Medicinal herbal raw materials and phytopreparations that have an effect on the cardiovascular system

Cardiovascular (CV) disorders are responsible for many years of ill health and multiple deaths around the world, and are mostly a consequence of lifestyle and diet as well as being linked to some extent to genetic predisposition.

Serious conditions such as heart failure may be treated only under the guidance of a qualified physician, but some minor forms of CV disease respond well to changes in diet and taking more exercise, as well as phytotherapy. Cardiology has benefited greatly from the introduction of some newer semi-synthetic drugs based on natural products, including aspirin, an antiplatelet agent derived from salicin, and warfarin, an anticoagulant derived from dicoumarol. Others have been developed using a natural product as a template. For example, verapamil, a calcium channel antagonist used to treat hypertension and angina, is based on the opium alkaloid papaverine; nifedipine, a calcium channel antagonist, and amiodarone, an anti-arrhythmic, were both developed from khellin, the active constituent of khella [*Visnaga daucoides* Gaertn., syn.: *Ammi visnaga* (L.) Lam.]. Cocaine has cardioactive as well as central nervous system effects, and was the starting material for the development of the anti-arrhythmics procaine and lignocaine, which are more effective and without the unwanted stimulant activity

Cardiovascular conditions discussed here include heart problems, venous insufficiency, thrombosis and atherosclerosis. Other conditions such as hypertension and cardiac arrhythmias are rarely treated with phytomedicines, although there are some natural products used in their treatment that will be mentioned briefly.

Synthetic diuretics are widely used as antihypertensives, but phytomedicines are not suitable for this purpose as they are not sufficiently potent to reduce blood pressure. Instead, they are often incorporated into remedies for urinary tract complaints or to reduce bloating (mild water retention, for example pre-menstrual).

HEART FAILURE AND ARRHYTHMIAS

These conditions can be treated with cardiac glycosides (cardenolides and bufadienolides) such as digoxin, isolated from the foxglove. Lily of the valley (*Convallaria majalis* L.) contains convallotoxin (a mixture of cardenolides), and squill [*Drimia maritima* (L.) Stearn] contains the bufadienolides scillaren A and proscillaridin, but these are rarely used now. Ouabain, isolated from *Strophanthus* spp., has been used in emergency cases. The cardiac glycosides have a positive inotropic effect, meaning that they increase the force of the contractions of the heart. They are emetic and toxic in large doses and have a cumulative effect and are therefore unsuitable for use in the form of herbal extracts.

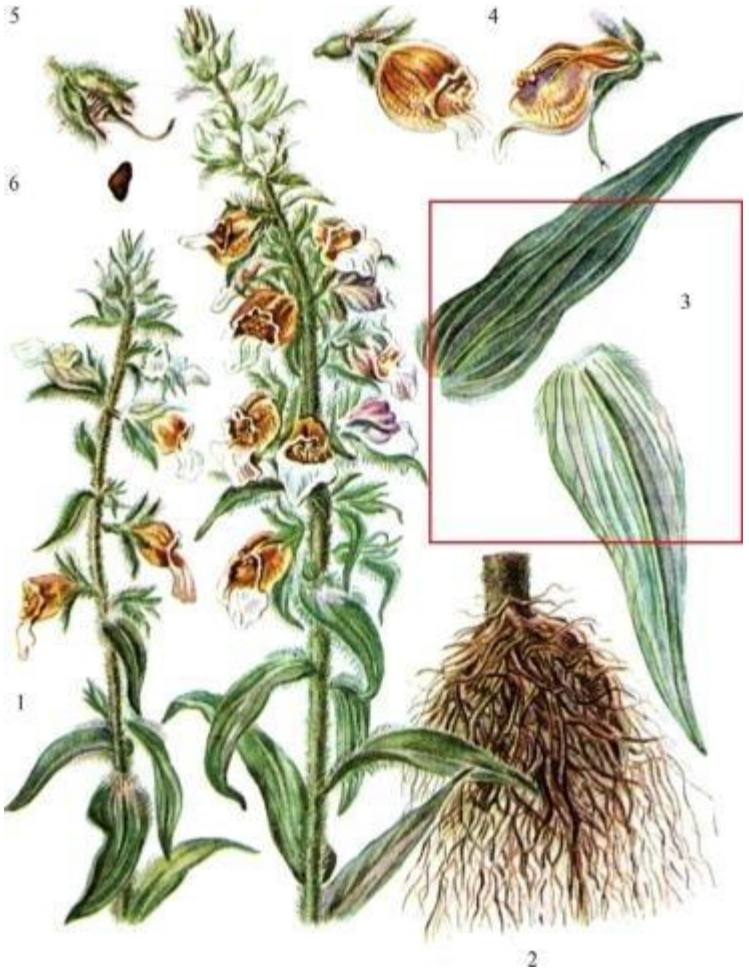
Single isolated compounds for which the pharmacokinetics can be monitored are used instead.

