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DRUGS USED IN HEART FAILURE

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Abstract

Cardiotonics (cardiostimulants) potentiate heart function by increasing heart rate (chronotropy) and myocardial contractility (inotropy), which increases cardiac output and arterial pressure. Many of them also have a positive dromotropic and lusitropic effect. Some of these drugs cause systemic vasodilation, while others have vasoconstrictive effects. The effects of these drugs on the heart muscle predispose them to use in heart failure, cardiogenic shock and hypotension. In the treatment of heart failure, procedures that reduce the demands on myocardial function are preferred over cardiotonics- ie reduce afterload or preload, or both (diuretics, organic nitrates, calcium channel blockers, ACE inhibitors).

Key words

Cardiac failure; apoprotein A-1.; digoxin; endogenous cardiotonic compounds; inotropic preparations; serum lipoproteins.

Introduction. cardiac glycosides play an important role in the treatment of heart failure. Glycosides are substances that break down into sugar glucones and sugar-free aglucon parts when hydrolyzed. Cardiotonic are drugs used to increase the efficiency and improve the contraction of the heart muscle, which leads to improved blood flow to all tissues of the body. Cardiotonic drugs increase the force of the contraction of the muscle (myocardium) of the heart. Cardiac glycosides are derived from plants and have a selective effect on the heart. Cardiac glycosides are obtained from several species of digitalis (Digitalis purpura, digitalis lanata), spring adonis (Adonis vernalis), mother-of-pearl (Konvalaria mayalis), chitrangi (Erysimum), strophant (storophantus combe), oleander (Oleander), hemp

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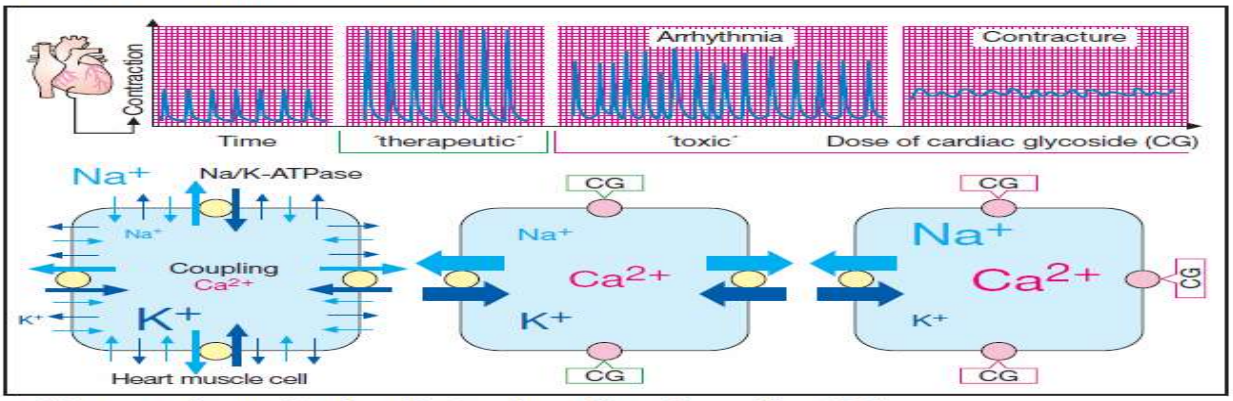
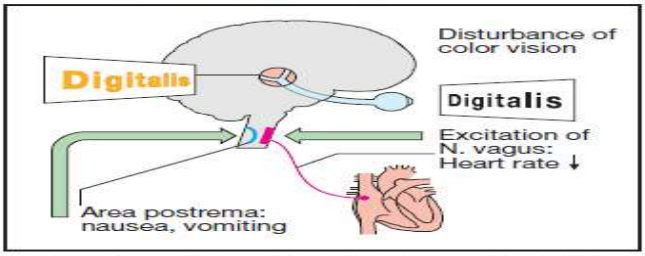
(Apocynum connabinuon) and others obtained from plants. In terms of chemical structure, cardiac glycosides are close to each other. The basis of the aglycon part has a steroid structure (stearin core) and is connected to an unsaturated lactone ring. In the cardiac glycoside molecule, the sugar moiety is composed of one or more sugars, including D-glucose, D-rhamnose, D-digitoxose, D-cemarase, and others. Cardiotonic effect of cardiac glycosides is associated with aglycone. The glucone part affects the toxicity, activity, solubility of glycosides and their binding to tissues. Cardiac glycosides selectively affect the heart and increase myocardial performance. In this case, the low consumption (saving) of heart activity, but the increase in strength, is due to the following:

