



## The evolution of pharmacy Theme C, Level 2

### The development of medicines

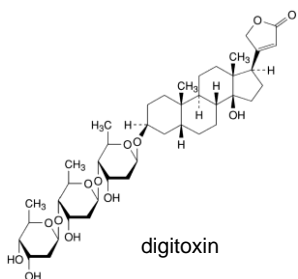
#### Digitalis

Dried leaves of the common foxglove, *Digitalis purpurea*.

The plant is poisonous and does not have a long history of herbal use, although the drug is reported by Trease to be a traditional Welsh remedy of the 'Physicians of Myddfai'. The leaves are collected, rapidly dried to avoid breakdown of the active principles and either powdered and tabletted or extracted to make a tincture. It contains inotropic cardiac glycosides which are used to strengthen the heart muscle. It was first recommended by Parkinson in 1640 and introduced into the *London Pharmacopoeia* of 1650. William Withering started to use digitalis leaf in the treatment of dropsy after investigating a herbal remedy supplied by Mrs Hutton of Shropshire, and published his work on its clinical use in 1785. Jenny Uglow describes the discovery:



Curiously the work that made him famous was provoked by the very lore he so despised. When he first came to Birmingham he used to drive back every week to see patients at the Stafford Infirmary. The horses had to be changed on the thirty-mile journey, and one day during this stop he was asked to look at an old woman with dropsy. His prognosis was bad and he was later astonished to find that she had recovered, helped by a mysterious herb tea, made according to an old family recipe, 'kept secret by an old woman in Shropshire, who had sometimes made cures after the more regular practitioners had failed'. It led to vomiting and purging, and Withering saw that it contained twenty or more different herbs, 'but it was not difficult for one conversant in these subjects to perceive that the active herb could be none other than the Foxglove.



Digitalis, although powerful, is a very toxic herb and the margin between the effective and toxic doses is very narrow; patients have to be carefully introduced to the drug and monitored frequently. The active principle, the secondary cardiac glycoside digitoxin, was isolated by Nativelle in 1869, crystallised by Schmiedeberg in 1875, and finally purified by Windaus in 1925. The drug has a narrow therapeutic index and is about 70% bound to blood protein, resulting in a slow onset of action and elimination from the body.

The potency (content of cardiac glycosides) was originally determined by biological assay in guinea pigs through comparison of the LD50 with that of a standardised preparation adjusted to the assumed potency of the sample, but was later replaced by a colorimetric method, using digitoxin as a standard.

In the 1920s, it was found that the related species *Digitalis lanata* (so called because of its woolly flowers) had a greater activity than *D. purpurea* and in 1930 Smith of Burroughs Wellcome announced the isolation of a new secondary glycoside, digoxin, which has become the standard treatment because of its lower protein binding and faster clearance from the body than the *D. purpurea* glycosides.

*Digitalis* is rarely used today; the pure, chemically standardised digoxin preparations having replaced it.

