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Review Article

# Cardiotropic medicinal products of plant origin. Prospects for use in modern clinical practice

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## Abstract

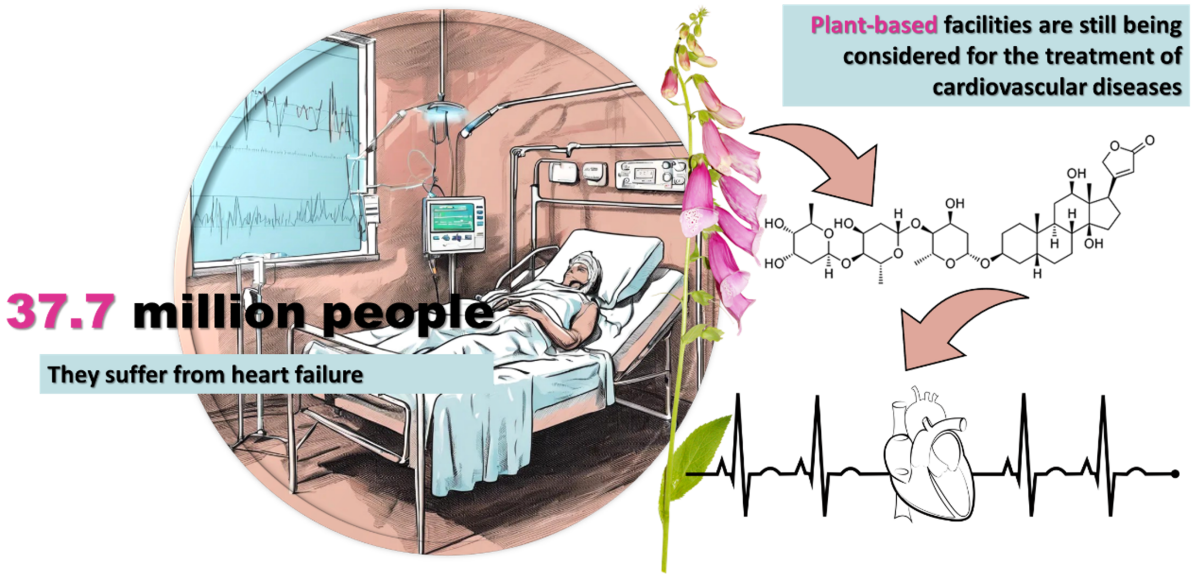
**Introduction:** The aim of the research was to study the current state of use and improvement of the prospects for the using cardiological medicinal products obtained on the basis of medicinal plant raw materials.

**Materials and Methods:** The work used content analysis, monitoring of scientific articles using the databases PubMed, Scopus, Google Scholar, ResearchGate, analysis of the nomenclature of the State Register of Medicines of the Russian Federation (2024) and the Register of Medicines of Russia (2024).

**Results and Discussion:** The study revealed that diseases of the cardiovascular system are some of the most common causes of death among the population, with at least 37.7 million people suffering from varying degrees of heart failure alone. Despite the constant growth of the range of medicines for the treatment of cardiovascular diseases, medicinal plants and preparations based on them, which are more often used in complex therapy, still play an important role in their therapy. In this review, we consider drugs derived from medicinal plant raw materials used for the treatment of heart failure and arrhythmia of various etiologies, as the most serious cardiovascular pathologies.

**Conclusion:** Preparations based on herbal remedies with cardiotropic and antiarrhythmic effects are relevant in the treatment of cardiovascular diseases. Cardiotropic action is characteristic of the group of cardiac glycosides, and antiarrhythmic activity is more pronounced in alkaloids and flavonoid substances. Taking into account the prospects for the use of herbal preparations with cardiotropic effects in the complex therapy of cardiovascular diseases, an important and unsolved problem today remains the problem of their interaction with other drugs, which in the future can be solved by creating artificial intelligence programs that contribute to the formation of optimal prescriptions for a particular patient.

## Graphical abstract




## Keywords

cardiotropic effect; antiarrhythmic effect; cardiac glycosides; alkaloids; side effects; polypharmacotherapy

## Introduction

Currently, diseases of the cardiovascular system are widespread in the world and are the leading cause of death in the population, with at least 37.7 million people suffering from heart failure alone (Shah et al. 2017; Clark and Velasquez 2020).

