

Foxglove

POISON!

Botanical: *Digitalis purpurea* (LINN.)

Family: N.O. Scrophulariaceae

Synonyms

Witches' Gloves. Dead Men's Bells. Fairy's Glove. Gloves of Our Lady. Bloody Fingers. Virgin's Glove. Fairy Caps. Folk's Glove. Fairy Thimbles.

(*Norwegian*) Revbielde.

(*German*) Fingerhut.

Part Used

Leaves.

Habitat

The Common Foxglove of the woods (*Digitalis purpurea*), perhaps the handsomest of our indigenous plants, is widely distributed throughout Europe and is common as a wild-flower in Great Britain, growing freely in woods and lanes, particularly in South Devon, ranging from Cornwall and Kent to Orkney, but not occurring in Shetland, or in some of the eastern counties of England. It flourishes best in siliceous soil and grows well in loam, but is entirely absent from some calcareous districts, such as the chain of the Jura, and is also not found in the Swiss Alps. It occurs in Madeira and the Azores, but is, perhaps, introduced there. The genus contains only this one indigenous species, though several are found on the Continent.

Needing little soil, it is found often in the crevices of granite walls, as well as in dry hilly pastures, rocky places and by roadsides. Seedling Foxgloves spring up rapidly from recently-turned earth. Turner (1548), says that it grows round rabbit-holes freely.

Description

The normal life of a Foxglove plant is two seasons, but sometimes the roots, which are formed of numerous, long, thick fibres, persist and throw up flowers for several seasons.

In the first year a rosette of leaves, but no stem, is sent up. In the second year, one or more flowering stems are thrown up, which are from 3 to 4 feet high, though even sometimes more, and bear long spikes of drooping flowers, which bloom in the early summer, though the time of flowering differs much, according to the locality. As a rule the flowers are in perfection in July. As the blossoms on the main stem gradually fall away, smaller lateral shoots are often thrown out from its lower parts, which remain in flower after the principal stem has shed its blossoms. These are also promptly developed if by mischance the central stem sustains any serious injury.

The radical leaves are often a foot or more long, contracted at the base into a long, winged footstalk, the wings formed by the lower veins running down into it some distance. They have slightly indented margins and sloping lateral veins, which are a very prominent feature. The flowering stems give off a few leaves, that gradually diminish in size from below upwards. All the leaves are covered with small, simple, unbranched hairs.

The flowers are bell-shaped and tubular, 1 1/2 to 2 1/2 inches long, flattened above, inflated beneath, crimson outside above and paler beneath, the lower lip furnished with long hairs inside and marked with numerous dark crimson spots, each surrounded with a white border. The shade of the flowers varies much, especially under cultivation, sometimes the corollas being found perfectly white.

In cultivated plants there frequently occurs a malformation, whereby one or two of the uppermost flowers become united, and form an erect, regular, cup-shaped flower, through the centre of which the upper extremity of the stem is more or less prolonged.

The Foxglove is a favourite flower of the honey-bee, and is entirely developed by the visits of this insect. For that reason, its tall and stately spikes of flowers are at their best in those sunny, midsummer days when the bees are busiest. The projecting lower lip of the corolla forms an alighting platform for the bee, and as he pushes his way up the bell, to get at the honey which lies in a ring round the seed vessel at the top of the flower, the anthers of the stamens which lie flat on the corolla above him, are rubbed against his back. Going from flower to flower up the spike, he rubs pollen thus from one blossom on to the cleft stigma of another blossom, and thus the flower is fertilized and seeds are able to be produced. The life of each flower, from the time the bud opens till the time it slips off its corolla, is about six days. An almost incredible number of seeds are produced, a single Foxglove plant providing from one to two million seeds to ensure its propagation.

It is noteworthy that although the flower is such a favourite with bees and is much visited by other smaller insects, who may be seen taking refuge from cold and wet in its drooping blossoms on chilly evenings, yet no animals will browse upon the plant, perhaps instinctively recognizing its poisonous character.

The Foxglove derives its common name from the shape of the flowers resembling the finger of a glove. It was originally Folksglove - the glove of the 'good folk' or fairies, whose favourite haunts were supposed to be in the deep hollows and woody dells, where the Foxglove delights to grow. Folksglove is one of its oldest names, and is mentioned in a list of plants in the time of Edward III. Its Norwegian name, *Revbjelde* (Foxbell), is the only foreign one that alludes to the Fox, though there is a northern legend that bad fairies gave these blossoms to the fox that he might put them on his toes to soften his tread when he prowled among the roosts.

The earliest known form of the word is the Anglo-Saxon *foxes glofa* (the glove of the fox).

