M.SC-Sem-IV, Elective Course – 1c , Organic Chemistry Special

UNIT – IV Drugs Cardiovascular drugs

INTRODUCTION

Cardiovascular drugs are a class of medications that have a significant effect on the heart or blood vessels. They can also be termed as those drugs that are used primarily to treat cardiovascular disorders. These drugs oftenregulate the total functioning of the heart as well as helps incirculating the blood to specific parts of the system. Cardiovascular drugs are used to treat heart failure, hypertension, and many other cardiovascular disorders.

Medications that have effect on the cardiovascular system are among those that are most utilised in medical practise and research. These drugs have three main mechanisms of action on the heart: they affect the strength with which the heart muscle contracts (inotropic effects), they affect the frequency with which the heart beats, or the rate at which the heart beats (chronotropic effects), and they affect the regularity with which the heart beats (rhythmic effects). Drugs that effect on blood vessels normally do so by modifying the state of contraction of the smooth muscle in the vessel wall, which in turn varies the diameter of the vessel and, as a result, controls the amount of blood flowing through the channel. High blood pressure (hypertension), a kind of chest discomfort known as angina pectoris, heart failure (insufficient output from the heart muscle), and arrhythmias (disturbances of cardiac rhythm)are just few conditions in which cardiovascular medicines may be beneficial.

There are many kinds of cardiovascular drugs, which are classified as follows:

4.1 OBJECTIVES

After that unit learners will be able to

- Introduction of cardiovascular drugs & diseases and drug inhibitors.
- Synthesis of cardiovascular drugs e.g. amyl sitrate, sorbitrate, diltiazem, guinidine, verapamil, methyedopa, aterolo & oxyprenolol

4.2 TYPE OF THE CARDUOVASCULAR DRUGS

There are many kinds of cardiovascular drugs, which are classified as follows:

1. Cardiac Glycosides
2. Anti-Anginal Drugs
3. Calcium Channel Blockers
4. β-Adrenergic Blocking Agents

5. Vasodilators
6. Anti-Arrhythmic Agents
7. Anti Hypercholesterolemic Agents
8. Sclerosing Agents

Fig. 4.1 cardiovascular drugs

4.2.1 *Cardiac Glycosides*

The Cardiac Glycosides are thefamily of naturally occurring drugs whose activity causes toxic as well as cardiotonic effects on the body. Cardiac glycosides are derived from variety of sources, including plants such as Digitalis and Strophanthus as well as animals such as the venomous toad. Cardiac glycosides have been utilised as both medicines and poisons throughout the history.

Steroids with cardioactive properties, as well as their glycosides, are abundant in nature and have distinct effects on the contractility and electrophysiology of the heart. Their finding is an example of folk medicine, which was known to ancient civilizations such as the Romans and the Egyptians. Most glycosides are derived from the leaves of the foxglove (Digitalis purpurea or Digitalis lanata), which are available in abundance. Cardiac glycosides are a mixture of an aglycone or genin and one to four sugars units that were discovered by William Withering (1785) and have been used since then to treat heart disease. The steroidal aglycone of glycosides is responsible for cardiac activity, while sugars facilitate solubility and dispersion, which affects the strength and duration of action of the glycosides in the body. These glycosides are being utilised less commonly these days. Calcium channel blockers (such as verapamil), Acetyl Choline Esterase Inhibitors (ACEIs), and diuretics are often used to treat patients with this condition.

9. Cardiac glycosides are harmful because they impede the Na^+, K^+, and ATP

pumps of the heart, resulting in elevated intracellular levels of calcium ions. The elevated amounts of Ca^{++} in the blood are mainly responsible for the occurrence of cardiac arrhythmias, which indicates glycoside poisoning.

