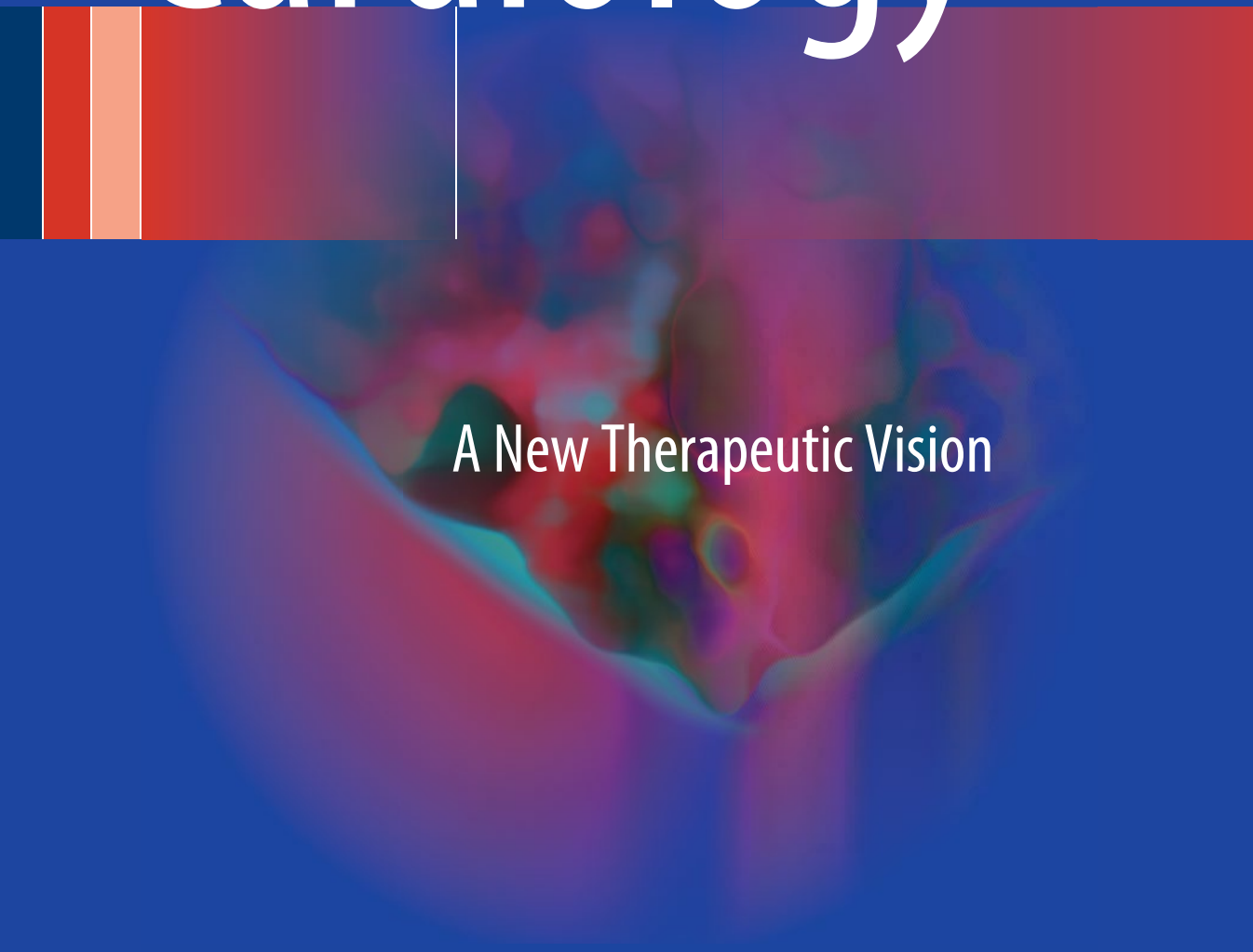
Massimo Fioranelli
Editor

Integrative Cardiology

A New Therapeutic Vision



Springer

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A New Therapeutic Vision

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Foreword

I've always been a little afraid of cardiology as a medical specialty. It always seemed to me a too delicate and, at the same time, "explosive" subject to be addressed by complementary medicine. Therefore, it is something to be handled with care, otherwise risking the health of a vital organ, and that of the patient.

It is a "dangerous" topic in which the general practitioner does not intervene if not carrying out the wishes of the specialist, as the complementary medicine practitioner does most of the time, often renouncing from the start to provide possible indications for natural substances useful in improving the clinical situation of patients with heart problems.

We often intervene in circulatory disorders and, in particular, in changes in blood pressure so frequently now, even when people are in their prime, but when it comes to real heart problems we proceed with caution, often fearfully, avoiding interference with conventional therapies prescribed to the patient as much as possible.

Yet, the heart is not only the vital organ par excellence, but it is also central to the holistic vision, which is the basis for the practice of complementary medicine.

On this issue, I allow myself to digress briefly before commenting. It is precisely the vital organs, with their function and physiology, that express more clearly the correspondence between the inner man, or the psychic and spiritual sphere of the person, and the outer man, the physical body with its organs and systems. Some organs and functions are related to the emotional side of the person, such as the heart and liver, and, on the other hand, some organs are connected to personal aspects, such as the digestive system (the stomach and intestines) and kidneys. The stomach, in fact, receives food and the intestine assimilates it, absorbing what is good for the body and rejecting what is dangerous or toxic, just as the intellect introjects what it considers true and eliminates the false.

The heart and circulatory system carry oxygen and nourishment to the tissues and they do not choose or select anything, holding for themselves only the minimum necessary for subsistence, distributing to the tissues as required according to their needs. What the heart receives from the pulmonary circulation is then donated. For this reason, we speak of a "person of heart" and the reference is a mother's love, unconditional love. For this correspondence, emotions such as love, hate, fear, or courage are felt in the heart and

therefore, the health of this organ; its integrity becomes essential for the continuation of life.

To take care of the heart, and all vital organs, is to take care of the whole person and coincides with the preservation of life. This concept emerges strongly when reading this book as a whole and in many of its parts.

Another important aspect of this book consists of the quality and the great expertise of each of the authors, starting with the curator Massimo Fioranelli. In this case, the reader can not only enjoy the fruits of experience gained in the field over decades of clinical activity, but also receive the teaching of true masters, each in their own discipline. The editorial proposal is therefore more of a real professional training manual than a book about unconventional therapies in cardiology.

We live in an age where information in all fields, but especially on health issues, come from a thousand different sources, primarily via social networks. None or very few of these are scientifically verified or evaluated based on the experience of competent professionals.

How then to judge the appropriateness of the treatment choices proposed? How to decide which path to take in the plethora of news that is often based on a desire for intellectual provocation or a need for glamour rather than on evidence for effectiveness?

Another aspect is the content of this text, which is based on three fundamental elements: the authority and expertise of the authors, the completeness of the information, and an updated bibliography.

We have already mentioned the authority of the masters, but equally important in the evaluation of text quality is the completeness of the information provided. These not only concern the range of possible interventions with the different complementary therapies—acupuncture, homeopathy, homotoxicology, herbal medicine, medicinal mushrooms, in addition to nutrition and meditation—but also the complex relationships between the cardiovascular system and the endocrine system, or the microbiota, interpreting the function of this system in the context of psycho-neuro-endocrine immunology (PNEI).