The annual increase in the number of cases of diagnosed arrhythmia per 1 thousand people in patients aged 45-49 years is 0.4%, and in patients aged 60-64 it has already increasing by 2 times (Schnabel et al. 2015).

Currently, the main risk factors for the development of cardiovascular diseases are considered to be arterial hypertension, dyslipidemia, diabetes mellitus, smoking, inactivity, obesity, and non-changeable biological characteristics such as age, gender, and heredity.

Taking into account the duration of use of drugs used in the treatment of cardiovascular diseases in the presence of chronic conditions in patients, often complicated by combined pathologies in complex therapy, it is still rational to use herbal medicines (Samylina et al. 2012).

Taking into account all the above, the purpose of this review is to study the current state of use and improvement of the prospects for the use of cardiological drugs obtained on the basis of medicinal plant raw materials

## Materials and Methods

The review used content analysis, monitoring of scientific articles using the databases PubMed, Scopus, Cyberleninka, Google Scholar, ResearchGate, analysis of the nomenclature of the State Register of Medicines of the Russian Federation (2024) and the Register of Medicines of Russia (2024).

# Results and Discussions

The State Register of Medicinal Products currently includes more than 40 names of medicinal products of plant origin used in the treatment of cardiovascular diseases.

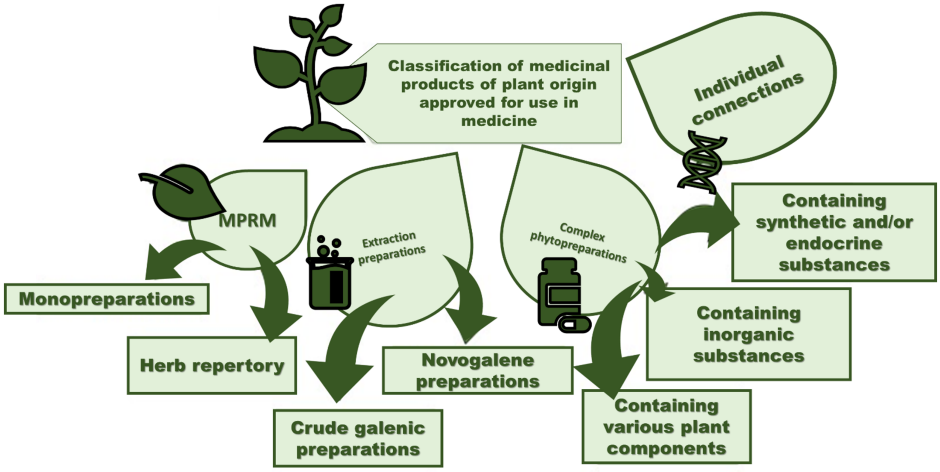



**Figure 1.** Classification of medicinal products of plant origin approved for use in medicine.

Taking into account the requirements of the accepted classification (Kaisheva and Gabrielyan 2016, presented in Figure 1, medicinal plant raw materials and plant-based products used in the treatment of cardiovascular diseases registered in the Russian Federation are presented in Tables 1-4.

**Table 1.** Medicinal plant raw materials approved for the production of cardiotropic products

| Raw material name | Composition | Pharmacological effect | Indications for use | Dosage form |
|---|---|---|---|---|
| Hawthorn fruit – *Fructus crataegi* | Complex of biologically active substances of hawthorn fruits | Antiarrhythmic, improving blood circulation in the vessels of the heart and brain, increasing the contraction of the heart muscle, increasing the sensitivity of the heart to the action of cardiac glycosides | Functional disorders of cardiac activity, angioneuroses, atrial fibrillation, paroxysmal tachycardia, initial forms of hypertension | In packs and filter bags |
| Hawthorn Flowers – *Flores Crataegi* | Complex of biologically active substances of hawthorn flowers | Antiarrhythmic, improving blood circulation in the vessels of the heart and brain, increasing the contraction of the heart muscle, increasing the sensitivity of the heart to the action of cardiac glycosides | Functional disorders of cardiac activity, hypertension, angioneurosis, atrial fibrillation, paroxysmal tachycardia | In packs and briquettes |
| Spring heis – *Herba Adonidis vernalis* | A complex of biologically active substances of Adonis herb, including cardiac glycosides: cymarin, adonitoxin, K-strophanthin-β. 1 g of herb contains 50-66 ICE, 6.3-8.0 KED | Cardiotonic | Mild forms of chronic circulatory insufficiency | Raw materials for obtaining infusion in pharmacies |