10. Table.1. Common cardiac glycosides
11.

Source	Structure	Aglycone	Glycoside
Leaf of Digitalis Lanata	Glucose-3 acetyldigitoxose-digitoxose$_2$-aglycone	Digitoxigenin Gitoxigenin Digitoxigenin	Lanatoside-A Lanatoside-B Lanatoside-C
Leaf of Digitalis Purpurea	Glucose-digitoxose$_3$-glycone	Digitoxigenin Gitoxigenin	Purpurea Glycoside A Purpurea Glycoside B
Leaf of Strophanthus Gratus	Rhamnose-Aglycone	Quabagenin	g-Strophanthin
Seed of Strophanthus Kombe	Glucose-glucose-cymarose-aglycone	Strophanthidin	k-Strophanthosi de

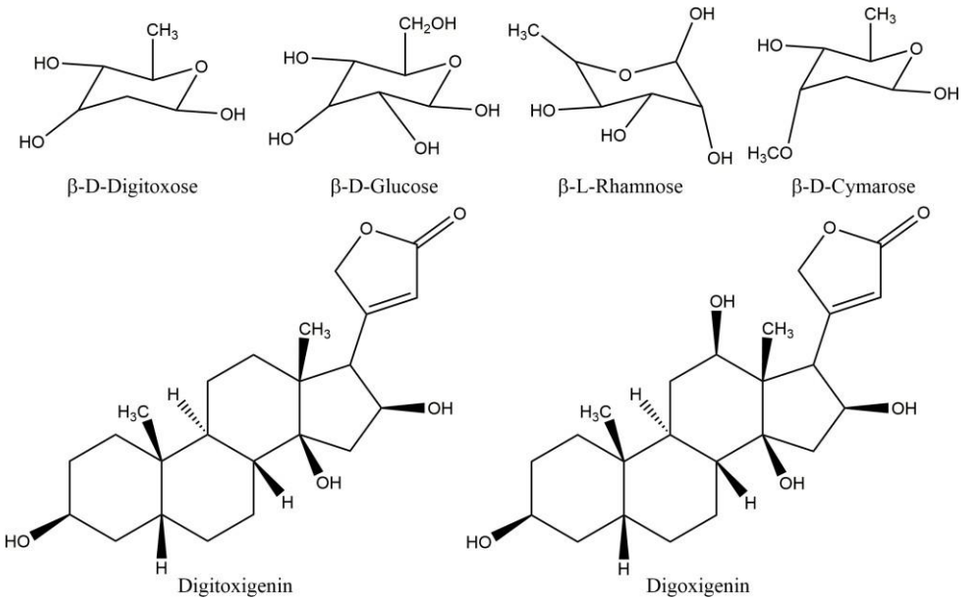


Fig.4.2 Structure of few cardiac glycosides and aglycones

4.2.2 *Anti-Anginal Medications*

When someone have angina pectoris, a sudden, acute pain in chest is felt that typically radiates to the left shoulder, and then moves down from the shoulder to the arm. The source of this kind of pain is thought to be the temporary condition of myocardial ischemia. This condition of myocardial ischemia occurs due to reducing of coronary blood flow and increasing need of myocardial oxygen. The increased energy demand caused by activity, emotion, eating, or coitus is known to cause attacks (stable angina), which then reduce when the increased energy demand is removed. Significant

arteriosclerosis of the major coronary arteries (conducting vessels), which flow epicardial and send perforating branches to serve the deeper tissue, is the underlying pathology in this case. The coronary occlusion is 'fixed'; blood flow does not rise in response to increased demand, despite dilatation of resistance arteries mediated by local causes, and ischemic discomfort is experienced as a result. The end diastolic left ventricular pressure rises from 5 to approximately 25 mm Hg because of the inadequacy of the ischaemic left ventricle, which causes subendocardial 'crunch' during diastole and aggravates the ischaemia in this region. A sort of quickly developing and rapidly reversible left ventricular failure results, which can be alleviated by resting and lessening the stress placed on the myocardium.All the organic nitrates undergo fast first-pass metabolism, which occurs in extrahepatic tissues such as blood vessels and liver because of the activity of the glutathione-nitrate reductase enzyme.Glyceryl trinitrate is the most often prescribed medication for the relief from acute anginal discomfort. In just less than two minutes, this medication is absorbed from the lingual, sublingual, and buccal mucosae, thusproviding immediate relief to the patient having angina pectoris.

Long-acting organic nitrate medications, such as orally givenisosorbide, dinitrate, pentaerythritol tetranitrate, and erythrityl tetranitrate, are used to avoid recurrent anginal discomfort. Also, orally given sustainedrelease formulations such as glyceryl trinitrate ointment, buccal pills, and transdermal patches are all utilized for treating the condition of angina pectoris.