Moreover, it is not only a theoretical text. The clear aim is to train doctors and provide useful tools for their therapeutic intervention in extremely complex pathological situations such as cardiovascular disease. Thus, valuable indications for the prevention and treatment of dyslipidemia, hypertension, but also of arrhythmias, coronary heart disease, heart failure and even the cardiac protection that is so important in cancer disease and its treatment, particularly in chemotherapy.

Obviously, this text is not opposed to conventional therapy but represents its natural complement. This does not mean, however, that, for some situations and settings, it may not be the first choice of treatment for the cardiologist.

How many are, in fact, the situations of suffering for which conventional medicine does not provide satisfactory answers, because it is ineffective in that specific case, or because it is poorly tolerated owing to the adverse effects produced by standard drugs?

As this book demonstrates, and especially from now on, the lack of integration of complementary therapies in cardiology in appropriate situations and settings can only be explained by the lack of knowledge and the resistance to change of most conservative conventional medicine practitioners.

In the future, this resistance will certainly be overcome, but it is very important that the future begins now, immediately. Not as a matter of principle, but namely the affirmation of the freedom of therapeutic choice, but for the patient's benefit.

Finally, I would like to sincerely acknowledge all the authors who participated in this project, which is important for our world and marks a point of no return for the development of a higher level of integration of complementary medicine into mainstream medicine.

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Foreword

A book can synthesize a shared knowledge or open a new territory in a scientific field.

The book *Integrative Cardiology* by Massimo Fioranelli encompasses both aspects.

Integrative medicine is a combination of conventional medicine and traditional healing modalities, not commonly taught in Western medical schools. Nutrition, low-dose therapy, herbal medicine, metabolic cardiology, acupuncture, psycho-neuro-endocrine immunology (PNEI), immunomodulation through the intervention on microbioma, and attention to mind–body influences cover many aspects of integrative cardiology.

Many medical conditions, such as hypertension, coronary artery disease, congestive heart failure, arrhythmias, and cardiac surgery can benefit from this natural approach.

This book translates this holistic strategy into the treatment of cardiovascular diseases.

The main merit of the Editor is to have collected the experience of eminent scholars in the field of integrative medicine and to highlight a new pathway in the treatment of cardiovascular diseases. This book is something very new in the publishing field that will be helpful to practitioners seeking to translate various bodies of knowledge into the clinical field.

Along with traditional therapy, in accordance with the current guidelines, I believe that there is space in the clinical field to integrate conventional medical treatment with nonconventional therapies.

My best wishes to Massimo Fioranelli for this new achievement in a field of medicine that deserves larger diffusion into the scientific community.

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Contents

Part I

The Basis of Integration

Herbal Medicine in Cardiology

1

Ivo Bianchi

All over the world, herbs are currently used in the treatment of cardiovascular disease. Ample evidence shows that heart diseases can be prevented or even reversed with traditional medicine using ethnobotanical remedies. Diet and lifestyle are a fundamental part of a strategy that is effective in the fight again atherosclerosis, the underlying cause of most cases of heart disease. There are few but very effective and well-studied herbs and herbal derivatives useful for pathological heart conditions; we describe the most important, some of which have been or are currently used in conventional medical practice [1–4]:

1. *Allium sativum* (garlic)
2. *Arnica montana*
3. *Astragalus membranaceus*
4. *Camelia sinensis* (green tea)
5. *Commiphora mukul* (guggul)
6. *Convallaria majalis*
7. *Crataegus oxyacantha* (hawthorn)
8. *Cytisus scoparius*
9. *Digitalis purpurea*
10. *Gelsemium sempervirens* (Carolina yellow jasmine)
11. *Ginkgo biloba*
12. *Hibiscus sabdariffa* (roselle)
13. *Leonurus cardiaca* (motherwort)
14. Nattokinase (fermented soybeans)
15. *Plectranthus barbatus* (forskolin)
16. *Rauvolfia serpentina*
17. *Ruscus aculeatus* (butcher's broom)
18. *Salvia miltiorrhiza* (danshen)
19. *Scilla maritima*
20. *Strophanthus kombe*
21. *Terminalia arjuna*
22. *Viscum album*

1.1 Primary Cardiological Herbs

1. *Arnica montana*
2. *Convallaria majalis*
3. *Crataegus oxyacantha* (hawthorn)
4. *Cytisus scoparius*
5. *Digitalis purpurea*
6. *Scilla maritima*
7. *Strophanthus kombe*
8. *Terminalia arjuna*

1.2 Metabolic Herbs

1. *Allium sativum* (garlic)
2. *Astragalus*
3. *Camelia sinensis* (green tea)

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4. *Commiphora mukul* (guggul)
5. Nattokinase (fermented soybeans)

1.3 Nervous Sedation and Neurovegetative Herbs

1. *Crataegus oxyacantha* (hawthorn)
2. *Gelsemium sempervirens* (Carolina yellow jasmine)
3. *Leonurus cardiaca* (motherwort)
4. *Plectranthus barbatus* (forskolin)
5. *Rauvolfia serpentina*
6. *Salvia miltiorrhiza* (danshen)

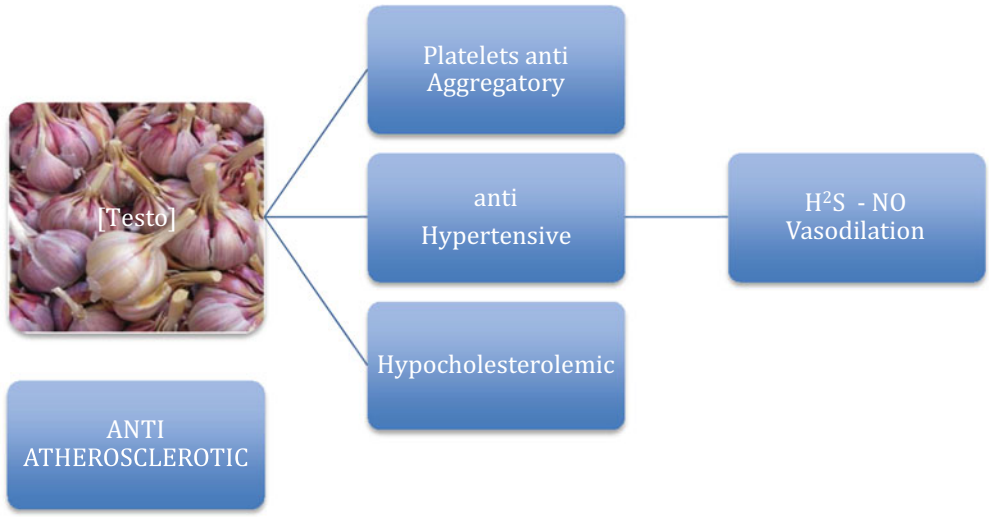
1.4 *Allium sativum* (Garlic)

Garlic is a perennial odiferous bulb containing 10–20 cloves, is native to the northern hemisphere, and belongs to the Liliaceae family. Its virtues were described in inscriptions on the Great Pyramid of Cheops. The pharmacologically active compound is allicin, which also gives crushed garlic its characteristic pungent odor (Fig. 1.1).

Allium sativum exerts **antiaggregatory effects** by inhibiting the adenosine diphosphate pathway; its mechanisms of action are comparable with those of conventional drugs [5]. Treatment with garlic tablets standardized to deliver 0.6% allicin, the active ingredient of garlic, produced a significantly greater **reduction in total cholesterol** and low-density lipoprotein (LDL) cholesterol and a moderate increase in high-density lipoprotein (HDL) cholesterol compared with placebo, whereas it has no significant effect on serum triglyceride levels.

