medullary rays than the official species, but resembles the latter in having sclerenchymatous cells. The bark of *R.fallax* has been recorded as a cascara substitute.

Marketed Products

It is one of the ingredients of the preparations known as Herbal Laxative (Trophic Canada Ltd.).

16.7. STEROL OR CARDIAC GLYCOSIDES

The cardiac glycosides are an important class of naturally occurring drugs whose actions include both beneficial and toxic effects on the heart. Plants containing cardiac steroids have been used as poisons and heart drugs at least since 1500 B.C. Throughout history these plants or their extracts have been variously used as arrow poisons, emetics, diuretics and heart tonics. Cardiac steroids are widely used in the modern treatment of congestive heart failure and for treatment of atrial fibrillation and flutter. Yet their toxicity remains a serious problem. These drugs all act by affecting the availability of intracellular Ca^{+2} for myocardial contraction or increasing the sensitivity of myocardial contractile proteins.

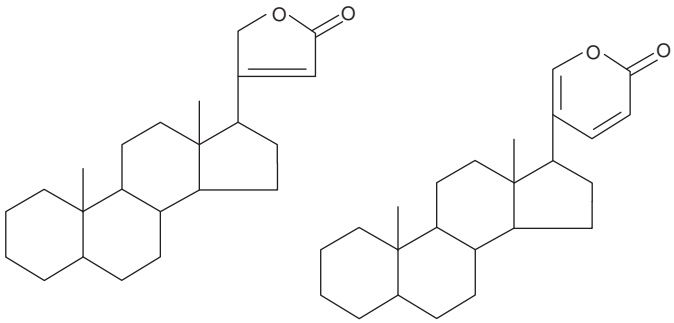
Cardiac glycosides are composed of two structural features: the sugar (glycone) and the nonsugar (aglycone–steroid) moieties.

The steroid nucleus has a unique set of fused ring system that makes the aglycone moiety structurally distinct from the other more common steroid ring systems. The steroid nucleus has hydroxyls at 3- and 14-positions of which the sugar attachment uses the 3-OH group. 14-OH is normally unsubstituted. Many genins have OH groups at 12- and 16-positions. These additional hydroxyl groups influence the partitioning of the cardiac glycosides into the aqueous media and greatly affect the duration of action. The lactone moiety at C-17 position is an important structural feature. The size and degree of unsaturation varies with the source of the glycoside. Normally plant sources provide a five-membered unsaturated lactone while animal sources give a six-membered unsaturated lactone.

One to four sugars are found to be present in most cardiac glycosides attached to the 3β-OH group. The sugars most commonly used include L-rhamnose, D-glucose, D-digitoxose, D-digitalose, D-digginose, D-sarmentose, L-vallarose and D-fructose. These sugars predominantly exist in the cardiac glycosides in the β-conformation. The presence of acetyl group on the sugar affects the lipophilic character and the kinetics of the entire glycoside.

Two classes have been observed in nature—the cardenolides and the bufadienolides.

The cardenolides have an unsaturated butyrolactone ring while the bufadienolides have a pyrone ring. The lactone of cardenolides has a single double bond and is attached at the C-17 position of steroidal nucleus. They are five-membered lactone ring and form a C_{23} steroids (Leguminosae, Cruciferae, Euphorbiaceae, etc.), while the lactone of bufadienolids have two double bond which is attached at the 17 α-position of the steroidal nucleus. They are six-memberd lactone ring and form C_{24} steroids (Liliaceae, Ranunculaceae).



Cardenolide

Bufadienolide

DIGITALIS LEAVES

Synonyms

Digitalis, purple foxglove, finger flower, lady's glove, Foxglove Leaves, Folia Digitalis.

Biological Sources

Digitalis consists of dried leaves of *Digitalis purpurea* Linn., belonging to family Scrophulariaceae.

Geographical Sources

It is mainly found in England, Germany, France, North America, India, Iraq, Japan, Kurdistan, Mexico, Nepal, Spain, Turkey.

Cultivation and Collection

Digitalis is a biennial herb growing wild but good quality of the drug is obtained especially from cultivated plant. 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, if it is desired to raise it by sown seed, 2 lb of seed to the acre are required. For cultivation special strains of the seeds are selected which would produce disease-resistant plants with maximum activity. Attention is specially paid to the structure of the soil in seed beds. As the seeds are so small and light, they should be mixed with fine sand in order to ensure even

distribution. Before sowing soil is sterilized. 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 6–9 inches apart. Sown in spring, the plant will not blossom till the following year. Seeds must be gathered as soon as ripe. In dry season sufficient water is supplied to the plant. In the first year, a long stalk with rosette of leaves is produced. The flowers of the true medicinal type must be pure, dull pink or magenta, not pale-coloured, white or spotted externally.