Angina may be relieved by three types of medications: organic nitrates, calcium channel antagonists (for both spasmatic and chronic stable angina), and beta-adrenergic antagonists (for both exertion-induced and non-exercise-induced angina). Anti-anginal medicines are primarily effective in relieving pain by lowering the oxygen demands of the heart, which in turn reduces the sensation of anginal discomfort. Each type of anti-anginal

drug employs a separate method for lowering cardiac strain, and as a result, many classes of anti-anginal agents may be used in conjunction to maximise the therapeutic impact.

4.2.3 *Calcium Channel Blockers*

Calcium Channel Blockers are medications that prevent calcium channels from opening. There are a variety of calcium channel blockers available, and they are particularly effective in treating myocardial insufficiency. Inhibiting calcium ion invasion into cardiac cells is beneficial in inhibitinganginal discomfort. Physiologically, calcium is present in the human body both intracellularly and extracellularly. Many medicines have been discovered to influence the transport and

availability of calcium. When medicinal drugs exert their effects by blocking calcium-dependent actions, they often achieve this blockage by lowering the levels of free calcium in the cytoplasm of the cell. It is possible to prepare the hydrochloride salt of each calcium channel blocker, which is delivered as oral tablets and capsules, by adding an amine group to the compound. Additionally, these medicines have a mainly hydrophobic nature, which accounts for their quick and full absorption upon oral administration. Around 75-95 percent of the medicine is detected in the bloodstream.

Most of these agents are found in the plasma primarily in the protein-bound (80-95 percent) state, even though they are active in the free form. The length of action for most agents is between 4 and 8 hours, except for amlodipine, which has 24-hour duration of action owing to the presence of the chlorine atom in the compound.

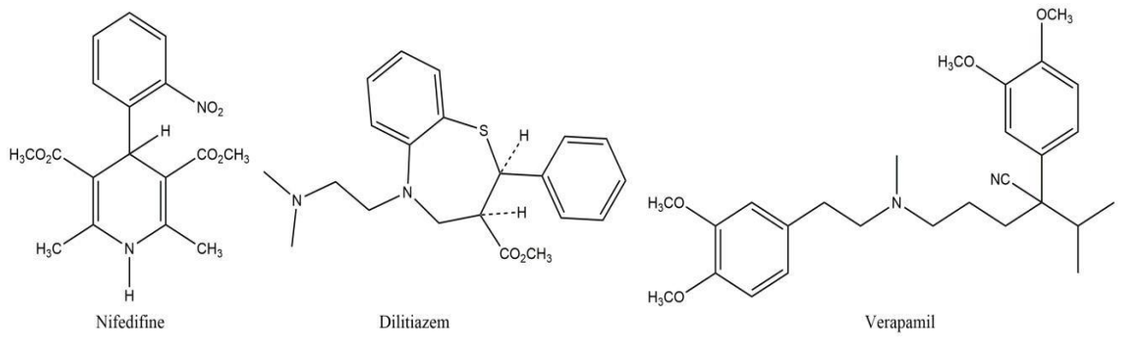


Fig.4.3 Structure of some Calcium Channel blocker

Mechanism: These medications work by selectively inhibiting calcium ion influx into heart muscle while also inhibiting calcium ion inflow into vascular smooth muscle, among other things. It dilates the main coronary arterioles, and by inhibiting coronary artery spasm, it increases myocardial oxygen delivery in patients with Prinzmetal's angina (Chronic Coronary Artery Disease).

4.2.4 *β-adrenergic receptor blockers*

These are the agents that blocks the action of the beta-adrenergic receptor. When it comes to the therapy of exertioninduced angina, beta-adrenergic blocking medications are utilised. These medications can be taken single as well, but they are mostly used in conjunction with calcium channel blockers, nitrates, or can be combination of both the drugs. Propranolol is a medication that serves as a prototype for this class.

Adrenergic nervous system plays a significant role in maintaining blood pressure, heart rate, bronchial tone, and gastrointestinal motility. Norepinephrine is generated and stored in granules inside the nerve terminals from where it is released as required. During neuronal depolarization, it is released into the synaptic vesicle in small quantities. Myocardial contraction is caused by an interaction with the β-receptor,

which also leads to increase in blood flow via vasodilation, relaxation of the bronchi, and enhanced glycolytic activity. β- adrenoreceptor stimulation is reduced or prevented in the presence of beta-adrenoreceptor blocking drug, which has the primary impact of lowering cardiac activity. They are used for the treatment of angina pectoris and cardiac arrhythmias as they help in reducing the heart's oxygen consumption while also boosting its tolerance to physical activity.