Garlic supplements have shown promise in the treatment of uncontrolled **hypertension**, lowering blood pressure (BP) by about 10 mmHg systolic and 8 mmHg diastolic, similar to standard BP medication. Modern garlic extract, which contains S-allylcysteine as the bioactive sulfur compound, is particularly standardizable and highly tolerable, with little or no known harmful interaction when taken with other BP-reducing or blood-thinning medications. Garlic-derived polysulfides stimulate the production of the vascular hydrogen sulfide (H_2S) and enhance the regulation of endothelial nitric oxide (NO), which induces **smooth muscle cell relaxation**, vasodilation, and BP reduction. Normally, several dietary and genetic factors influence the efficiency of the H_2S and NO signaling pathways and may contribute to the development of hypertension. Sulfur deficiency may play a part in the etiology of hypertension and could be alleviated with supplementation of organosulfur compounds derived from garlic. The available data suggest that garlic might be of value in either the prevention or treatment of atherosclerotic diseases [6–12].

Fig. 1.1 *Allium sativum*



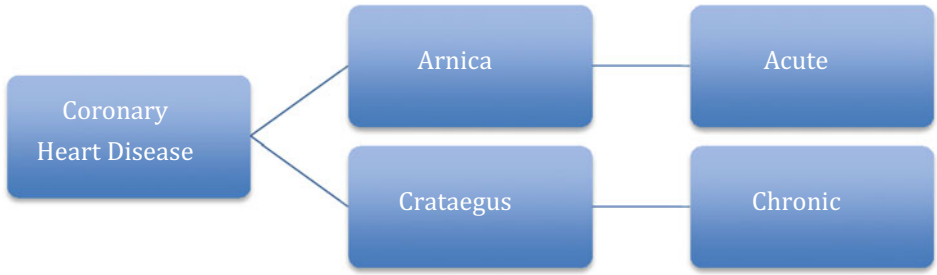
1.5 *Arnica montana*

Arnica is a perennial herb native to the mountainous regions of Europe and southern Russia and belong to the Asteraceae family. *Arnica* flowers contain helenanolide-type sesquiterpene lactones, flavonoids (isoquercetin, astragalin, etc.), volatile oils, and coumarins. Goethe recommended it for coronary heart disease and acute treatment of angina pectoris. Although *Arnica* can improve coronary circulation in much the same manner as *Crataegus*, it has a more rapid onset of action. Therefore, *Arnica* is preferred for **acute** and *Crataegus* for long-term treatment of **coronary heart disease** [7–9, 13, 14] (Fig. 1.2).

Fig. 1.2 *Arnica montana*

1.6 *Astragalus membranaceus*

Astragalus is a small shrub native to temperate regions of the northern hemisphere and belongs to the Fabaceae family. Use of *Astragalus* roots is very old and well known in traditional Chinese medicine, employed principally as a tonic and for the treatment of diabetes and kidney diseases. *Astragalus* root contains a series of cycloartane triterpene glycosides named astragalosides I to VII. Several saponins based on the oleanane skeleton have also been reported. *Astragalus* saponins demonstrated a positive **inotropic action**, improving walking distance and quality of life in patients with chronic heart failure. Oral administration of extracts of the root countered the rise in blood pressure and plasma renin activity in a hypertensive model. Astragaloside IV improved **homocysteine-**induced endothelial dysfunction in rat aortic rings via antioxidant activity and exhibited vasodilatory effects. Oral administration of *Astragalus* has an **inhibitory effect on left ventricular hypertrophy** induced



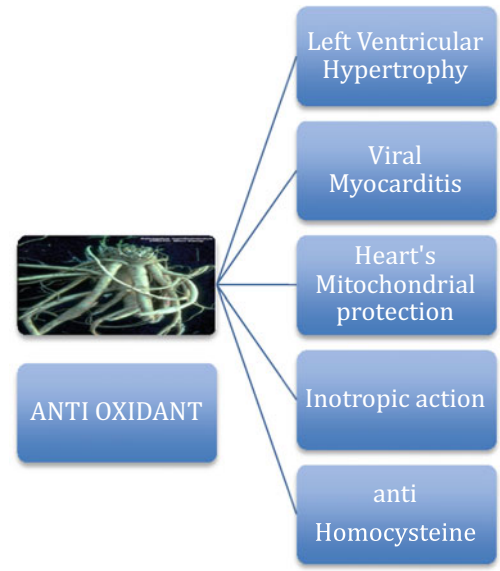
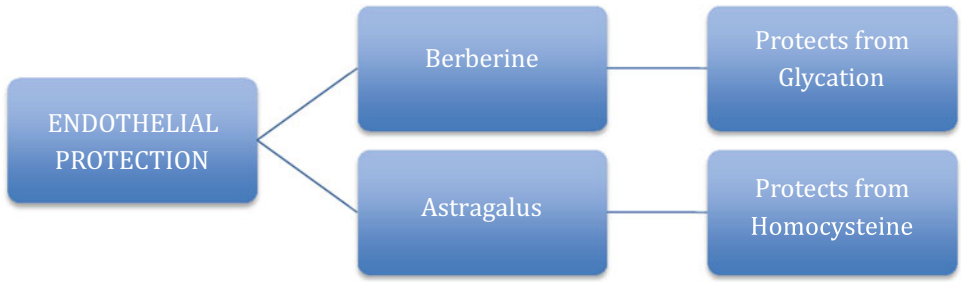


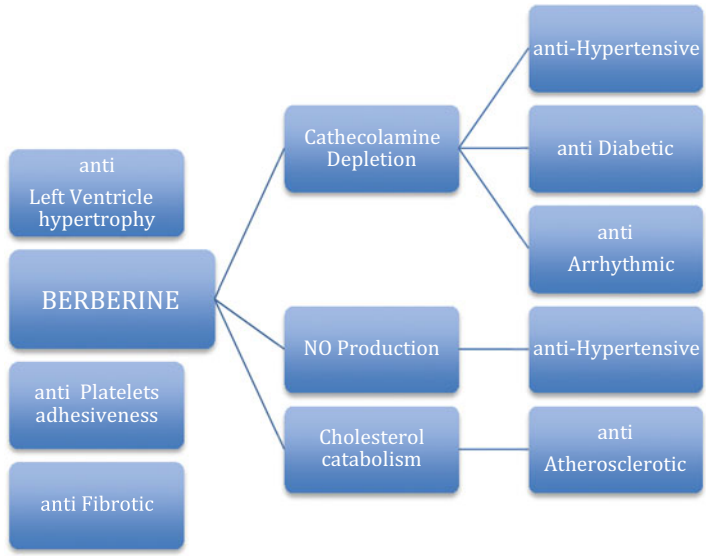
Fig. 1.3 *Astragalus membranaceus*

by pressure overload in rats. After acute myocardial infarction, there is an anti-free radical effect and amelioration of left ventricular function. *Astragalus* increases the survival rate and improves some abnormal electrophysiological parameters in **acute viral myocarditis**. Routine therapy combined with oral administration of *Astragalus* in these patients significantly enhanced immune parameters compared with patients receiving routine therapy alone. **Heart mitochondria** are also **protected** by toxic insult experimentally produced with daunorubicin [13, 15–18] (Fig. 1.3).