The mottlings of the blossoms of the Foxglove and the Cowslip, like the spots on butterfly wings and on the tails of peacocks and pheasants, were said to mark where the elves had placed their fingers, and one legend ran that the marks on the Foxglove

were a warning sign of the baneful juices secreted by the plant, which in Ireland gain it the popular name of 'Dead Man's Thimbles.' In Scotland, it forms the badge of the Farquharsons, as the Thistle does of the Stuarts. The German name *Fingerhut* (thimble) suggested to Leonhard Fuchs (the well-known German herbalist of the sixteenth century, after whom the Fuchsia has been named) the employment of the Latin adjective *Digitalis* (from *Digitabulum*, a thimble) as a designation for the plant, which, as he remarked, up to the time when he thus named it, in 1542, had had no name in either Greek or Latin.

The Foxglove was employed by the old herbalists for various purposes in medicine, most of them wholly without reference to those valuable properties which render it useful as a remedy in the hands of modern physicians. Gerard recommends it to those 'who have fallen from high places,' and Parkinson speaks highly of the bruised herb or of its expressed juice for scrofulous swellings, when applied outwardly in the form of an ointment, and the bruised leaves for cleansing for old sores and ulcers. Dodoens (1554) prescribed it boiled in wine as an expectorant, and it seems to have been in frequent use in cases in which the practitioners of the present day would consider it highly dangerous. Culpepper says it is of: 'a gentle, cleansing nature and withal very friendly to nature. The Herb is familiarly and frequently used by the Italians to heal any fresh or green wound, the leaves being but bruised and bound thereon and the juice thereof is also used in old sores, to cleanse, dry and heal them. It has been found by experience to be available for the King's evil, the herb bruised and applied, or an ointment made with the juice thereof, and so used.... I am confident that an ointment of it is one of the best remedies for a scabby head that is.' Strangely enough, the Foxglove, so handsome and striking in our landscape, is not mentioned by Shakespeare, or by any of the old English poets. The earliest known descriptions of it are those given about the middle of the sixteenth century by Fuchs and Tragus in their Herbals. According to an old manuscript, the Welsh physicians of the thirteenth century appear to have frequently made use of it in the preparation of external medicines. Gerard and Parkinson advocate its use for a number of complaints, and later Salmon, in the *New London Dispensatory*, praised the plant. It was introduced into the London Pharmacopoeia in 1650, though it did not come into frequent use until a century later, and was first brought prominently under the notice of the medical profession by Dr. W. Withering, who in his *Account of the Foxglove*, 1785, gave details of upwards of 200 cases, chiefly dropsical, in which it was used.

A domestic use of the Foxglove was general throughout North Wales at one time, when the leaves were used to darken the lines engraved on the stone floors which were fashionable then. This gave them a mosaiclike appearance.

The plant is both cultivated and collected in quantities for commercial purposes in the Harz Mountains and the Thuringian Forest.

Cultivation

The Foxglove is cultivated by a few growers in this country in order to provide a drug of uniform activity from a true type of *Digitalis purpurea*. It is absolutely necessary to have the true medicinal seeds to supply the drug market: crops must be obtained from carefully selected wild seed and all variations from the new type struck out.

The plant will flourish best in well-drained loose soil, preferably of siliceous origin, with some slight shade. The plants growing in sunny situations possess the active qualities of the herb in a much greater degree than those shaded by trees, and it has been proved that those grown on a hot, sunny bank, protected by a wood, give the best results.

It grows best when allowed to seed itself, but if it is desired to raise it by sown seed, 2 lb. of seed to the acre are required. As the seeds are so small and light, they should be mixed with fine sand in order to ensure even distribution. They should be thinly covered with soil. The seeds are uncertain in germination, but the seedlings may be readily and safely transplanted in damp weather, and should be pricked out to 6 to 9 inches apart. Sown in spring, the plant will not blossom till the following year. Seeds must be gathered as soon as ripe. The flowers of the true medicinal type must be pure, dull pink or magenta, not pale-coloured, white or spotted externally.

It is estimated that one acre of good soil will grow at least two tons of the Foxglove foliage, producing about 1/2 ton of the dried leaves.

Preparation for Market

The leaves alone are now used for the extraction of the drug, although formerly the seeds were also official.

No leaves are to be used for medicinal purposes that are not taken from the two-year-old plants, picked when the bloom spike has run up and about two-thirds of the flowers are expanded, because at this time, before the ripening of the seeds, the leaves are in the most active state. They may be collected as long as they are in good condition: only green, perfect leaves being picked, all those that are insect-eaten or diseased, or tinged with purple or otherwise discoloured, must be discarded. Leaves from seedlings are valueless, and they must also not be collected in the spring, before the plant flowers, or in the autumn, when it has seeded, as the activity of the alkaloids is in each case too low.

