiv mecarbil as an effective treatment which improves heart function while reducing heart failure events for patients who have severe systolic dysfunction. The new mechanism-based treatment method provides patients with a safer and more effective choice than traditional medical procedures. The research that operates at present will establish the correct methods for choosing patients and dosing medications and using various treatment methods together while cardiac myosin activation treatment should become essential for treating heart failure according to individual patient needs and it will enhance treatment results in this group of patients who face high health risks.

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