1.7 Berberine

Berberine is a quaternary ammonium salt derived from protoberberine, and belongs to the isoquinoline alkaloid family. This molecule is found in the roots, rhizomes, stems, and bark of plants such as *Berberis aquifolium* and *vulgaris*, *Hydrastis canadensis*, *Xanthorhiza simplicissima*, *Tinospora cordifolia*, and *Eschscholzia californica*. A detailed review concluded that berberine possesses a range of cardiovascular properties, including **positive inotropic, negative chronotropic, antiarrhythmic, and vasodilatory activities**. In experiments, berberine prevented the development of pressure overload induced by **left ventricular hypertrophy** in vivo after aortic banding. Oral administration of 10 mg/kg decreased left ventricular, **diastolic pressure,** and **plasma levels of adrenaline and noradrenaline**. In a rat model of hypertension, 5–10 mg/kg of berberine improved cardiac contractility and inhibited left ventricular remodeling and global **myocardial fibrosis**. Such effects might be





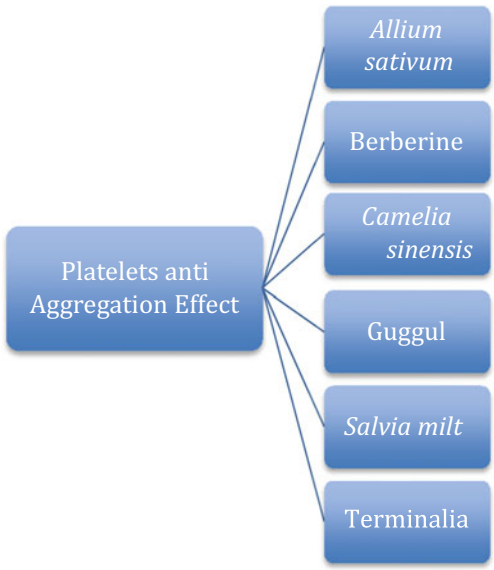
partially associated with increased nitric oxide and cAMP in left ventricular tissue. Berberine **inhibits platelet aggregation and adhesiveness** and levels of thromboxane B2, and these could be the important factors behind the **anti-ischemic activity** of berberine.

Recent research focused on the **cholesterol-lowering activity** of berberine mediated by the upregulation of hepatic LDL receptor expression and inhibition of cholesterol and triglyceride synthesis. Oral administration of berberine to hyperlipidemic hamsters for 10 days resulted in 26 and 42% decreases in total cholesterol and LDL cholesterol respectively. Human studies seem to demonstrate that berberine might **benefit the integrity and function of vascular endothelial cells** by improving protective mechanisms: increasing the **production of NO** and enhancing resistance to hyperglycemia-induced injury [7, 8, 19].

1.8 *Camelia sinensis* (Green Tea)

Green tea is produced from leaves of *Camellia sinensis*, an evergreen shrub native to Eastern Asia from Teaceae family. Green tea is the dried leaf component, whereas black tea is produced by a complex wilting and fermentation process. Tea leaves contain varying amounts of polyphenols (most of which are catechins) in addition to smaller quantities of caffeine, theanine, theobromine, theophylline, and phenolic acids. Evidence from clinical trials suggests that green tea might play a role in **metabolic syndrome** because it may have an impact on body weight, glucose homeostasis, and other cardiovascular risk factors. Green tea helps to reduce the oxidation of low-density lipoproteins, **improving cholesterol profiles**, **reducing**

Fig. 1.4 *Camelia sinensis*



platelet aggregation, and finally antagonizing atherosclerosis [7, 8, 19–22] (Fig. 1.4).

1.9 *Commiphora mukul* (Guggul)

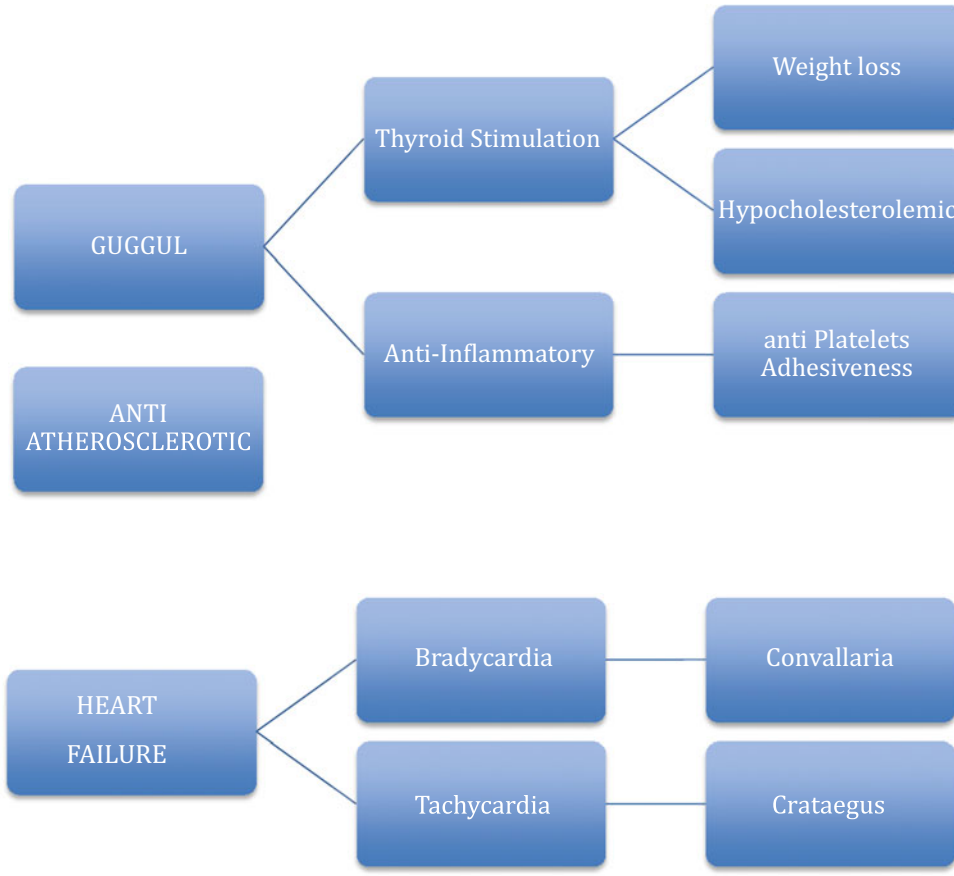
Guggul is a small shrub that is widely distributed in India and adjacent dry regions from the Burseraceae family. The gum has been used in Indian medicine for centuries as a cardiac tonic, and as a weight-reducing and anti-inflammatory agent.

The dry gum resin obtained from the bark of the tree **downregulates the expression of all inflammatory mediators**. Research shows that the resin of the guggul tree contains ketonic steroid compounds called guggulsterones and these have the ability to reduce the cholesterol-containing plaque. Guggul also helps to increase the metabolic rate of the body and thus is useful for **weight loss**.

Guggul, in animal experiments, was as effective as phenylbutazone and ibuprofen in acute and chronic inflammation. A study in 200 patients with **ischemic heart disease** demonstrated an improvement on electrocardiography and a decrease in episodes of dyspnea and chest pain. Guggul increases fibrinolytic activity and **decreases platelet adhesiveness,** but the most interesting activity is the improvement of **hypothyroid conditions** and an increase in triiodothyronine levels. In most studies, the use of guggul leads to a **reduction in total cholesterol** and HDL. Globally, guggul is considered an important natural remedy for preventing coronary heart disease [23, 24].