**Table 2.** Galenic and new galenic preparations

| Name | Composition | Pharmacological effect | Indications for use | Dosage form |
|---|---|---|---|---|
| Adonisid – *Adonisidum* | New galenic preparation from the herb *Adonis vernalis* (*Ranunculaceae*). 1 ml contains 23_27 LED or 2.7-3.5 KED | Cardiotonic | Chronic circulatory insufficiency of the I and II degrees, autonomic neuroses | In flasks of 15 mL |
| Dry Adonizide – *Adonisidum siccum* | Extract from sping herb Adonis. 1 g contains 20000 LED or 2083 ED, which corresponds to 670 mL of liquid adoniside. | Cardiotonic | Chronic circulatory insufficiency of the I and II degrees, autonomic neuroses | Tablets of 0.00075 g, in a package of 30 pcs. |
| Hawthorn fruit tincture | Alcoholic extract from the fruits of blood-red hawthorn (*Crataegus* sanguinea Pall.), prickly hawthorn (*C.oxyacantha Pojark*.) and other species of hawthorn of the Rosaceae family | Antiarrhythmic, improving blood circulation in the vessels of the heart and brain, increasing the contraction of the heart muscle, increasing the sensitivity of the heart to the action of cardiac glycosides | Functional disorders of cardiac activity, hypertension, angioneuroses, atrial fibrillation, paroxysmal tachycardia | in bottles of 10,15,20,25 mL |
| Hawthorn tincture – *Tinctura Crataegi* | Alcoholic extract from the flowers of blood-red hawthorn (*Crataegus sanguinea Pall.*), prickly hawthorn (*C. oxyacantha* Pojark.) and other species of hawthorn of the Rosaceae family | Antiarrhythmic, improving blood circulation in the vessels of the heart and brain, increasing the contraction of the heart muscle, increasing the sensitivity of the heart to the action of cardiac glycosides | Functional disorders of cardiac activity, hypertension, angioneuroses, atrial fibrillation, paroxysmal tachycardia | In bottles of 25, 50 and 100 mL |
| Hawthorn extract liquid | Extract from the fruits of blood-red hawthorn (*Crataegus sanguinea Pall.),* prickly hawthorn (*C. oxyacantha* Pojark.) and other species of hawthorn of the Rosaceae family | Antiarrhythmic, improving blood circulation in the vessels of the heart and brain, increasing the contraction of the heart muscle, increasing the sensitivity of the heart to the action of cardiac glycosides | Functional disorders of cardiac activity, hypertension, angioneurosis, atrial fibrillation, paroxysmal tachycardia | In bottles of 25 mL |
| Corglycone Lily-of-the-Valley Leaf Glycoside | Preparation containing the sum of cardiac glycosides from the flowers, leaves and herbs of lily-of-the-valley, lily-of-the- valley of Transcaucasia or Lily-of-the-Convallaria keiskei (Liliaceae) | Cardiotonic | Acute and chronic circulatory failure, cardiac decompensation, paroxysmal tachycardia attacks | Solution in ampoules |
| Lily-of-the-valley tincture | Tincture of lily-of- the-valley herb sem. Lily and other species containing cardiac glycosides | Cardiotonic | Cardioneurosis, cardiac disorders (without signs of decompensation) | Bottles of 25 mL |
| — Erysimum diffusum liquid extract | Liquid extract from Erysimi herb Sam. Cruciferous | Cardiotonic | Cardioneurosis, cardiac disorders (without signs of decompensation) | Bottles of 25 mL |