Propranolol is a nonselective adrenergic receptor antagonist that is often used to treat heart failure and bronchitis. It is commonly used for the treatment of exertion-induced angina, which is caused by coronary atherosclerosis. As a result, medications with beta- blocking activity lower the heart rate and reduce the power of muscle contraction, making them effective in the treatment of hypertension and cardiac arrhythmias, as well as angina and other cardiovascular diseases. The anti-anginal effectiveness of propanolol is often enhanced using organic nitrates or calcium channel blockers in conjunction with other medications.

Mechanism: It is believed that the β-Adrenergic Antagonist works by decreasing sympathetic activation of the heart, which lowers the heart rate and lessens the contractibility of the heart muscle. These actions, in turn, lower the oxygen needs of the myocardium, which is beneficial both during exercise and during resting state.

4.2.5 *Vasodilators*

Vasodilators are a class of medications that influence the circulatory system and are used to treat various medical conditions. Their therapeutic activity is attributed to its capacity to widen coronary arteries, and are also used to treat coronary artery disease, notably angina discomfort, among other conditions. It is a naturally occurring vasodilatory chemical that is secreted by the myocardium during hypoxia-induced events. Inhibition of adenosine absorption byred blood cells (RBCs) and the vasculature is said to be the mechanism through which dipyridamole produces its long-lasting and selective coronary vasodilation. These medications are used to treat or prevent many conditions such as hypertension, Pulmonary hypertension, heart failure, high blood pressure during pregnancy and chest pain caused due to reduced blood flow to the heart.

Mechanism: A single unifying mechanism does not exist; instead, different vasodilators may operate at different points in the cascade of events that link excitatory signals to contractions in vascular smooth muscle cells. For example, the vasodilators known as calcium channel antagonists prevent or limit the entry of calcium into vascular smooth muscle cells through voltage-dependent channels in the membranous membrane of these cells. Calcium channel blockers work in this fashion by limiting the amount of free intracellular calcium that is accessible to interact with smooth muscle

contractile proteins in the body.

Some other vasodilators, such as diazoxide and minoxidil, induce blood arteries to dilate by activating potassium channels in the vascular smooth muscle. An increase in potassium conductance causes hyperpolarization of the cell membrane, which results in relaxation of the smooth muscle of the vascular system.

4.2.6 *Antiarrhythmic Agents*

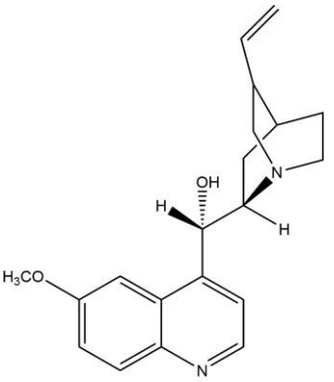
When it comes to the therapy of cardiac arrhythmias, antiarrhythmic medicines are quite helpful. Cardiac arrhythmias are characterised by a disruption in the conduction of impulses across the heart because of disturbances in the production of impulses.

Mechanism: Cardiac arrhythmias may arise because of a disruption in the origin of the impulse, which are the pacemaker cells. Those cells may have impaired automaticity, which is the rhythmic trait that allows them to depolarize their membranes at the appropriate pace. Disruption of the automaticity of pacemaker cells may be caused by underlying disorders such as hypertension, atherosclerosis, hyperthyroidism, or lung disease, among others. The genesis of impulses in cells other than pacemaker cells may result in the development of several types of arrhythmias. Ectopic arrhythmias are what they are referred to as. Excessive myocardial catecholamine production, myocardial ischemia, and the toxicity of cardiac glycosides are all potential causes of ectopic arrhythmias.Additionally, arrhythmias may be created when the electrical impulse does not fully die down before the beginning of phase 0 of the heartbeat. Consequently, a part of the previous impulse that remains at the end re-enters and re-excites the cardiac muscles prematurely, resulting in the phenomenon known as asynchronous depolarization. Pre-mature heartbeats are distinguished by the presence of this distinctive shape. Re-entrant arrhythmias are prevalent in patients with coronary artery disease.