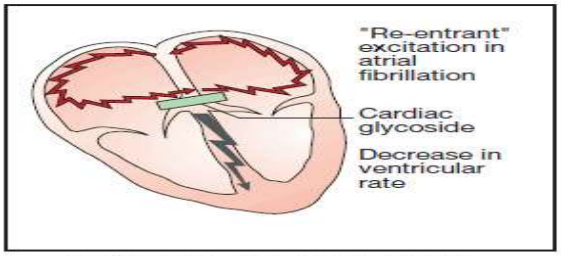
A. Plants containing cardiac glycosides



Therapeutic and toxic effects of cardiac glycosides (CG)



Cardiac glycoside effects on the CNS



Cardiac glycoside effects in atrial fibrillation

Source : Color Atlas of Pharmacology 2nd Ed (Thieme,2000)

increased heart contraction (systole) (positive inotrope) (inos-muscular-tsropos-direction),

- cardiotonic effect, that is, heart contractions are fast and strong (Q-T interval on ECG is shortened). This is due to the direct effect of glycosides on the myocardium. In heart failure (myogenic dilatation), cardiac glycosides significantly

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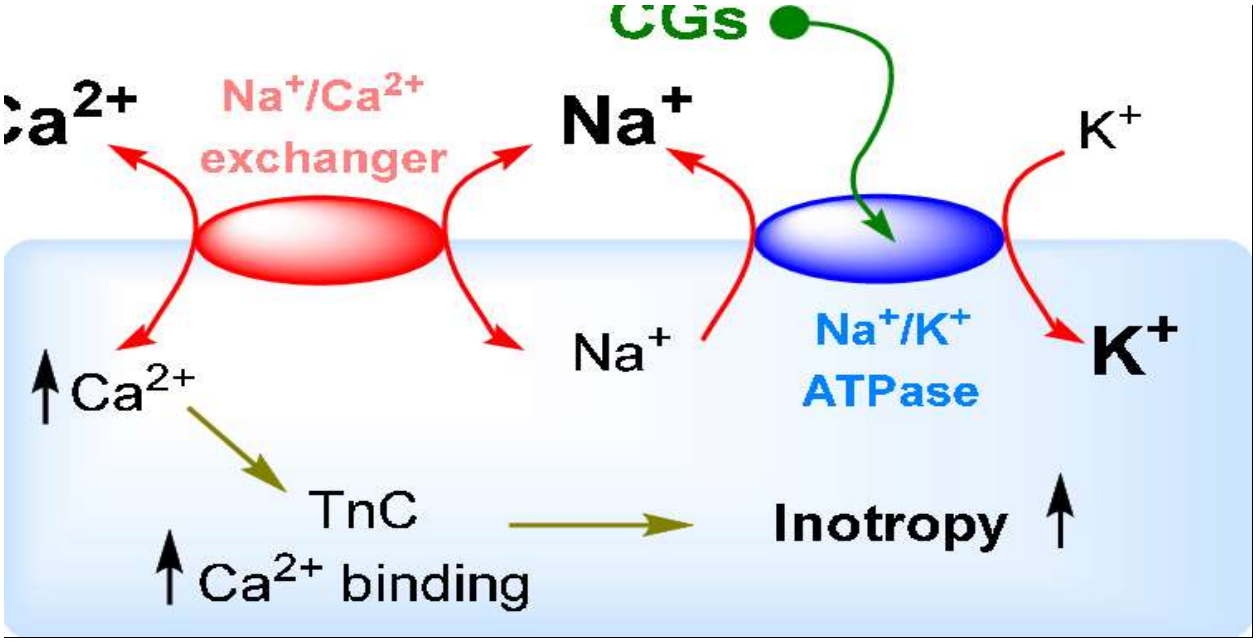
increase the systolic and per minute volume of blood pumped by the heart without increasing the demand for oxygen[1,2,3,4].