Collection of these leaves is carried out from September to November by hand and thus other organic matter and discoloured leaves are avoided. After collection the leaves should be dried as soon as possible at 60°C. By quick drying characteristic green colour of the leaves is maintained. Drying is carried out till moisture is not more than 5%. Leaves are packed under pressure in airtight containers.

Morphology

Colour	Dark greyish green in colour
Odour	Odourless
Taste	Bitter
Shape	Ovatelanceolate to broadly ovate. Leaves have a subacute apex, decurrent base and crenate or dentate margin. The upper surface of leaf is hairy, slightly pubescent, dark green and little wrinkled. The lower surface of leaf is hairy, greyish-green and very pubescent.
Size	10–30 cm long and 4–10 cm wide

Fig. 16.8 *Digitalis purpurea*

Microscopy

Digitalis has dorsiventral leaf structure. It has plenty of simple covering and glandular trichomes on both the surfaces. The covering trichomes are uniseriate, usually three to four cells long, having collapsed cells, acute apex and finely warty cuticle. The glandular trichomes have a short, unicellular stalk and bicellular or rarely unicellular head. It has anomocytic or ranunculaceous type of stomata. Trichomes and stomata are more in lower surface. The pericycle is parenchymatous above and collenchymatous below. Calcium oxalate crystals are absent.

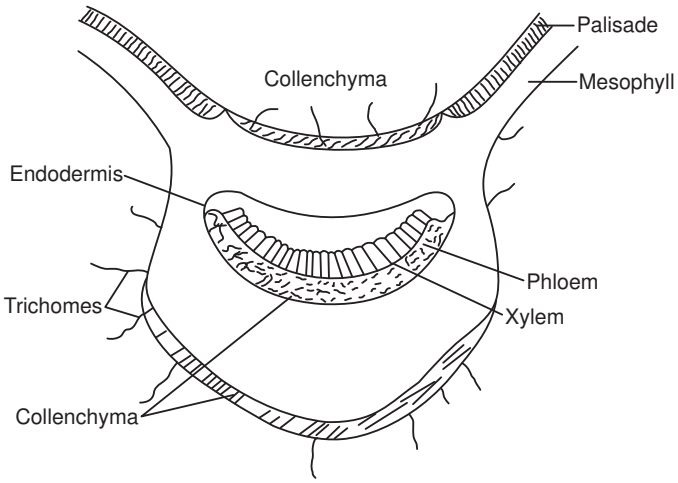


Fig. 16.9 T.S. (schematic) of Digitalis leaf

Chemical Constituents

Digitalis leaves contains 0.2–0.45% of both primary and secondary glycosides. Purpurea glycosides A and B and glucogitoloxin are primary glycosides. Because of greater stability of secondary glycosides, and lesser absorption of primary glycosides a higher content of primary glycosides are not considered ideal and secondary glycosides are used. Purpurea glycosides A and B are present in fresh leaves and by their hydrolysis digitoxin and glucose or gitoxin and glucose are obtained respectively. Hydrolysis of purpurea glycosides can take place by digipuridase (enzyme) present in the leaves. Digitoxin yields on hydrolysis digitoxigenin and three digitoxose. By hydrolysis of verodoxin, gitaloxigenin and digitalose are obtained. Digitalis leaves also contains glycosides like odoroside-H, gitaloxin, verodoxin and glucoverodoxin.

Verodoxin was found to potentiate the activity of digitoxin by synergism. Digitoxose and digitalose are desoxy sugars found only in cardiac glycosides and answers Keller–Killiani test. The important saponins include digitonin, tigonin and gitonin, and luteolin, a flavone responsible for the colour of the drug are also present in the leaves.