There are, however, other herbal drugs that have beneficial effects upon the heart, the most important of which are hawthorn (*Crataegus* spp.) and motherwort (*Leonurus cardiaca* L.). Hawthorn has anti-arrhythmic activity, and will be discussed briefly below. There is not enough evidence available at present to justify the inclusion of motherwort. In general, however, arrhythmias are treated with isolated compounds, most of which are synthetic, although quinidine (an alkaloid from Cinchona spp.) is still used occasionally. Ajmaline, from Rauvolfia spp., is used as an antiarrhythmic in some parts of the world; sparteine, from broom [Cytisus scoparius (L.) Link], was formerly employed. Both of these compounds are alkaloids.

DIGITALIS LANATA LEAVES -DIGITALIS LANATA FOLIA

It consists of the dried leaves of *Digitalis lanata*J. F. Ehrh., belonging to family Scrophulariaceae

Digitalis lanata is a biennial or perennial growing from a woody, horizontal rootstock. There is a tidy rosette before the spike goes up, and it is neatly arranged around the purple-tinged stems. The plant commonly forms a single, upright, more or less uniformly leafy stem that is partly ascending at the base. The plant send up these stems and flowers in usually in its second year. The stems are 0.3 to 0.6 meters in height.



The leaves are moderately green in colour, woolly, veined, and covered with white hairs on the underside. They have a very bitter taste. The lower cauline leaves are 6 to 12 cm (sometimes to 20 cm) long and 1.5 to 3.5 cm wide, the upper cauline leaves are 4 to 10 cm long and lanceolate shaped, usually with entire margins, and with a distinctive mid-rib. The leaves along the stalks are alternate. The lower stem leaves wither by early flowering. Both flowers and stems are also woolly or hairy.

The inflorescence axisis densely covered with densely matted woolly hairs (tomentose), and the flowers are densely arranged into a raceme that is pyramidal in shape. The flowers are tubular and bell shaped, pale yellow to whitish with brown or violet lines (ferruginous reticulated markings),and the centre lobe of the lower lip is 8 to 13 mm long.

The fruit is a conical capsule with a blunt end topped by a short beak. The seeds which develop within are quadrangular or prismatic in shape, and are about 0.6 mm broad and 1.1 to 1.3 mm long.