1.10 *Convallaria majalis* (Lily of the Valley)

Lily of the valley is an herbaceous perennial plant native to the forests of Northern Hemisphere of the Asparagaceae family (previously classified in the Liliaceae family). The aerial parts contain cardenolides and glycosides whose potency is not comparable to that of *Digitalis* and is also weaker than that of *Scilla*. Hence *Convallaria* is mainly used in patients with **mild heart failure**. The main advantage of *Convallaria* is its rapid onset of effects and the only remote risk of accumulation of glycosides. Furthermore, the glycosides in *Convallaria* do not affect the nerve impulse conduction system of the heart; thus, there is no risk of arrhythmias. This plant is therefore very well suited for the treatment of heart failure associated with



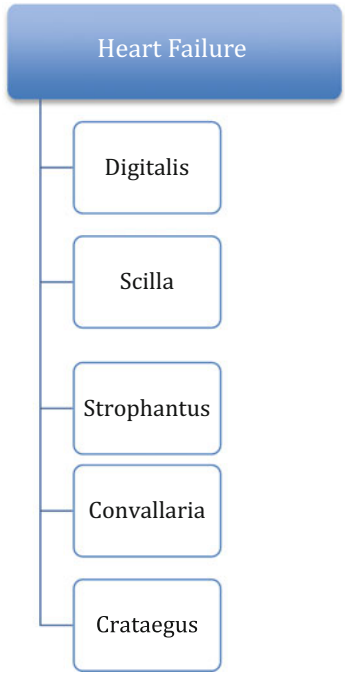
bradycardia. *Crataegus* complements *Convallaria* in the case of an "aging heart." We can classify lily of the valley as a **cardiosedative remedy**, well suited to the treatment of functional heart disorders [25].

1.11 *Crataegus oxyacantha* (Hawthorn)

Hawthorn is a spiny tree native to temperate regions in the Northern Hemisphere belonging to Rosaceae family. The use of this herb for the treatment of heart problems dates back to 1800, but the ancients probably knew already the virtues of this plant that they not casually named *Crataegus*: in the Greek language *krátos* means strength and this suggests that this plant might give the body energy through the enhancement of heart activity. Today, hawthorn is an official drug in the pharmacopoeias of Brazil, China, Czechoslovakia, France, Germany, Hungary, Russia, and Switzerland. As a measure of its incredible popularity, it is an ingredient in 213 commercial European herbal formulas, mostly for cardiovascular system.

For many years, it has been suggested that hawthorn could be used as an alternative therapy for various cardiovascular diseases, such as **angina, hypertension, hyperlipidemia, arrhythmia, and initial congestive heart failure**. Besides the **antioxidant**, **positive inotropic**, **anti-inflammatory**, and **anticardiac remodeling effects** and other **cardiovascular protective effects** of the hawthorn, active ingredients have been demonstrated in various in vivo and in vitro experiments.

The clinical efficacy of hawthorn can therefore no longer be disputed, but this plant still has



not found its rightful place in modern cardiology. Therapy shows effects after 7–8 weeks, but the pharmacologically measurable effects on the myocardium and coronary flow volume persist for several weeks, even after the administration of *Crataegus* has been discontinued.

The constituents of hawthorn are:

1. Active **dehydrocatechins** of the flavan type, also classified as oligomeric procyanidins, responsible for the **effects on coronary circulation**
2. Monomeric **flavonoids** (hyperoside, quercetin, vitexin rhamnoside), which are important for **myocardial metabolism**
3. Biogenic amines
4. Triterpene acids
5. Sterols
6. Purines
7. Catechin tannins

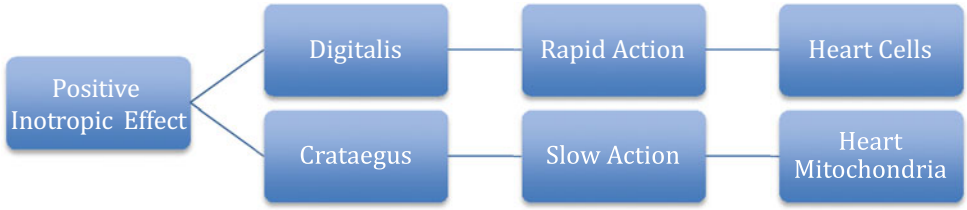
In any case, the research confirms that the overall effect of the extract as a whole is more significant than that of its individual constituents.

Many experimental studies in animals have confirmed that *Crataegus* increases coronary blood flow, inhibiting cAMP. Several studies also documented stimulation of myocardial contractility, through a different mechanism to that of *Digitalis*, indirectly improving myocardial energy metabolism through mitochondrial activation. This also explains why hawthorn requires a much longer period than *Digitalis* to take effect and why myocardial reactivity must exist so that the herbal drug can take effect.

It has been verified pharmacologically that *Crataegus* regulates heart rhythm and standard extracts of the plant demonstrated positive chronotropic and dromotropic effects in addition to negative bathmotropic effects. *Crataegus* increases myocardial tolerance to oxygen deficiency. An increase in cardiac volume, a reduction of peripheral vascular resistance, and an increase in cardiac performance have also been documented in various studies on animals.

Summarizing *Crataegus*:

1. Increases **coronary** and myocardial **circulation**
2. Improves myocardial contractility, mostly stimulating and **protecting mitochondria** from lipid peroxidative damage, preventing left ventricular hypertrophy and most functional and structural problems of the heart.
3. Exerts an eurythmic effect on certain types of electrical heart instabilities. *Crataegus* extract prolongs action potential duration and delays recovery. The effect is similar to the action of class III **antiarrhythmic drugs**, with a significant decrease in the total number of ventricular ectopic beats, mainly by reducing the number of beats, i.e., ventricular tachycardia.
4. Increases **myocardial tolerance to oxygen deficiency**
5. Has positive **inotropic activity**: the force of contraction of the left ventricle is clearly enhanced.
6. Has an **anti-inflammatory effect**, downregulating COX-2, TNF-α, IL-1β, and

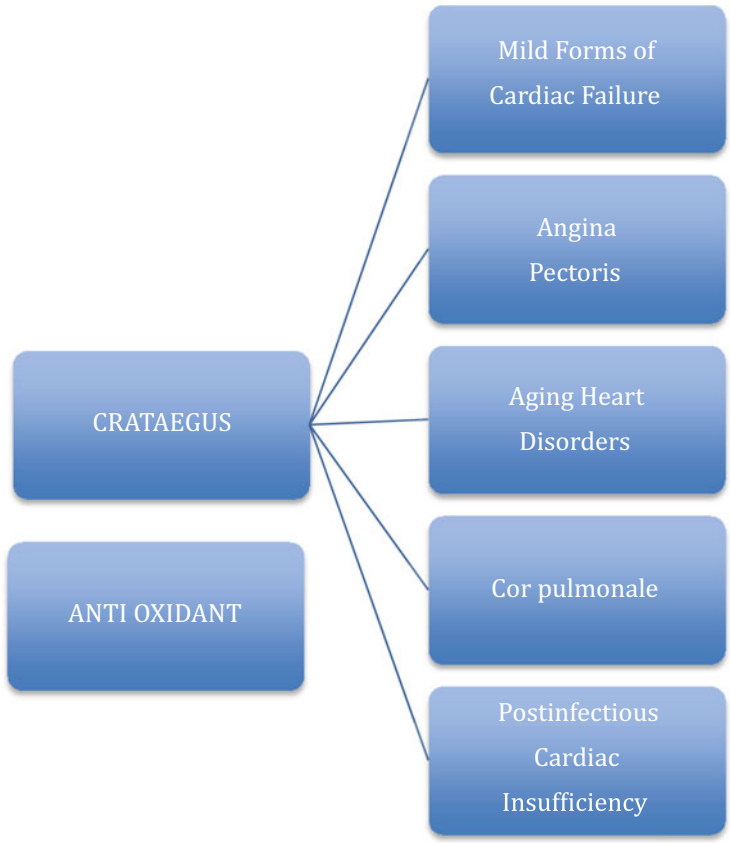


IL-6 expression, in addition to reducing nitrative stress and oxidative stress, and thus decreasing apoptosis of myocardial cells.