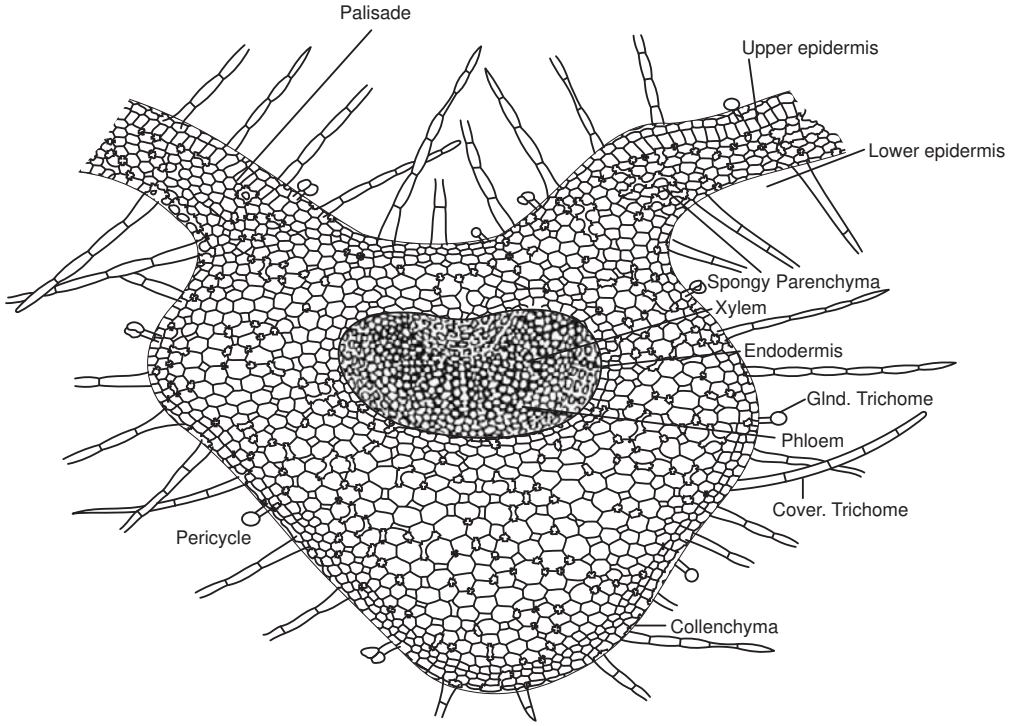
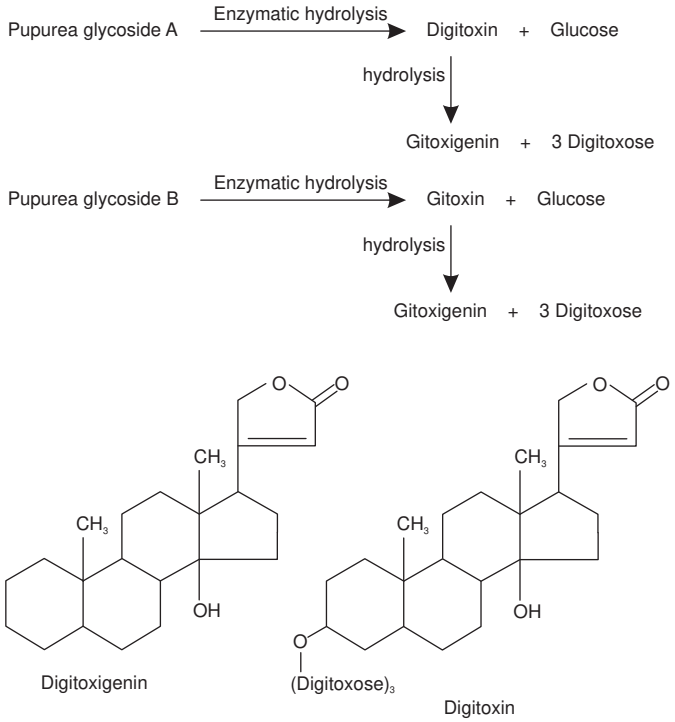


Fig. 16.10 Transverse section of Digitalis leaf



Chemical Tests

Digitalis glycosides having five membered lactone ring answers positive for the following tests which are due to the intact lactone.

1. *Baljet Test:* To a thick section of the leaf sodium picrate reagent is added. Yellow to orange colour indicates the presence of glycoside.
2. *Legal Test:* Glycoside is dissolved in pyridine and sodium nitroprusside solution is added to it and made alkaline. Pink to red colour is produced.
3. *Keller–Killiani Test:* The isolated glycoside is dissolved in glacial acetic acid and a drop of ferric chloride solution is added followed by the addition of sulphuric acid which forms the lower layer. A reddish-brown colour is seen in between two liquids and the upper layer becomes bluish green.