These drugs are further classified into four different types:

(a) Class I Drugs: Class I antiarrhythmic medicines are often local anaesthetics that act on the myocardial membrane and nerve to slow the conduction of electrical impulses in the heart. These medications also slow down the pace of depolarization without altering the resting potential of the brain. Quinidine is an example of this kind of medication.

Quinidine is a drug that is used to treat a variety of ailments. Quinidine is a medication that is commonly used for the acute and chronic treatment of ventricular and supraventricular arrhythmias, especially supraventricular tachycardia, in both adults and children. Cinchona bark contains a group of alkaloids that are known as cinchona alkaloids. It has a close relationship to the drug quinine.



Quinidine

Fig.4.4. Structure of Quinidine

(a) **Class II drugs:**β-adrenergic receptor blockers are used to treat arrhythmias in the class II category. They go through the process as described below:

i) Specifically, they reduce adrenergic ally enhanced phase 4 depolarization by inhibiting B receptor function.

ii) At typical therapeutic levels, these drugs have been shown to reduce neurologically induced automaticity.

iii) These medicines produce excitability when used in greater dosages.

As an example, **Propranolol** is a beta-adrenergic receptor antagonist that is used to treat heart failure.

(b) **Class III drugs:** Antiarrhythmic medications of class III produce a homogenouslengthening of the duration of action potential throughout the body.

Bretylium is a genus of plants that includes the species Bretylium.

(c) **Class IV drugs:** Class IV antiarrhythmic pharmaceuticals work by inhibiting the sluggish inward current carried by calcium.Supraventricular arrhythmias are treated extremely well by blocking the conduction of premature impulses at the AV-node, which is accomplished by the actions described above.

(d) **Verapamil** is a calcium channel blocker that is used in the treatment of angina pectoris and supraventricular arrhythmias (supraventricular tachycardia).

Table.2. Classes of Antiarrhythmic Drugs

Class	Antiarrhythmic Drugs	Pharmacological Effects
IA	Quinidine, Procainamide, Disopyramide	Duration of action potential is also decreased; Rate of depolarization is decreased
IB	Lidocaine, Phenytoin, Tocainide Mexiletine	Rate of depolarization is decreased; Duration of action potential is also decreased
IC	Flecainide	Rate of depolarization is decreased; No change in duration of action potential is observed
II	Propranolol	Sympathetic activity is inhibited
III	Bretylium, Amiodarone	Duration of action potential is prolonged
IV	Verapamil	Inward calcium current is inhibited

4.1.1 *Anti-Hypercholesteraemic drug*

Coronary artery disease is one of the most common causes of death throughout the world. High cholesterol levels in the blood are one of the major causes of this disease. High cholesterol levels are caused by a variety of genetic abnormalities that are related with the accumulation of specific classes of lipoprotein particles in the bloodstream. Several medications, including statins, fibrates, bile acid sequestrants, niacin, ezetimibe, omega-3 fatty acids, and natural extracts are used to treat hypercholesterolemia. Statins are the most prescribed medication. It has been noted that these medications produce a wide range of responses in various people.

Atherosclerosis is a condition in which fat deposits in the inside walls of arteries developed in humans. High blood pressure and heart attack may be caused due to cholesterol buildup in the arteries, which can further lead to high blood pressure and heart failure. The amount of cholesterol may be controlled by using the following anti-hypercholesteromic medications i.e.Aluminium Nicotinate also called as Niclex, Clofibrate also known as Atromid-S and D-Thiroxine Sodium.

4.1.2 *Sclerosing Agents*

These drugs are those substances that cause scarring.They cause irritation of the intimal layer of the vessel wall, resulting in the formation of a thrombus. It induces endothelium to adhere to one another and occludes the arteries. These medications are used in the treatment of varicose veins or commonly termed as dilated veins.