- Decreased heart rate (bradycardia-negative chronotropic effect) and prolongation of diastole. As a result, the systole interval becomes longer, and during the prolonged diastole, more blood collects in the ventricles of the heart. This ensures that the heart works most economically: strong systolic contraction alternates with continuous rest, which in turn creates conditions for the restoration of energy potential in the myocardium. In the origin of bradycardia, stimulation of the stray nerve is important (stimulation of baroreceptors in the carotid ball, cardio-cardiac reflexes). Bradycardia is reflected in the prolongation of the R-frequency on the ECG.



- the slowing down of the speed of propagation of excitation impulses (negative dromatrope-dromos-yul) occurs due to the increase in the refractory period of the atrioventricular node (atrioventricular) and the gis bundle (R-R on the ECG). A large dose of cardiac glycosides blocks the atrioventricular node. Therefore, cardiac glycosides have a direct effect on the conduction system of the heart.

- increase in the excitability of the myocardium (positive bathmotrope effect is bathmos-threshold), that is, the re-response of the myocardium to impulses increases, or even weak impulses strongly excite the myocardium. This usually occurs in small doses of glycosides, and large doses reduce the excitability of heart muscles and increase automaticity, thus creating conditions for the development of extrostole. Changes in the excitability and automatism of the myocardium are a consequence of the indirect myotropic effect of cardiac glycosides. The mechanism of cardiotonic action of cardiac glycosides is associated with the reduction of the activity of ATPases involved in the transfer of K+ and Na+ ions through the

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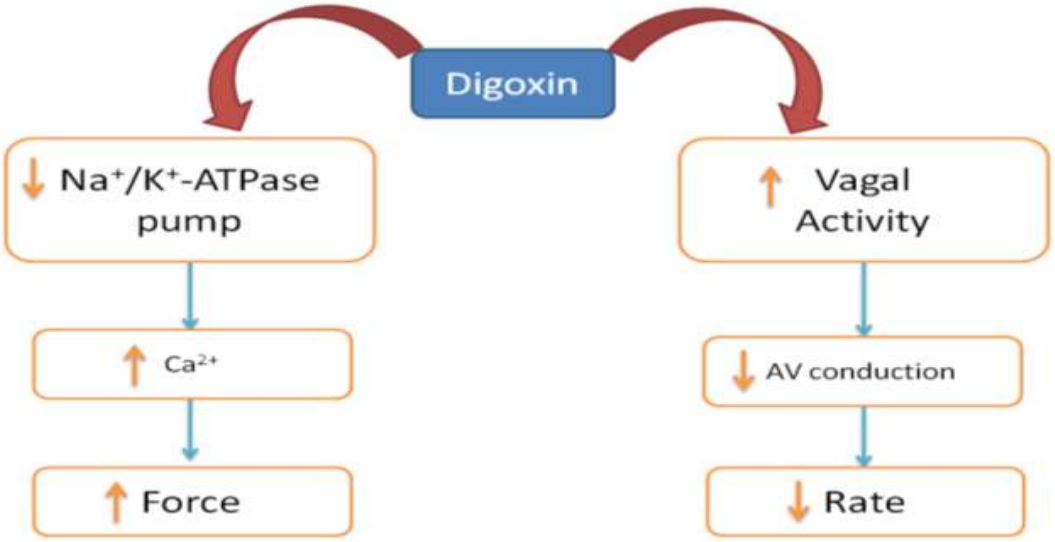
cardiomyocyte membrane. As a result, the amount of Na+ ions inside the cells (intracellular) increases, and the amount of K+ ions decreases. An increase in Na ions increases their exchange with Ca++ ions outside the cell and leads to additional release of Ca++ ions from the sarcoplasmic reticulum. These two processes lead to an increase in sarcolemma-free Ca ++ ions and thereby increase the binding of Ca ++ ions to the tropin complex. As a result, it eliminates the inhibitory effect of tropine on myocardial contractile (actin-mycin) proteins, and fast and strong contraction of myocardium is observed when actin combines with mycin.