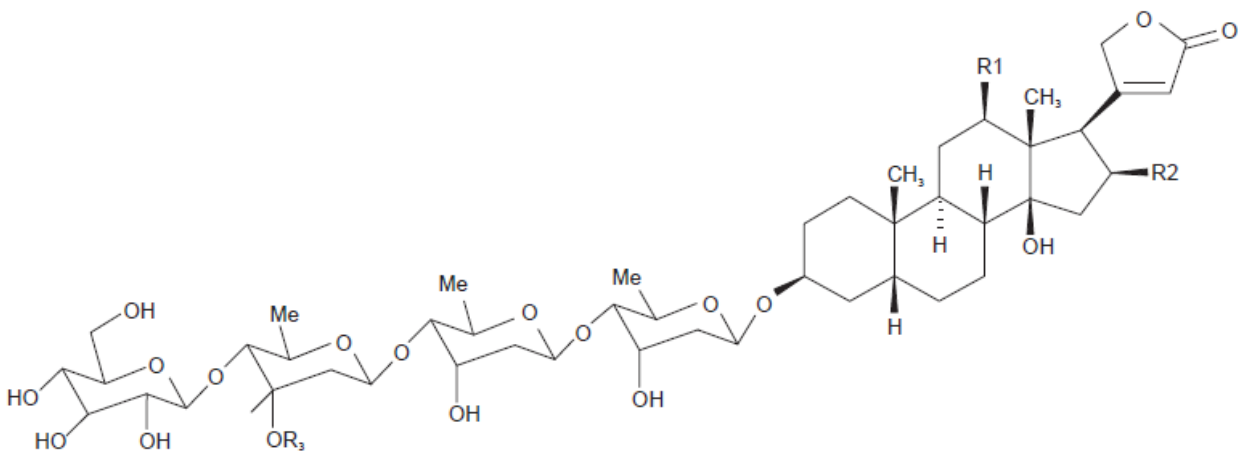
Geographical Source

It is mainly found in Central and Southern Europe, England, California and India.

They are indigenous to Europe and cultivated elsewhere. They do not have a long history of herbal use because of their toxicity, although in 1870, based on reports from a local herbalist in Shropshire, the famous surgeon William Withering described their use for ‘dropsy’ (an old term for congestive heart ailure), and this was the first time an effective treatment for this condition had been found. The leaves are the source of the drug and are usually gathered in the second year of growth.

Chemical Constituents

Digitalis lanata contains higher concentrations of glycosides, including digoxin and lanatosides, and is the main source of digoxin for the pharmaceutical industry.



	R1	R2	R3
Lanatoside A	H	H	CH_3CO
Lanatoside B	H	OH	CH_3CO
Lanatoside C	OH	H	CH_3CO

Therapeutic uses and available evidence

Digoxin increases the force of myocardial contractility and reduces conductivity within the atrioventricular node. It is used primarily in the treatment of upraventricular tachycardia and heart failure and is given as a once-daily dosage in the range 62.5–250 micrograms. Digitalis glycosides increase the force of the contractions of the heart without increasing the oxygen consumption, and slow the heart rate when atrial fibrillation is present. Due to their cumulative effect, the glycosides can easily give rise to toxic symptoms, such as nausea, vomiting and anorexia, especially in the elderly, thus blood levels should be monitored.

HAWTHORN FLOWERS - CRATAEGI FLORES
HAWTHORN FRUITS - CRATAEGI FRUCTUS

Collected at the beginning of flowering and dried inflorescences or collected in the phase of full ripening and dried fruits of wild and cultivated shrubs or small trees are used as medicinal plant material. *Crataequs sanquinea, C. laevigata* (*C.oxyacantha*), *C. Dahurica, C.monogyna; C. pentagyna; C. Curvisepala* and some others.

Family *Rosaceae*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Constituents. The main constituents of the leaf are flavonoids, including vitexin, vitexin-4-rhamnoside, quercetin and quercetin-3-galactoside, hyperoside, rutin, vicentin, orientin; the fruit contains flavonoids, procyanidins, catechins and epicatechin dimers, as well as phenolic acids such as chlorogenic and caffeic acids. Amines such as phenethylamine and its methoxy derivative, as well as dopamine, acetylcholine and tyramine, have also been isolated.

It is thought that a mixture of active constituents may be necessary for the therapeutic effect. The drug prepared from hawthorn is often standardized to contain 4–30 mg of flavonoids, calculated as hyperoside, or 30–160 mg of procyanidins, calculated as epicatechin. In the Eur. Ph., the leaf and flower, and also the berries, are identified using a thin-layer chromatography (TLC) method with the hyperoside, rutin and chlorogenic acid as reference standards. The assays are different, however: hereas the leaf and flower use the flavonoid content, the berries are assayed for anthocyanin content.