Creasing chemicals produce irreversible endothelial injury, which results in inflammation and thrombosis of the vessels, which ultimately results in the creation of fibrous tissues. Sclerosing chemicals, when injected into blood arteries or lymphatics, cause the walls of the vessels to shrink and eventually obliterate the vessel. Pleural effusion is another condition that can be treated with sclerosing drugs. As a result of

their injection, these drugs cause inflammation of the pleura, which results in adhesions of the pleural membranes and the closure of the cavity, preventing the build-up of fluid in the pleura again.

4.2 CARDIOVASCULAR DISEASES

Diseases affecting the human heart and other organs of the circulatory system are referred to as cardiovascular diseases. A set of conditions affecting the heart and blood arteries is referred to as cardiovascular diseases (CVDs). It is a group of diseases that affect the blood vessels that supply the heart muscle, brain, and arms and legs. Heart attacks and strokes are sudden and severe events that are primarily caused by blockage in supply of blood to the heart or brain. It is most often caused by a build-up of fatty deposits on the inner walls of the blood arteries that supply the heart or the brain. Stroke can be caused by bleeding from a blood artery in the brain or by blood clots clotting the blood vessels in the brain. Several other common cardiovascular diseases occur in human beings, some of them are discussed below:

4.2.7 *Cardiac Failure*

Cardiac failure, also known as congestive heart failure, is characterised by a reduction in the contractility of the ventricles, resulting in a decreased cardiac output that is insufficient to meet the metabolic needs of the body. Greater blood volume, end-diastolic volume, and venous return are all associated with increased cardiac failure, resulting in a reduction in systemic blood pressure as the degree of cardiac failure rises. A typical heart would attempt to raise the force with which it contracts in response to these modifications. Therefore, it leads to a rise in heart rate, systemic vascular resistance, and venous load, among other things. When sympathetic tone is elevated, it is possible that myocardial contractility will be raised as well. As the severity of cardiac failure increases, the heart gets dilated, which may result in swelling and ascites in the lungs, among other complications.

It can also be termed as a medical disorder in which the heart is unable to adequately pump blood to the rest of the body's organs. The "failing" heart continues to beat, but it does so at a lower rate than it should. People who suffer from heart failure are unable to exercise because they get short of breath and exhausted. The slowing of blood flow out of the heart results in a back-up of blood returning to the heart through the veins, which causes congestion in the tissues. Swelling is a common side effect. It is most common to see swelling in the legs and ankles, but it can manifest itself in other places of the body as well. Occasionally, fluid accumulates in the lungs and interferes with breathing, resulting in shortness of breath, particularly when a person is lying down. Heart failure impairs the kidneys' ability to excrete salt and water, as well as their overall function.

4.2.8 *Ischemic Heart Disease*

Ischemic heart disease is a kind of heart disease that occurs because of advanced atherosclerosis. Angina pectoris is a common side effect of this medication. Angina pectoris is a kind of myocardial ischemia characterised by a sudden, acute pain that originates in the myocardium and is caused by a reduction in coronary blood flow and an increase in myocardial oxygen demand.

Angina pain is caused in certain people by atherosclerotic constriction of the coronary blood arteries, which is caused by atherosclerosis. Specifically, in these individuals, the reduction in myocardial oxygen demand, which is caused by nitrate administration, happens as a direct consequence of changes in the systemic circulation. In these patients, the administration of nitrates results in dilatation of both resistance and capacitance vessels in the chest, with symptoms often extends to the left shoulder and down the left arm.

Angina may be classified into two types:

(1) Typical

(2) Variant

This categorization is based on the causes that precipitated the attack as well as the electrophysiologic alterations that were seen during the assault. It doesn't matter which angioplasty is used since the underlying reason is myocardial ischemia, which is caused by a reduction in coronary blood flow and an increase in myocardial oxygen demand. In the treatment of acute angina pain, organic nitrates, calcium channel blockers, and B-adrenergic blocking medications are used. According to the labour load of the heart, which comprises the function of the heart rate, systolic pressure, thickness of the ventricular heart muscle, and diameter of the heart, the oxygen need of the myocardial tissues is determined.

Myocardial ischemia occurs when there is insufficient oxygen available to satisfy the demands of the myocardium. Depending on the cause, this might be caused by atherosclerotic constriction of the coronary circulation or by vasospasm of the coronary veins. Angina pain is caused in certain people by atherosclerotic constriction of the coronary blood arteries, which is caused by atherosclerosis. Specifically, in these individuals, the reduction in myocardial oxygen demand, which is caused by nitrate administration, occurs as a direct consequence of changes in the systemic circulation. In these patients, the administration of nitrates results in the dilatation of both resistance and capacitance capillaries.