If the *fresh* leaves are sent to the manufacturing druggists for Extract-making, they should be in 1/2 cwt. bundles, packed in air-covered railway cattle-trucks, or if in an open truck, must be covered with tarpaulin. The fresh crop should, if possible, be delivered to the wholesale buyer the same day as cut, but if this is impossible, on account of distance, they should be picked before the dew falls in the late afternoon and despatched the same evening, packed loosely in wicker baskets, lined with an open kind of muslin. Consignments by rail should be labelled: 'Urgent, Medicinal Herbs,' to ensure quick delivery. The weather for picking must be absolutely dry - no damp or rain in the air and the leaves must be kept out of the sun and not packed too closely, or they may heat and turn yellow.

The odour of the fresh leaves is unpleasant, and the taste of both fresh and dried leaves is disagreeably bitter.

Foxglove leaves have in some places been recklessly gathered by over-zealous and thoughtless collectors without due regard to the future supply of the plants. The plant should not be roughly treated and never cut off just above the root, but the bottom

leaves should in all cases be left to nourish the flower-spikes, in order that the seed may be ripened. In patches where Foxgloves grow thickly, the collection and redistribution of seed in likely places is much to be recommended.

The dried leaves as imported have occasionally been found adulterated with the leaves of various other plants. The chief of these are *Inula Conyza* (Ploughman's Spikenard), which may be distinguished by their greater roughness, the less-divided margins, the teeth of which have horny points, and odour when rubbed; *I. Helenium* (Elecampane), the leaves of which resemble Foxglove leaves, though they are less pointed, and the lower lateral veins do not form a 'wing' as in the Foxglove, the leaves of *Symphytum officinale* (Comfrey), which, however, may be recognized by the isolated stiff hairs they bear, and *Verbascum Thapsus* (Great Mullein), the leaves of which, unlike those of the Foxglove, have woolly upper and under surfaces, and the hairs of which, examined under a lens, are seen to be branched. Primrose leaves are also sometimes mingled with the drug, though they are much smaller than the average Foxglove leaf, and may be readily distinguished by the straight, lateral veins, which divide near the margins of the leaves. Foxglove leaves are easy to distinguish by their veins running down the leaf.

There is no reason why Foxglove leaves, properly prepared, should not become a national export.

Digitalis has lately been grown in Government Cinchona plantations in the Nilgiris, Madras, India. The leaves are coarser and rather darker in colour than British or German-grown leaves, wild or cultivated, but tests show that the tincture prepared from them contains glucosides of more than average value.

Constituents

Digitalis contains four important glucosides of which three are cardiac stimulants. The most powerful is Digitoxin, an extremely poisonous and cumulative drug, insoluble in water, Digitalin, which is crystalline and also insoluble in water; Digitalein, amorphous, but readily soluble in water, rendering it, therefore, capable of being administered subcutaneously, in doses so minute as rarely to exceed of a grain; Digitonin, which is a cardiac depressant, containing none of the physiological action peculiar to *Digitalis*, and is identical with Saponin, the chief constituent of Senega root. Other constituents are volatile oil, fatty matter, starch, gum, sugar, etc.

The amount and character of the active constituents vary according to season and soil: 100 parts of dried leaves yield about 1.25 of Digitalin, which is generally found in a larger proportion in the wild than in the cultivated plants.

The active constituents of *Digitalis* are not yet sufficiently explored to render a chemical assay effective in standardizing for therapeutic activity. The different glucosides contained varying from each other in their physiological action, it is impossible to assay the leaves by determining one only of these, such as Digitoxin. No method of determining Digitalin is known. Hence the chemical means of assay fail, and the drug is usually standardized by a physiological test. One of our oldest firms of manufacturing druggists standardizes preparations of this extremely powerful and important drug by testing their action upon frogs.

Preparations

The preparations of Foxglove on the market vary considerably in composition and strength. Powdered Digitalis leaf is administered in pill form. The pharmacopoeial tincture, which is the preparation in commonest use, is given in doses of 5.15 minims, and the infusion is the unusually small dose of 2 to 4 drachms, the dose of other infusions being an ounce or more. The tincture contains a fair proportion of both Digitalin and Digitoxin.