**Table 3.** Complex preparations

| Name | Composition | Pharmacological effect | Indications for use | Dosage form |
|---|---|---|---|---|
| Adonis-bromine | Dry redflower extract 0.25, potassium bromide 0.25 | Cardiotonic, sedative | Neuroses and mild forms of circulatory insufficiency | Coated blets |
| Valocordin | Combined preparation containing ethylbromoisovalerianate 2.00 g, phenobarbital 2.00, mint oil 0.14, hop oil 0.02 55 vol% ethanol up to 100 ml | Sedative, antispasmodic | Neuroses, spasms of coronary vessels, tachycardia, early stages of hypertension | In dropper bottles of 15 and 25 mL |
| Valocormid | A combined drug containing 10 mL of valerian and lily-of-the-valley tinctures, 5 mL of sodium bromide 4 g. belladonna tinctures. menthol 0.25 g, water distilled to 30 mL | Sedative, antispasmodic | Cardioneuroses accompanied by bradycardia | In bottles of 30 mL |
| Valoserdin | 100 g of the drug includes ethyl ester of a-bromoisovaleric acid 2 g, phenobarital 2 g, peppermint oil 0.14 g, oregano oil 0.02 g | Sedative, antispasmodic | Neuroses, cardialgia, arterial hypertension, spasms of coronary vessels, tachycardia | In dropper bottles of 15 mL |
| Green drops - Guttae Zelenini | Lily-of-the-valley tinctures and valerian tinctures 10 mL each, belladonna tinctures 5 mL, menthol 0.2 g. | Sedative, antispasmodic | Cardioneurosis accompanied by bradycardia | In bottles of 25 mL |
| Cardiovalenum | Complex preparation containing jaundice juice 17.2 mL, concentrated adonizide 30.3 mL, tincture of fresh rhizomes with valerian roots 48.6 mL, hawthorn extract 2.2 mL, camphor 0.4 g, sodium bromide 2 g, ethyl alcohol 95% 1.6 mL, chlorobutpnol hydrate 0.25 g. | Cardiotonic, sedative | Rheumatic heart defects, cardiosclerosis with heart failure and circulatory disorders I IIA | In bottles of 15, 20, 25 mL |
| Cardiplant | 1 capsule contains 80 mg of dry extracts of hawthorn leaves and flowers, 15 mg of procyanidin oligomer | Cardiotonic, adaptogenic | Heart failure (initial stage) | Capsules |
| Corvalol | Combined preparation containing ethyl ester of a-bromoisovaleric acid 20 g, phenobarbital 18.26 g, caustic soda 3.15 g, peppermint oil 1.42 g, ethyl alcohol 580 ml, purified water 420 ml | Sedative, antispasmodic | Spasms of coronary vessels, tachycardia, early stages of hypertension. | In dropper bottles of 15 and 25 mL |
| Lily-of-the-valley drops -Tinctura Convallariae et Tinctura Valerianae | Lily-of-the-valley tinctures and valerian tinctures in equal proportions | Cardiotonic | Cardioneurosis, cardiac disorders (without signs of decompensation) | In bottles of 30 mL |
| Lily-of-the-valley motherwort drops -Tinctura Convallariae et Tinctura Leonuri | Lily-of-the-valley tinctures and motherwort tinctures in equal proportions | Cardiotonic, Sedative | Cardioneurosis, cardiac disorders (without signs of decompensation) | In bottles of 25 mL |
| Lily-of-the-valley drops with adoniside-Tinctura Convallariae et Tinctura Valerianae Adonisido | Lily-of-the-valley tinctures. tinctures of valerian and adoniside in equal proportions | Cardiotonic | Cardioneurosis, cardiac disorders (without signs of decompensation) | In bottles of 30 mL |

**Table 4.** Individual compounds used in the treatment of cardiovascular diseases

| Name | Composition | Pharmacological effect | Indications for use | Dosage form |
|---|---|---|---|---|
| Allapinin – Allapininum | The alkaloid lappaconitin (with an admixture of concomitant alkaloids isolated from the herb aconite (*Aconitum leucostonum* Worosch.) *Ranunculaceae Family* | Antiarrhythmic | Supraventricular and ventricular extrasystoles, atrial fibrillation and flutter, paroxysmal tachycardia, arrhythmias secondary to myocardial infarction | Tablets of 0.025 g, 0.5% solution in ampoules of 2 mL |
| Digoxin | Cardiac glycoside isolated from the leaves of *Digitalis lanata* Ehrh. fam. *Scrophulariaceae* | Cardiotonic | Chronic heart failure, supraventicular tachyarrhythmias (especially atrial fibrillation) | Tablets of 0.25 and 0.1 mg, 0.025% solution in ampoules |
| Raunatin | Sum of alkaloids from the roots of Rauwolfia serpentine of the *Apocynaceae Family* | Hypotensive. Antiarrhythmic. Sedative | Hypertension | Film-coated tablets |