The main indication for the use of cardiac glycosides is heart defects in the stage of decompensation (paroc) with venous blood thinning. Myogenic dilatation in this case does not allow to carry out the usual physiological load, that is, the blood coming from the veins of the veins is not transferred to the heart arteries, as a result, the blood in the veins becomes damp, the pressure in the vein increases. Reflex tachycardia develops due to the Bainbridge reflex. Blood circulation slows down, the liver swells, urine production slows down, swelling occurs in the limbs, gas exchange is disturbed (circulatory and tissue hypoxia), skin bruising and shortness of breath are observed.

Under the influence of therapeutic doses of cardiac glycosides, the heart easily copes with physiological loads, and symptoms of hypothermia disappear. Myogenic dilatation decreases, venous pressure decreases, blood circulation accelerates, urine output increases, edema decreases and disappears, including bruising and shortness of breath. the general resistance of peripheral vessels decreases, blood circulation in tissues and their oxygen supply increases. Due to this, the functions of MIT members will be restored. Acceleration of urine excretion ensures that the body gets rid of excess water, which in turn reduces the total volume of blood in circulation and reduces the load on the heart.

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Preparations containing cardiac glycosides differ from each other in the strength of action, the time of development of the effect, its duration and pharmacokinetics. Cardiac glycosides vary greatly in potency. Since it is difficult to identify glycosides in plants by a chemical method, their standardization is mainly carried out by a biological method (that is, in frogs, cats, pigeons and other animals).

The effect of cardiac glycosides depends on the dose and route of administration. Their effect is fully manifested, especially when administered intravenously. In particular, the effects of strophantin and konvalyatoxins develop the fastest - after 1/2-1.5 hours, after 1-5 hours of celanid and digoxin. Digidoxine reaches its peak after 4-12 hours.

The duration of the effect of cardiac glycosides depends on the rate of their breakdown in the body, and their distribution with blood proteins. Biotransformation of cardiac glycosides takes place mainly in the liver (the sugar part is separated, hydroxylated, conjugated with glucuronic acid). Metabolites are excreted in urine and bile. A small amount of digoxin is metabolised almost all of digoxin. Strophanthin is generally metabolized. After absorption from MIT, cardiac glycosides are distributed to various organs, and in the heart, 1% of the administered amount is detected, but when calculated relative to the weight of the organ, it is greater than that of other organs. Therefore, the main direction of the effect of cardiac glycosides is explained by the sensitivity of the myocardium to these drugs.

A certain part of glycosides combines with albumin in blood serum, for example: 30-35% of digoxi, less than 5% of strophanthin, but the pharmacological effect is shown by free (not bound to protein) glycosides, so the effect of digoxi is 5-10 minutes later than that of strophanthin, i.e. It starts in 30 minutes[5,6,7,8,9].

The difference between glycosides is also related to their property of accumulation. The longer the exposure to cardiac glycosides, the greater the material accumulation (material)

Conclusion. Medicinal preparations currently used for the treatment of patients with chronic cardiac failure involve those that reduce the heart load (vasodilators, diuretics, beta-blockers, and angiotensin- converting enzyme (ACE) inhibitors). Cardiotonic drugs with the cAMP-dependent mechanism are unsuitable for long-term administration due to the intensification of metabolic processes and an increase in the oxygen demand of the myocardium and all tissues of the body. For many years, digoxin has remained the only preparation enhancing the efficiency of myocardial performance. The detection of digoxin and ouabain in intact animals has initiated a search for other compounds with cardiotonic activity. The review summarizes current data on the effect exerted on the heart performance

by endogenous compounds, from simple, such as NO and CO, to steroids, fatty acids, polypeptides, and proteins. Controversial questions and problems with the introduction of scientific achievements into clinical practice are discussed. The results obtained by the authors and their colleagues after many years of studies on the cardiotropic properties of serum lipoproteins are also reported. The experimentally established cardiotonic activity of apoprotein A-1, which is accompanied by a decrease in the relative consumption of oxygen, maybe of great interest.

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