The following note from the *Chemist and Druggist* (December 30, 1922) is of interest here:

Cultivation of Digitalis

'As is well known, for many years prior to the War digitalis was successfully cultivated on a large scale in various parts of the former Austro-Hungarian monarchy, and indeed the Government actively promoted the cultivation of this as well as of other medicinal plants. B. Pater, of Klausenburg, gives a résumé of his experiences in this direction (*Pharmazeutische Monatshefte*, 7, 1922), dealing not only with the best methods for cultivating digitalis from the seeds of this plant, but also with his investigations into certain differences and abnormalities peculiar to *Digitalis purpurea*. Apart from the fact that, occasionally, some plants bear flowers already in the first year of growth, the observation was made that the colour of the flowers showed a wide scale of variation, ranging from the well-known distinctive purple shade through dark rose, light rose, to white. These variations in colour of the flowers of cultivated digitalis plants induced the author to undertake a study of the activity of the several varieties, based on the digitoxin content of the stem leaves collected from flowering plants. In the case of *Digitalis purpurea* with normal purple flowers, the content of purified digitoxin, ascertained by Keller's method, averaged 0.17 per cent, while the leaves of plants bearing white flowers showed a slightly lower content, i.e. an average of 0.155 per cent of purified digitoxin. On the other hand, the plants with rose-coloured flowers were found to possess a very low content of digitoxin, averaging only 0.059 per cent. In the course of these investigations the fact was confirmed that the upper stem leaves are more active than the lower leaves.'

Medicinal Action and Uses

Digitalis has been used from early times in heart cases. It increases the activity of all forms of muscle tissue, but more especially that of the heart and arterioles, the all-important property of the drug being its action on the circulation. The first consequence of its absorption is a contraction of the heart and arteries, causing a very high rise in the blood pressure.

After the taking of a moderate dose, the pulse is markedly slowed. Digitalis also causes an irregular pulse to become regular. Added to the greater force of cardiac contraction is a permanent tonic contraction of the organ, so that its internal capacity is reduced, which is a beneficial effect in cases of cardiac dilatation, and it improves the nutrition of the heart by increasing the amount of blood.

In ordinary conditions it takes about twelve hours or more before its effects on the heart muscle is appreciated, and it must thus always be combined with other remedies to tide the patient over this period and never prescribed in large doses at first, as some patients are unable to take it, the drug being apt to cause considerable digestive disturbances, varying in different cases. This action is probably due to the Digitonin, an undesirable constituent.

The action of the drug on the kidneys is of importance only second to its action on the circulation. In small or moderate doses, it is a powerful diuretic and a valuable remedy in dropsy, especially when this is connected with affections of the heart.

It has also been employed in the treatment of internal haemorrhage, in inflammatory diseases, in delirium tremens, in epilepsy, in acute mania and various other diseases, with real or supposed benefits.

The action of Digitalis in all the forms in which it is administered should be carefully watched, and when given over a prolonged period it should be employed with caution, as it is liable to accumulate in the system and to manifest its presence all at once by its poisonous action, indicated by the pulse becoming irregular, the blood-pressure low and gastro-intestinal irritation setting in. The constant use of Digitalis, also, by increasing the activity of the heart, leads to hypertrophy of that organ.

Digitalis is an excellent antidote in Aconite poisoning, given as a hypodermic injection.

When Digitalis fails to act on the heart as desired, Lily-of-the-Valley may be substituted and will often be found of service.

In large doses, the action of Digitalis on the circulation will cause various cerebral symptoms, such as seeing all objects blue, and various other disturbances of the special senses. In cases of poisoning by Digitalis, with a very slow and irregular pulse, the administration of Atropine is generally all that is necessary. In the more severe cases, with the very rapid heart-beat, the stomach pump must be used, and drugs may be used which depress and diminish the irritability of the heart, such as chloral and chloroform.

Preparations of Digitalis come under Table II of the Poison Schedule.

Preparations and Dosages

Tincture, B.P., 5 to 15 drops. Infusion, B.P., 2 to 4 drachms. Powdered leaves, 1/2 to 2 grains. Fluid extract, 1 to 3 drops. Solid extract, U.S.P., 1/8 grain.

A method of preparing the drug in a noninjurious manner is given in the *Chemist and Druggist* (December 30, 1922):

Digitalis Maceration

'On preparing an infusion of digitalis leaves in the usual manner, one of the active principles, gitalin, is destroyed by the action of the boiling water. To obviate the

possibility of destroying any of the active principles in the leaves, Th. Koch (*Süddeutsche Apotheker-Zeitung*, 63, 1922) has for some years past adopted the following procedure: 20 gm. powdered standardized digitalis leaves, 1000 gm. chloroform water (7.1000) and 40 drops of 10 per cent. Solution of Sodium Carbonate are shaken for four hours. The liquid is then passed through a flannel cloth, and, after standing for some time, filtered in the ordinary way, taking the precaution to cover the filter with a glass plate. The use of chloroform water as the solvent serves a threefold purpose: It promotes the solution of the gitalin present in the leaves, ensures the stability and keeping properties of the maceration, and prevents the occurrence of gastric troubles. The presence of Sodium Carbonate prevents the plant acid from reacting with the chloroform to produce hydrochloric acid. In this maceration no digitoxin is present, the principle which is assumed to exert a deleterious action on the heart as well as a cumulative effect.'