There is no doubt that the most important group of herbal remedies used in the treatment of cardiovascular diseases for many decades has been cardiac glycosides (cardiosteroids), which are still used today. In therapeutic doses, cardiac glycosides affect all myocardial functions, increasing excitability and contractility, reducing sinus automatism and conduction. The main indications for the prescription of cardiac glycosides are chronic heart failure, tachyarrhythmias – paroxysmal atrial fibrillation, and paroxysmal supraventricular tachycardia. The mechanism of action of cardiac glycosides (Gurevich and Gavrilin 2014) and their characteristic pharmacological effects are shown in the figures below.

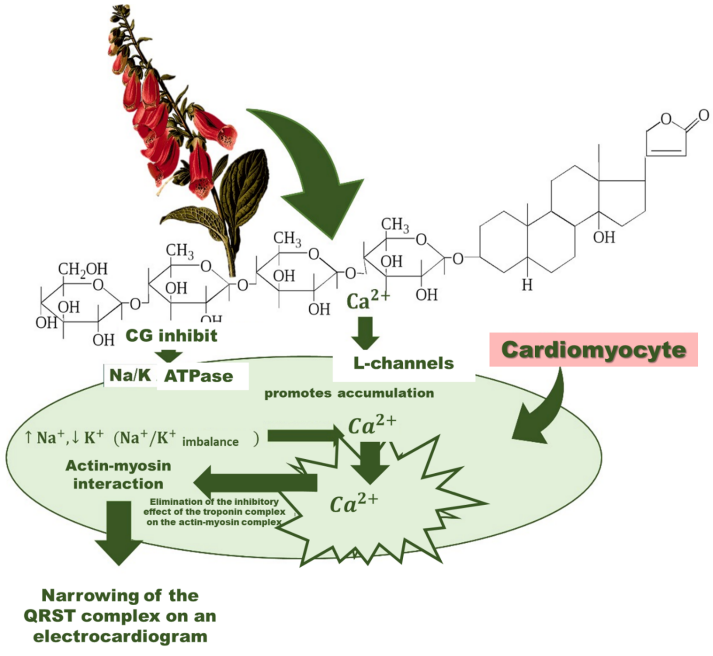



**Figure 2.** Mechanism of action of cardiosteroids

These substances have a positive inotropic effect. It blocks the t-transport Na/K-ATPASE, resulting in an increase in the Na content in the cardiomyocyte, which leads to the opening of Ca channels and the entry of Ca-into cardiomyocytes. Excess Na causes activation of sodium/calcium metabolism, which accelerates the release of Ca from the SPR and increases the content of calcium ions, which, in turn, increases the strength of myocardial contraction. An increase in the strength and speed of myocardial contraction occurs by a mechanism other than the Frank-Starling mechanism (it does not depend on a degree of pre-stretching of the myocardium). Systole becomes shorter and more energy-efficient.