7. Has an **anti-platelet aggregation effect** at low doses, as indicated by the increase in bleeding time, decrease in platelet aggregation, and reduction in serum levels of thromboxane.
8. Is effective in **lowering blood lipid levels** and significantly reducing the ratio between low-density and high lipoprotein. It also increases bile acid excretion and depresses hepatic cholesterol by upregulating hepatic LDL receptors with a consequently greater influx of plasma cholesterol into the liver.
9. Significantly restores the **activity of antioxidant** enzymes such as superoxide dismutase, catalase, glutathione peroxidase, and glutathione.
10. Antagonizes **left ventricular hypertrophy** related to hypertension
11. Has a vasodilatory action on both coronary and peripheral circulation that may be mediated by the inhibition of angiotensin-converting enzyme (ACE).
12. Effectively protects against endothelial barrier dysfunction by its action on key determinants of endothelial permeability (adherens junctions, actin cytoskeleton, and contractile apparatus). Past and ongoing studies also suggest that the chronic intake of *Crataegus* might have prevented aging-related endothelial dysfunction by reducing the prostanoid-mediated contractile responses.
13. **Decreases heart rate** by sinus node suppression and progressive atrio-ventricular blockade owing to direct stimulation of the muscarinic receptor M2 and possible blockade of β-receptors
14. Significantly reduces the **deterioration of contractile function** and infarct size in rat myocardium exposed to prolonged ischemia and reperfusion. Besides, it showed an evident effect against reperfusion arrhythmias by reducing the average prevalence of malignant arrhythmias (VF + flutter) and the average prevalence of ventricular tachycardia (VT). Moreover, it prevents the isoproterenol-induced decrease in antioxidant enzyme activity .
15. Has **hypotensive action as it enhances nitric oxide** release
16. Is a support to conventional treatment because of its **positive inotropic, antiarrhythmic, and vasodilator properties**, and may provide additional benefit in symptom control (fatigue, listlessness, dyspnea under strain, pretibial edema, and rapid exhaustion), frequency of nocturnal urination, and exercise tolerance (distance walked and number of stairs ascended without fatigue).
17. Reduces **sudden cardiac death** by 39.7% and is safe for patients with heart failure. The maximal tolerated workload during bicycle exercise showed that typical heart failure symptoms as rated by the patients were reduced to a greater extent [7, 8, 13, 19, 23, 26–28].

1.12 *Cytisus scoparius* (Broom)

Cytisus is deciduous bush native to central and southern Europe and belongs to the Fabaceae family. The main alkaloid in the floral parts of the plant is sparteine, classified as an antiarrhythmic drug. Sparteine inhibits the transport of sodium ions across the cell membrane, thereby reducing overstimulation of the nerve impulse conduction system of the heart. Pathological change in the impulse arising in the atrium is



also normalized. Unlike *Digitalis* glycosides, sparteine does not have a positive inotropic effect, but still extends diastole. Broom is contraindicated in hypertension and should also be avoided in pregnancy because it increases the tonicity of the gravid uterus. The indications for *Cytisus* are **primarily functional cardiac arrhythmias mostly of the tachycardiac type, in combination with a tendency toward low blood pressure** [29].

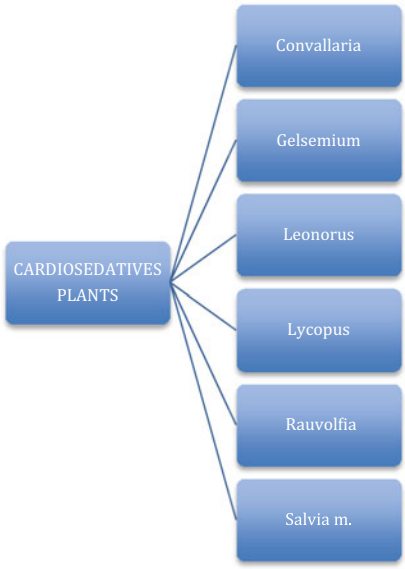
1.13 *Digitalis purpurea*

Digitalis is a biennial plant native to Western Europe, but is found today as an ornamental plant through the world. It belongs to the Scrophulariaceae family. In Europe, its use for the treatment of heart failure has been traced back to the 10th century. In 1875, digitoxin was isolated from *Digitalis* and since then this plant has been recognized by all major pharmacopeias.

Cardiac glycosides from the leaves of *Digitalis* possess **positive inotropic effects** owing to inhibition of sodium–potassium adenosine triphosphatase; this allows calcium to accumulate in myocytes leading to the enhancement of cardiac contractility. *Digitalis* causes some **antiarrhythmic activity**, but the therapeutic index is quite narrow and it can only induce arrhythmias at higher dosages [7, 8, 19, 30].

1.14 *Gelsemium sempervirens* (Yellow Jasmine)

Gelsemium is a climbing plant native to Mexico and Guatemala and belongs to Loganiaceae family. The rootstock is used to make a tincture containing indole alkaloids. *Gelsemium* reduces



the overstimulation of the sympathetic nervous system and calms the overtonicized vascular system. This plant can be classified as **cardiosedative**. Unlike broom, it does not have a specific effect on the nerve impulse conduction system; nevertheless, it does have a calming effect on the heart in patients with **extrasystoles** and **functional heart disorders** [31, 32].

1.15 *Ginkgo biloba*

Ginkgo can be traced back more than 200 million years to fossils of the Permian geological period and is the sole survivor of the Ginkgoaceae family. Individual trees may live as long as 1,000 years and grow to a height of approximately 40 m. The main medicinal constituents are found in the leaves and include flavonoids and several terpene trilactones unique to the family. There is a seasonal variation in the content of active compounds in leaves, with the highest amounts in autumn. *Ginkgo* is traditionally used to treat **peripheral arterial occlusion** and has been demonstrated to be useful for **improving walking distances** for patients with **intermittent claudication**. *Ginkgo* extracts are used in China to treat **short-term ischemic stroke** and may be useful to shorten general and neurological recovery [7, 8, 19, 33–36].

1.16 *Hibiscus sabdariffa* (Roselle)

Hibiscus is an annual herb native to Central and West Africa and belongs to the Malvaceae family. It has a long history of traditional use for many conditions, including hypertension, liver disease, cancer, constipation, and fever. Its flowers contain various polyphenols, including anthocyanins, proanthocyanidins, flavonoids, and other pigments. Aqueous preparations of *Hibiscus* showed a dose-dependent **decreased effect on systolic** and **diastolic pressure** comparable with that of captopril and lisinopril. A **natriuretic effect** was also observed in various studies [37].

1.17 *Leonorus cardiaca* (Motherwort)

Leonorus cardiaca is an herbaceous perennial plant native to Central Asia and South East Europe and belongs to the Lamiaceae (mint) family. It contains alkaloids, bitter glycosides, and bufenolides. In particular, the alkaloid leonurine is a mild vasodilator with a relaxant effect on smooth muscles. *Leonorus* is indicated in patients with vegetative and functional heart complaints, and like valerian seems to have a primarily **sedative effect**. It must usually be used for several months to achieve adequate treatment results [38].