4.2.9 *Cardiac Arrhythmias*

Cardiac Arrhythmias are irregular heartbeats. Various reasons, including a disruption

in the conduction of impulses via myocardial, problems of impulse production, or a combination

thereof, may produce cardiac arrhythmias. There are a variety of variables that alter the natural rhythm of electrical activity inside the heart.

Arrhythmias may develop for a variety of causes, the most common of which are:

(a) Pacemaker cells are unable to perform their functions adequately.

(b) The transmission via the AV-node is prevented from proceeding.

Arrhythmias may be triggered by a variety of conditions including pulmonary illness, hyperthyroidism, and atherosclerosis. Ectopic arrhythmias are among of the most prevalent types of arrhythmias. Ectopic electrical signals develop when electrical signals spontaneously emerge in areas other than the pacemaker and then compete with the regular electrical impulses. Ectopic foci are also induced by myocardial. Another factor that contributes to the development of arrhythmias is a process known as re-entry. During this process, the electrical impulse does not terminate once it has been fired, but instead continues to circulate and excite resting cardiac cells into depolarizing.

4.2.10 *Thrombosis*

Thrombosis is a kind of blood clot. Thrombosis, which includes coronary, embolic, venous, and traumatic thrombosis, is responsible for a significant number of fatalities each year under the category of cardiovascular illnesses, according to the American Heart Association. In addition to vascular damage, blood stasis and blood hypercoagulability may all contribute to thrombosis (intravascular clotting). When the subendothelial cells of a blood artery or the cells of tissue are wounded, a vasoconstrictive reflex is triggered, which lowers the volume of blood flow and causes the platelets to stick to the injured cells of tissue. In response, platelets release ADP and prostaglandin peroxide molecules and aggregate into a plug-like structure, which is formed by the platelets. Platelets release and platelets aggregation are the terms used to describe these two processes, respectively. It is possible that the release of biochemicals from platelets will result in the production of thromboxane A2, which is synthesised by the platelets and promotes platelet aggregation, or the production of prostacyclin (PGI2), which is synthesised by the blood vessel cells and inhibits platelet aggregation.

4.2.11 *Platelet aggregation*

It has been implicated in the production of thrombi, notably in the arterial system, as well as in the pathophysiology of atherosclerosis in general and in specific. Atherosclerotic illness is caused by the accumulation of platelets. Because it

acetylates cyclo-oxygenase, a platelet

enzyme, aspirin functions as an anti-platelet medication by decreasing platelet aggregation, thus preventing blood clot formation. This prevents the production of thromboxane A2, which is a potent vasoconstrictor as well as an inducer of the platelet release response and platelet aggregation in the bloodstream. The irreversible impact lasts for the duration of the acetylated platelet's life, which is typically 4-7 days after injection. According to recent clinical research conducted by the Food and Drug Administration of US (FAO), taking a aspirin tablet each daydecreases the risk of having a second heart attack by almost 20% for those people who have previously had one heart attack.

4.2.12 *Kawasaki Disease*

Kawasaki illness is a condition that affects children between the ages of 6 months and 4 years that causes coronary aneurysms and may result in heart attack and death. The results of a recent clinical investigation suggest that aspirin, taken in large dosages, may be useful in the treatment of the complications of Kawasaki illness.Due to the enlargement of glands (lymph nodes) and mucous membranes within the mouth, nose, eyes, and throat, Kawasaki illness was originally referred to as Mucocutaneous Lymph Node Syndrome (MCLNS).

Children who have Kawasaki illness experience high fever, swollen hands and feet with skin peeling, red eyes and tongue. However, Kawasaki illness is frequently curable, and most children who receive therapy within 10 days ofonset of the condition recover without experiencing any serious complications.

The complications due to this disease include inflammation of the blood vessels and coronary arteries. Usually the coronary arteries, that supplies blood to the heart and heart muscle is affected which can also lead to weakening and bulging of the artery wall (aneurysm). This increases the risk of blood clotting, which could further lead to a heart attack or cause life-threatening internal bleeding.