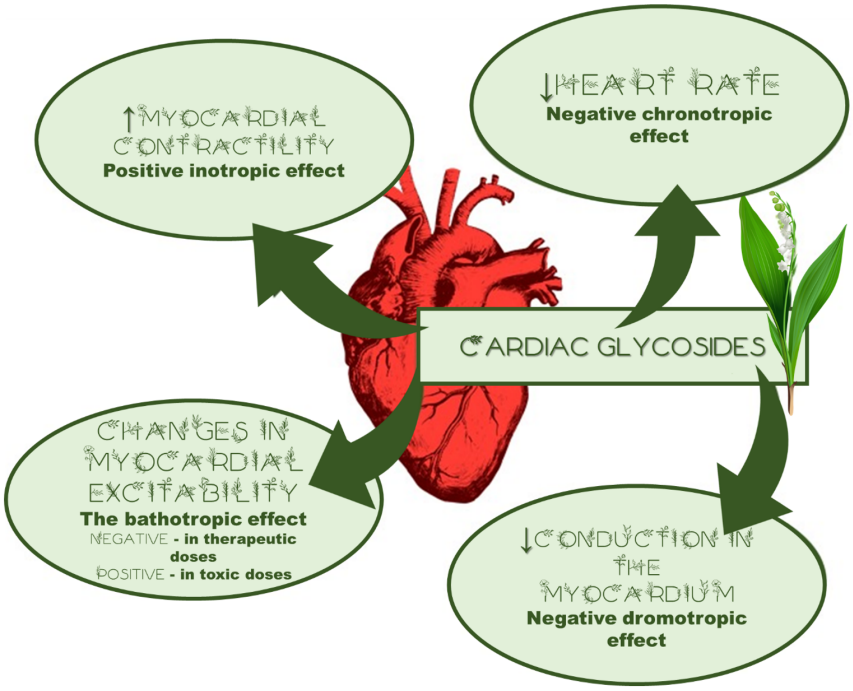



**Figure 3.** Main pharmacological effects of cardiac glycosides (Gurevich and Gavrilin 2014).

Despite the fact that the basic principles of therapy using cardiac glycosides have been known for a long time, some features are still revealed in the course of clinical observation of patients. Thus, it was found that when digoxin is prescribed in low doses (0.25, mg/day) in patients with synapse rhythm, the drug develops mainly a neuromodulatory effect, causing a decrease in the activity of the sympathoadrenal system (Hood et al. 2014). Currently, clinicians are ambivalent about prescribing cardiosteroids, for example, concerns are raised about the safety of using digoxin in atrial fibrillation (AF) (Moiseev 2011; Elayi et al. 2020).

Dr. Chris J. Kapelios found that digoxin use is statistically characterized by lower mortality/morbidity rates in patients with atrial fibrillation, but higher rates in patients without AF.

According to the literature, the group of cardiovascular diseases, the treatment of which is considered difficult, includes cardiac arrhythmias.

It should be noted that the improvement of treatment standards in this area, as well as the growth in the range of antiarrhythmic drugs, paradoxically leads to a noticeable increase in complicated conditions (Nedostup 2008).

Historically, one of the first drugs for the treatment of arrhythmia was the alkaloid quinine isolated from the bark of the quinine tree and its right-rotating isomer quinidine, whose antiarrhythmic activity is associated with the blockade of sodium channels and slowing the rate of depolarization of the action potential. Despite the rejection of the drug in many countries due to the risk of ventricular arrhythmias and a number of other side effects, there is evidence that quinidine can be considered as the only oral drug that consistently shows effectiveness in preventing arrhythmias and reducing storms in patients with Brugada syndrome (Stelios et al. 2013). Later, the alkaloid Rauvólfia

serpentína aimalin was introduced into medical practice, which is active in relieving paroxysms of AF, supraventricular tachycardia, ventricular tachycardia, as well as in the complex therapy of extrasystole. Aimalin is used in a pharmacological test to diagnose Brugada syndrome (BrS) and identify patients at higher risk of developing life-threatening arrhythmias and sudden death as a result of cardiac arrest. (Monasky et al. 2021a, 2021b).

For the prevention of tachyarrhythmias in patients with Wolff-Parkinson-White syndrome syndrome (WPW), as well as with moderate bradycardia, allapinin is prescribed, which is a hydrobromide of lappaconitine, and an alkaloid contained in the grass of white Aconite (*Aconitum leucostomum Worosch*.), Ranunculaceae (Buttercup) Family. The antiarrhythmic effect of allapinin is realized by inhibiting potential-dependent sodium channels sensitive to tetrodotoxin (Chuikin and Shtanko 2013). Relatively few non-randomized studies of allapinin have demonstrated its effectiveness in the prevention of AF paroxysms (Syrkin et al. 2010).

Unfortunately, this drug is registered only in the Russian Federation and is not included in international recommendations, which makes it a reserve drug. In order to assess the safety of using lappaconitine preparations, further full-fledged study of its pharmacokinetics is necessary, and research in this area is underway (Archakova et al. 2021). To correct a number of drawbacks of the drug, such as high toxicity (Gutser et al. 1997; Archakova et al. 2021), problems with calculating the therapeutic dose due to its possible accumulation in organs and tissues, nonlinear pharmacokinetics (Mishra et al. 2022), and a number of side effects (Liu et al. 2022), studies are being conducted aimed at immobilizing allapinin in order to prolong its release process (Sun et al. 2016; Salikhov et al. 2024).