Therapeutic uses and available evidence

Hawthorn is used as a cardiac tonic, hypotensive, coronary and peripheral vasodilator, anti-atherosclerotic and antiarrhythmic. Animal studies have shown beneficial effects on coronary blood flow, blood pressure and heart rate, as well as improved circulation to the extremities.

Hawthorn extract inhibits myocardial Na^{+}, K^{+}-ATPase and exerts a positive inotropic effect and relaxes the coronary artery. It blocks the repolarizing potassium current in the ventricular muscle and so prolongs the refractory period, thus exerting an anti-arrhythmic effect. It seems to protect heart muscle by regulating Akt and HIF-1 signaling pathways, and reducing oxidative stress.

There are as yet few clinical trials of the drug, although a double-blind pilot study indicated a promising role for hawthorn extract in mild essential hypertension. A large consistent positive outcome from clinical trials using hawthorn extracts for cardiovascular disease has been reported but there are inconsistencies in terms of the clinical criteria used (sample size, preparation, dosage, among others). Tolerance to exercise was not improved in patients with class II congestive heart failure. It seems likely that hawthorn can be used as an adjunct or sole treatment only in milder cases of heart disease. The usual recommended dose of standardized extract (see Constituents, above) is 160–900 mg daily. Few side effects have been observed, and both patients and physicians rated the tolerance of the drug as good, although nausea and headache have been reported infrequently.

YELLOW MILKVETCH HERB

- *ASTRAGALI DASYANTHI HERBA*

Astragalus dasyanthus Pall.
Family Fabaceae

Perennial herbaceous plant with a rod-shaped multi-headed root. Stems are numerous, ascending, 30-40 cm tall. Leaves up to 20 cm long, alternate, non-pinnately pinnately compound with 21-27 elliptic or oblong-elliptic leaflets 6-20 mm long. Flowers are 10-20 in dense head-like inflorescences on long pedicels, with light yellow moth-like corolla and five-lobed bell-shaped grey-green calyx. The fruit is a bloated, ovoid or elliptic, leathery bean, 10-12 mm long, with a spout 2-3 mm long. All parts of the plant, except the corolla, are pubescent with whitish spurred hairs.

Distribution. Black Sea species. Grows in the south of European Russia, Ukraine and Moldova. In the east it reaches the Volga River.

Harvesting. The herb is cut in the phase of mass flowering before fruit formation at a height of 5-7 cm from the soil surface, leaving rough, almost leafless stem bases. Dry quickly in attics or well-ventilated barns, under sheds, spread in a layer of 3-5 cm on paper or cloth, often turning. Artificial drying at a temperature not exceeding 55 ºC is allowed.

Chemical composition. Astragalus herb contains triterpene saponins - dasyanthosides, derivatives of dasyanthogenin (cycloartan series); flavonoids (kaempferol, quercetin, isoramnetin, astragaloside); tannins; coumarins; amino acids; vitamins, including alpha-tocopherol (vitamin E). Astragalus is one of the plants that accumulate selenium (up to 1.5 mg%). The plant contains a variety of macro- and microelements (calcium, silicon, aluminium, iron, magnesium, cobalt, zinc, copper, manganese, molybdenum, chromium).

Usage. Astragalus woolly-flowered used in the initial forms of hypertension. When treated with an infusion of astragalus patients significantly improved health, lowered blood pressure, disappeared headache, dizziness, tinnitus, flushes to the head, insomnia, interruptions and pain in the heart. Microcirculation was improved under the influence of astragalus treatment. Improvement of cerebral circulation in patients with hypertension was accompanied by a decrease in blood pressure in the central retinal artery and temporal artery. When treating patients with ischaemic heart disease with astragalus, in addition to hypotensive and cardiotonic properties, its ability to inhibit vasomotor regulatory centres was taken into consideration.