If the powdered leaves are used, 1 gm of the powdered leaves is extracted with 10 ml of 70% alcohol for couple of minutes, filtered and to 5 ml of filtrate 10 ml of water and 0.5 ml of strong solution of lead acetate is added and filtered and the filtrate is shaken with 5 ml of chloroform. Chloroform layer is separated in a porcelain dish and the test is carried out as mentioned above.

Uses

The foxglove is a widely used herbal medicine with a recognized stimulatory effect upon the heart. It is also used in allopathic medicine in the treatment of heart complaints. It has a profound tonic effect upon a diseased heart, enabling the heart to beat more slowly, powerfully and regularly without requiring more oxygen. At the same time it stimulates the flow of urine which lowers the volume of the blood and

lessens the load on 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. Digitalis has a cumulative effect in the body, so the dose has to be decided very carefully.

Adulterants

Verbascum thapsus also known as Mullelin leaves. These leaves are covered with large woolly branched candelabra trichomes.

Primula vulgaris (Primrose leaves) can be detected by the presence of long eight- to nine-celled covering trichomes in them.

Symphytum officinale (Comfrey leaves), this leaves contains multicellular trichomes forming hook at the top.

Inula conyza (Ploughman's Spikenard), may be distinguished by their greater roughness, the less-divided margins, the teeth of which have horny points and odour when rubbed.

Marketed Products

It is one of the ingredients of the preparation known as Lanoxin tablets (Glaxo Smith Kline).

DIGITALIS LANATA

Synonym

Grecian Foxglove.

Biological Source

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

Geographical Source

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

Cultivation and Collection

It is an evergreen biennial/Perennial growing to 0.6 m by 0.3 m. The plant prefers light (sandy), medium (loamy) and heavy (clay) soils. The plant prefers acid, neutral and alkaline soils. It can grow in semishade or no shade. It requires dry or moist soil. It grows well even in ordinary garden soil, especially if it is rich in organic matter. It is propagated by seeds. Seed are sown on early spring in a cold frame. The seed usually germinates in 2–4 weeks at 20°C. When they are large enough to handle, seedlings are transplanted into individual pots and planted them out in the summer.

Characteristics

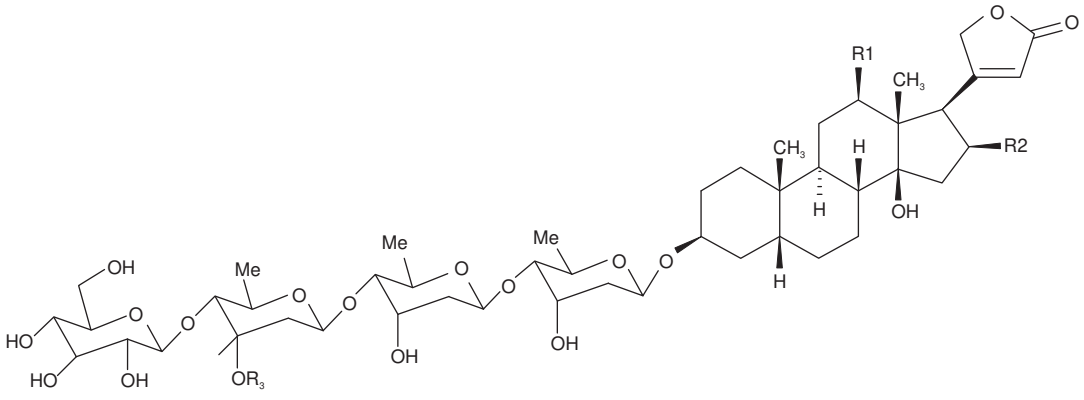
The leaves are sessile, linear-lanceolate, about 30 cm long and 4 cm broad with entire margin and apex is acuminate. The veins leave the midrib at an acute-angle. The epidermal cells are beaded with anticlinal walls, has 10–14 celled nonglandular trichomes, and the glandular one.

Chemical Constituents

Digitalis lanata contains cardiac glycosides like lanatoside A, B, C and E. Lanatosides A and B are acetyl derivatives of purpurea glycosides A and B respectively. Hydrolysis of Lanatoside C yields digoxin, a crystalline active glycoside.

Uses

It has gained much importance in recent years because of the less cumulative effect and three to four times greater activity than *D. purpurea.* They have the same actions as that of the *D. purpurea.* It is the commercial source of digoxin. Employed in the treatment of auricular fibrillation and congestive heart failure. Their use should always be supervised by a qualified practitioner since in excess they cause nausea, vomiting, slow pulse, visual disturbance, anorexia and fainting.



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