Salikhov et al. (2024) showed that the complex of allapinin with monoammonium salt of glycyrrhizic acid is characterized by reduced toxicity and improved antiarrhythmic activity. Prolonging the release of the alkaloid, which reduces the residual side effects, is achieved by encapsulating the allapinin complex with a monoammonium salt of glycyrizzic acid in polyelectrolyte microcapsules based on polyallylamine and polystyrene sulfonate.

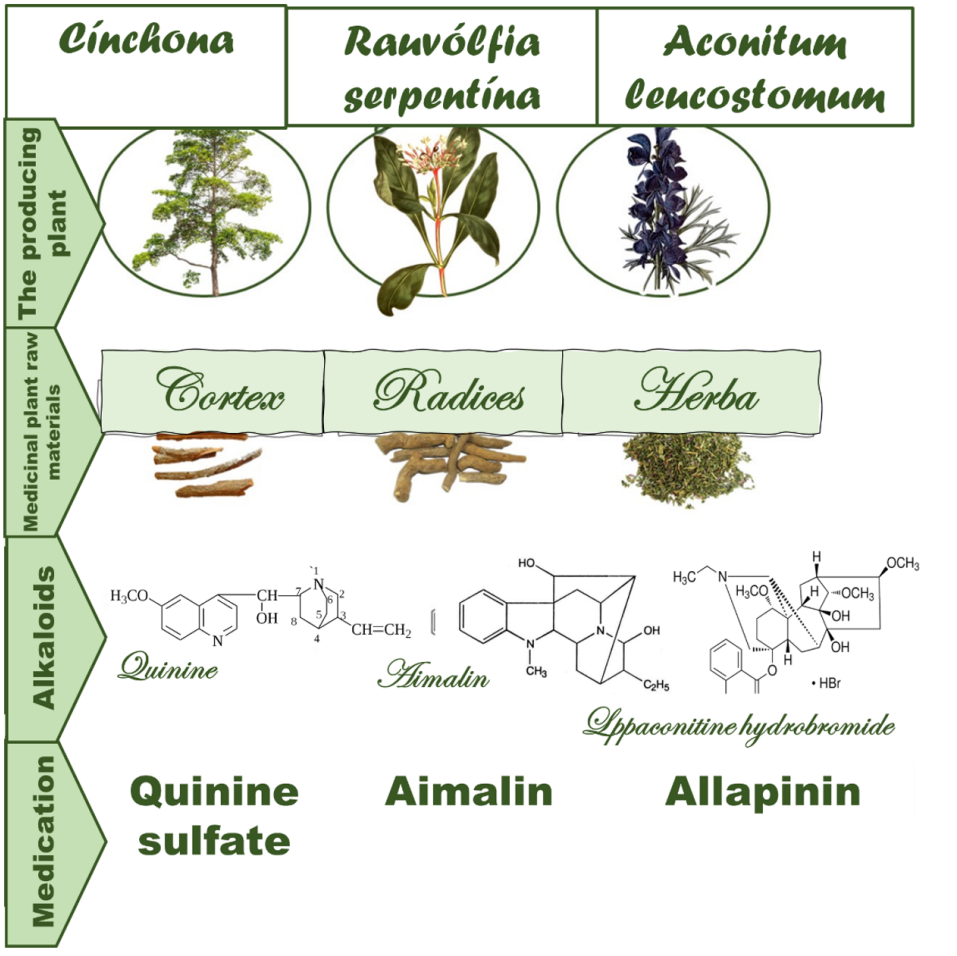



**Figure 4.** Alkaloids with antiarrhythmic activity.

Antiarrhythmic action is characteristic of hawthorn flowers and fruits, which also exhibit coronary-expanding and hypotensive effects (Wang et al. 2013; Kurkin et al. 2017; Orha 2018; Nazhand et al. 2020).

The antiarrhythmic effect of extracts from hawthorn raw materials, which manifests itself in the form of shortening the duration of arrhythmia and reducing its severity in comparison with the control group, as well as the presence of antifibrillator activity, has been repeatedly experimentally proven both on the aconitin and calcium chloride models (Trofimova et al. 2011).