1.18 *Lycopus virginicus/europeus*

Lycopus virginicus/europeus is a herbaceous perennial plant growing in the wet habitats of North America and Europe. It belongs to the Lamiaceae (mint) family. Phenolic compounds, lithospermic, rosarinic, chlorogenic, and caffeic acid have been identified in both European and American plants. This herb is mainly used for hyperthyroidism and related symptoms. Extracts of the plant **reduce prolactin levels** and may be related to the suppression of TSH. Its thyrostatic activity, due to the inhibition of iodine transport and the release of preformed thyroid hormones, can be useful for tachycardia in patients with even slight hyperfunction of the thyroid gland [13, 39].

1.19 Nattokinase (Fermented Soybeans)

Nattokinase is an **enzyme** produced when the bacterium *Bacillus subtilis* natto is added to boiled soybeans of the Fabaceae family. The fermentation of soybeans is common in traditional Asian culinary practice and natto is a traditional Japanese food that has been consumed for at least 1,000 years as breakfast with rice, on toast, or as sushi. It has traditionally been used to treat heart conditions.

This enzyme catalyzes the cleavage of protein to polypeptides and is inactivated in acid conditions, and tablets of nattokinase must be have an enteric coating. It increases the activity of tissue plasminogen activator and promotes the conversion of plasminogen to plasmin, with a resultant increase in clot and thrombolysis. This enzyme has also been reported to degrade amyloid fibrils. Dietary supplements with nattokinase **suppress intimal thickening**, **modulate the lysis of mural thrombi,** and **improve arterial blood flow**. In dogs, its oral administration completely dissolves induced clots from major leg veins within 5 h. Nattokinase, in combination with pycnogenol, taken 2 h before a long flight, and every 2 h during the flight can reduce thrombotic events and edema [40–42].

1.20 *Plectranthus barbatus* (Forskolin)

This plant, also named forskolin or Indian coleus, is a perennial herb native to East Africa and the tropical regions of India and belongs to the Lamiaceae (mints) family. The main constituents are essential oils (mono and sesquiterpenes) and diterpenoids (at least 70), the most active compounds. The principal mechanism by which this plant exerts its activity is by stimulating adenylate cyclase (AC), thereby increasing cellular cAMP, which is involved in glycogen and lipid metabolism and in the relaxation of smooth muscles.

Positive inotropic action (related to the activation of AC), **augments coronary blood flow**, **increases the heart rate, decreases blood pressure**, and has been demonstrated in animal and human tests [43]. A concentration-dependent **inhibition of vascular contractility** and a **vasodilatory action** was shown in rats and rabbits. Owing to poor water solubility and low oral bioavailability, the clinical use of this plant is limited. A derived water-soluble molecule (colforsin) has been developed and is currently used in Japan (Adehl).

In addition to **smooth muscle relaxation,** forskolin exerts **strong activity on inflammatory mediators** and is often used to treat asthma due to histamine, inflammatory interleukins, and leukotrienes.

1.21 *Rauvolfia serpentina* (Indian Snakeroot)

Rauvolfia is a flowering plant native to the Indian Subcontinent and East Asia of the Apocynaceae family. It was mentioned in Sanskrit writings from around 200 B.C. There are reports of its use in a wide variety of diseases, but it was primarily used as a universal sedative. The drug is derived from the root containing more than 50 different alkaloids belonging to the monoterpenoid indole family. It exerts **sympatholytic action** via **depletion of norepinephrine** uptake into the vesicles of the noradrenergic nerve endings. As a result, reserpine has **antihypertensive and sedative properties**. Ajmaline, another constituent of the root, is known to have **anti-arrhythmic action** for membrane stabilization. *Rauvolfia* also has antimicrobial, antifungal, anti-inflammatory, anticholinergic, and antiproliferative actions. It is one of the 50 fundamental herbs of traditional Chinese medicine. Contraindications are related to vagotonic stimulation, which can result in depression, ulcers, and impotence [7, 8, 13, 44, 45].

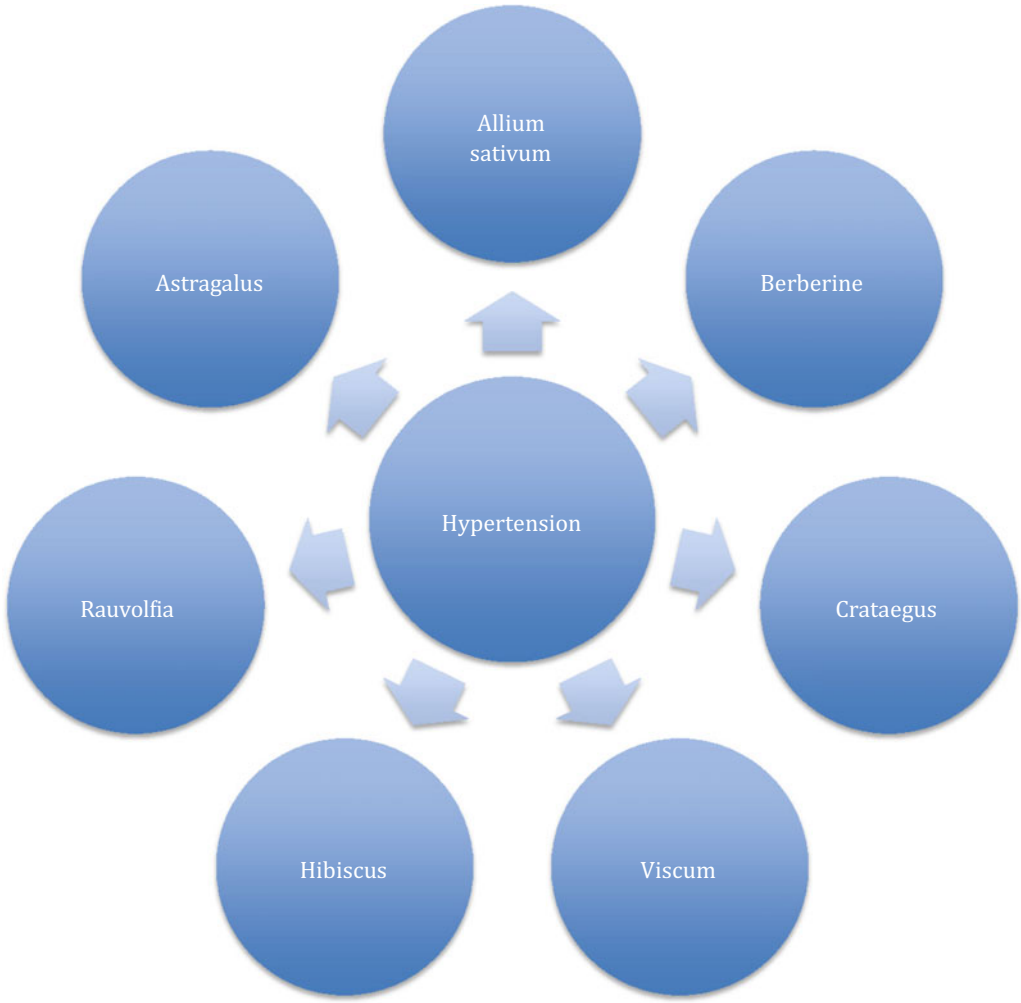
1.22 *Ruscus aculeatus* (Butcher's Broom)

Ruscus is a low-growing common evergreen shrub that is widely distributed in Mediterranean regions and belongs to the Liliaceae family. It has a long history of use as a laxative, **diuretic,** and phlebotherapeutic agent. Early investigations during the 1950s indicated that extracts of the rhizomes of butcher's broom could induce **vasoconstriction** and therefore may be of use in the treatment of circulatory diseases. *Ruscus* is used to treat **orthostatic hypotension** and does not cause supine hypertension like other related drug therapies [46–48].