The data of clinical observation in dynamics showed that the addition of dry hawthorn extract to the standard therapy of chronic heart failure, which was standardized according to hyperoside, has a positive effect on the rhythmic activity of the heart, suppressing initially increased ventricular ectopic activity and preventing the persistence and development of new ventricular extrasystoles of high gradations, which significantly optimizes therapeutic measures and improves the prognosis in patients with chronic heart failure, especially in cases where the use of antiarrhythmic drugs recommended by the standard treatment is contraindicated for some reason (Trofimova et al. 2011; Miller et al. 2019; Elayi et al. 2020; Doschitsin and Tarzimanova 2022).

The antiarrhythmic activity of hawthorn raw materials is associated with the presence of flavonoids quercitin and hyperoside in the raw material (Orhan 2018). It was experimentally established that quercitin, rutin, and (+)-catechin have an antiarrhythmic effect on aconitin-induced arrhythmia, while the pharmacological effect, according to the researchers, may be due to the modulation of the activity of Na+and CaCa2+channels in cardiomyocytes (Lazuko et al. 2009; Trofimova et al. 2011; Chuikin and Shtanko 2013; Khushmatov et al. 2015).

Further search for medicinal plants with cardiotropic effects is associated with the study of promising sources of flavonoids. Thus, embinin, a flavone C-glycoside, was isolated from the aboveground part of Iris lactea, the inotropic effect of which was compared with digoxin in a Langendorff model of perfusion of an isolated rat heart. (Ivkin et al. 2018).

There is also experimental evidence in the scientific literature of the use of "non-traditional" antiarrhythmic drugs, such as omega-3-polyunsaturated fatty acids in the prevention and complex therapy of arrhythmias (Moiseev 2011). When studying the Omacor preparation, as well as a number of vegetable oils, the effect of polyunsaturated fatty acids on the transport of sodium and calcium ions was established by blocking fast potential-dependent sodium channels and reducing the intake of calcium ions. The effect of omega-3 polyunsaturated fatty acids on the expression of connexins in the myocardium has also been revealed, which contributes to the achievement of an antiarrhythmic effect. (Gaikova 2010).

Thus, there is a significant potential for obtaining drugs for treatment and prevention based on medicinal plant raw materials for use in the complex therapy of cardiovascular diseases.

When considering the role of herbal preparations in the treatment of cardiovascular diseases, it is necessary to strictly distinguish between drugs used in pure form (digoxin, lappaconitine) and those included in the list of vital and essential drugs (VED) and extracts, infusions, tinctures, etc. medicinal forms of various plants that are not always standardized by specific ingredients (Bhat and Bhat 2021; Dinan et al. 2021; Liu et al. 2022; Nawrot et al. 2022; Saqib et al. 2022; Xulu et al. 2022; Barratt et al. 2023; Joubert et al. 2023; Gorchakova et al. 2024; Macwan et al. 2024). Since many herbal medicines do not always have proven clinical benefits, even minor side effects may not be acceptable for patients with cardiovascular diseases (Boyko et al. 2017).

The solution of the problem of prescribing herbal cardiotonic drugs in the complex therapy of cardiovascular diseases, taking into account the factor of possible interaction with other drugs of complex therapy, is possible using artificial intelligence (Fersht et al. 2020; Chen et al. 2023; Garcia et al. 2024).

# Conclusion

Medicinal plant raw materials and drugs based on it, which have cardiotropic and antiarrhythmic effects, are still relevant tools in the treatment of cardiovascular diseases. Cardiotropic action is characteristic of the group of cardiac glycosides, and antiarrhythmic action is shown by the alkaloids quinidine, aimalin and allapinin, which exhibit a significant range of side effects, but are still used in medical practice for certain heart pathologies. A mild antiarrhythmic effect is characteristic of hawthorn raw materials

of various types, whose biologically active substances, especially flavonoids, provide not only the main cardiotropic effect, but also such effects as anti-inflammatory, antispasmodic, diuretic, etc., which contributes to the optimal achievement of the therapeutic effect in complex therapy.

Considering the future prospects for the use of herbal preparations with cardiotropic effects in the complex therapy of cardiovascular diseases, an important and unsolved problem today remains the problem of their interaction with other drugs, which in the future can be solved by creating artificial intelligence programs that contribute to the formation of optimal prescriptions for a particular patient.

# Additional information

### Conflict of interest

The authors have declared that no competing interests exist.

### Acknowledgements

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### Data availability

All of the data that support the findings of this study are available in the main text.

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