1.23 *Salvia miltiorrhiza* (Danshen)

Danshen is a perennial herb native to China's hills and belongs to the Lamiaceae (mints) family. It is considered one of the most important traditional Chinese medicines and has widespread use in Asian countries. It was the first traditional Chinese medicine to pass phase 2 clinical trials for cardiovascular indications in the USA. More than 50 compounds have been identified in danshen, mainly of two classes:

1. Lipophilic diterpenes, named tanshinones, with antibacterial, antioxidant, and antineoplastic effects.



2. Polar phenolic compounds, mostly caffeic acid derivates with antioxidant and anticoagulant effects.

Many studies report the extensive use of this plant as a standard treatment for **acute ischemic stroke** in China. The injury to the vasculature following ischemia and reperfusion may be ameliorated by treatment with this plant. In vitro data suggest that this type of *Salvia* inhibits vascular smooth muscle cell proliferation and reduces intimal hyperplasia. Animal experiments demonstrated **increased cerebral microcirculation**. After ischemic stroke, the use of danshen improved neurological deficits. Animal data showed the cardioprotective activity of danshen with regard to infarct size and mortality. A meta-analysis of trials among patients with angina demonstrated an improvement in symptoms and electrocardiogram parameters compared with nitrates. Efficacy in the treatment of myocardial infarction may be due to **sedative, antioxidant, and antiplatelet effects** in addition to **improved coronary microcirculation**. Various studies demonstrated a reduction in cholesterol, triglycerides, and LDL levels with the use of the plant. Danshen is used for the management of hypertension in China, Korea, and Japan, and is thought to act via inhibition of angiotensin converting enzymes (ACE inhibitors) [39, 49, 50].

1.24 *Scilla maritima*

Scilla or *Urginea maritima* is a perennial herb native to the Mediterranean region of Liliaceae family. The bulbs of this plant contain a large number of cardioactive glycosides and *Scilla* is a cardiotonic similar to *Digitalis*. Herbalists used to claim that *Scilla* had a specific effect on right-sided heart failure. This bulb is indicated in all types of **mild to moderate heart failure**, especially when **diuretic action** is desired. Cor pulmonale associated with emphysema is a special indication for the use of the plant. Like *Digitalis, Scilla* causes dose-dependent effects such as nausea, vomiting, and cardiac arrhythmias, which are quickly reversible.

1.25 *Strophantus kombe*

This is a climbing plant found in the jungles of tropical Africa from the Apocynaceae family. The drug is made from the seeds and the tincture has a mild **cardiotonic** effect in patients with mild myocardial or coronary impairment of a primarily functional nature. It combines very well with other **antispasmodic** tinctures of herbs, such as *Convallaria*, *Valeriana,* and *Belladonna*. Administration should last for several months. In vagotonic patients, it can determine meteorism, which can be avoided by adding carminative herbs and belladonna [7, 8].

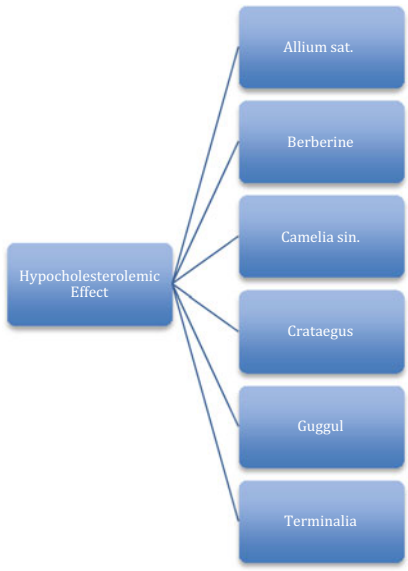
1.26 *Terminalia arjuna*

Terminalia is an evergreen tree that reaches 30 m in height and is native to northern India and Tibet. It belongs to the Combretaceae family. The bark has been used in Indian medicine for at least 3,000 years as a remedy, mostly for heart ailments. Experiments with rats demonstrated **antiplatelet** and **anticoagulant** actions similar to those of acetylsalicylic acid. Clinical studies have revealed that the use of this bark significantly reduces episodes of angina and improves diastolic function in patients with **ischemic mitral regurgitation**.

Terminalia also exerts **antioxidant**, **hypocholesterolemic,** and **hepatoprotective** actions, activities very useful in cardiac patients [51].

1.27 *Viscum album* (Mistletoe)

Viscum is a spherical evergreen shrub, which is hemiparasitic, growing on a wide variety of host trees (pine, oak, birch, and apple). It belongs to the Loranthaceae family. *Viscum* preparations have been used medicinally in Europe for centuries to treat epilepsy, infertility, hypertension, and arthritis. The most distinctive



constituents are viscotoxins, lectins, flavonoids, biogenic amines, phenylpropane derivates, and lignans. None of these compounds is specifically responsible for the **antihypertensive properties** of the plant. Its effect on blood pressure is mild compared with *Rauvolfia*, but the patients report beneficial effects on **subjective symptoms of hypertension** such as **headache, dizziness, and irritability**. *Viscum* does not have any unpleasant side effects and is the long-term therapy of choice for hypertensive patients [9, 19, 52, 53].

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Homeopathy and Cardiovascular Disease 2

Ivo Bianchi

2.1 Historical Background and Basic Concepts

Homoeopathy is the name given by Samuel Hahnemann in the first years of the eighteenth century to a new therapeutic approach that was indeed as ancient as medicine. Hahnemann was not a revolutionary, but a restorer of traditional values related to a comprehensive view of medicine originating from Hippocrates, the founder of Western medicine, who recognized two different and somewhat opposing approaches to the problem of illness that were both useful for healing suffering people. The still current dichotomy of medicine is descended from these concepts:

- *Official rationalist Galenic medicine*, based on the immediacy of its conclusions and on the linearity of its concepts. This approach gave rise to the tendency to face illnesses directly, with poison to kill the germ and the bistoury to remove it. This tendency is directly connected with the modern, official form of medicine, which is quick, safe, and technically perfect.
- *Alternative empiristic Celsus medicine*, based on a global concept of man and nature, giving much importance to spiritual and psychic factors and giving rise to the tendency to face illness by far, trying to stimulate an organic reaction against the disease and often ignoring the ultimate cause of the disease itself. This approach is very important because it is directed toward the comprehension of natural laws, with an effort to find a therapy strictly related to them. This tendency, which also gave rise to alchemical research, was not and is still not immediately comprehensible. Homeopathy is within this range: it can be slow and empirical, based mostly on the intuition of the doctor, but is often successful, providing long-lasting results without side effects and at a low cost.

Homoeopathy proposes to use a wide variety of substances, both to fight the disease directly and to stimulate the physiological reactivity of the organism. This was possible by studying very carefully the toxicological reports of various activities from the plant, mineral, and animal kingdoms. There is experimental evidence that even very diluted substances are still effective if they are well prescribed. The basic principle is that the symptom or the damage caused by a toxic substance in the healthy body can be healed if present in the illness, using this same very diluted and activated substance. The skill of the doctor is to look for the specific symptoms and signs in the patient, not focussing his attention only on the pathognomonic known expressions

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