A Miracle Cure

The theme of medicinal plants has been extensively explored in the University of Oxford Botanic Garden and was one of the themes for a joint study day at the Museum in December.

The accompanying activities are designed to make the relevance of science clearer and give an insight into how scientists really work, as well as reveal more about the origin of medicines and the processes of their discovery, production, approval and use. Plants are used to explain these processes, with examples that are familiar, enlightening and provocative.

So where do our medicines come from? Some modern medicines have their origins in plants that have been used for centuries. In the 1700s, Reverend Edmund Stone wrote about the success of the bark of white willow, *Salix alba*, in the cure of the "agues," or fevers with aches. In 1897, a German chemist, Felix Hoffman synthesised a more effective version of the active ingredient of willow bark. Today this is sold as aspirin and it is the most administered medicine in the world, predominantly for its use as an anticoagulant.

In contrast, the discovery of breast cancer treatment Taxol was a relatively recent, chance discovery. In 1962 an American research group collected a range of botanical specimens. Extracts from Pacific yew, *Taxus brevifolia*, were mixed with a human cell line in a series of in-vitro tests. Unexpectedly the chemicals in the plant extract were observed to act in a novel way, interfering with the process of cell division. When used in human trials the chemical halted the progression of a significant number of cases of breast cancer. This chance discovery was a consequence of the approach, then current, to screen as many new specimens as possible and look for molecules that behave in a potentially useful way.

Once an interesting plant derivative has been shown to have an effect in in-vitro experiments, the chemical has to be sourced or synthesised. Plant biochemistry if often a complex process and sometimes it is easier and more cost effective to harvest the chemical than to synthesise it. As a result such plants are often grown on a large scale. This is the case for digoxin and digitoxin, two drugs that treat heart conditions are harvested from the British foxglove, *Digitalis purpurea* and the woolly foxglove, *Digitalis lanata*.

In the case of Taxol the story was more complex. This chemical was produced in low concentrations in the living tissue of the trees, directly beneath the bark. Removing this material eventually weakens and kills the Pacific yew, and it was soon apparent that it would be impossible to treat everyone suffering with breast cancer using the plant as the only source of Taxol. However, further research revealed that English yew, *Taxus baccata* produced a similar chemical in its leaves. With some chemical tinkering it was shown to work in the same way as Taxol. If fact, this form of the drug was more soluble,

and therefore easier to administer. This modified form is still used today and is commercially known as Taxotere.
Ironically, when Jacob Bobart was trimming his decorative yew plants in the Garden he was unwittingly harvesting something arguably more potent than all the other medicinal plants growing in his Garden put together.

However synthesising the chemical can have its advantages. If a company synthesises a modified form of a drug and patents the process then the revenue the patent generates can offset costly clinical trials. Proving the drug works is more important than understanding how it works. St John' wort, *Hypericum perforatum* is hailed as a miracle cure for mild depression. The active ingredient, hypericin has been isolated and has shown to be effective in trials. How it works, however, is still a mystery.

Sometimes the biochemical processes needed to create a drug from scratch are too complex to recreate in a cost effective way in the lab. This does not necessarily mean that the discovery leads to a dead end. Probably the most famous of all plant based cancer drugs are those derived from the rosy periwinkle, *Catharanthus roseus.*
In the 1950's the American pharmaceutical company Eli Lily patented the process of extraction of the active chemicals from the plant. This patent covered the cost of clinical trials and today the drugs, Vincristne and Vinblastin earn Eli Lilly over £75,000,000 annually.

This discovery and eventual patenting of the extraction process saved the rosy periwinkle from the brink of extinction. It may be too late for other potential miracle cures. Fewer than 10% of the world plants have been screened for their medicinal properties. The Gran Canaria Group, whose members include major biodiversity conservation organisations and botanic gardens, recently reported that 1 in 4 of Earth's 40,000 plant species are already on the brink of extinction. Environments are changing faster than plants can migrate, and this could cause half of Europe's plant species to be lost in the next 80 years. The figures speak for themselves.

The development of new medicines, from discovery to development, is a complex and intriguing process. However this is not the end of the story. New medicines have to be approved before they can be prescribed. This final barrier can sometimes be the most difficult to overcome, particularly if the medicine is derived form a controversial source. Sufferers of conditions such as MS were increasingly resorting to the use of cannabis to treat chronic pain. Although the effectiveness of this treatment was dependent on the highly variable nature of the source, increasing numbers of MS sufferers were ending up in court, and receiving light sentences, or effectively being let off. Concerned that this was bringing the drug laws into disrepute, the government began making positive, if cautious, noises about legalising medicinal cannabis if a pharmaceutical form could be developed. In November 2005 Sativex, derived form the plant *Cannabis sativa*, was

licensed in the UK. Since then there has been a flurry of controversy about its effectiveness from renowned scientists around the world.

The following activities allow students discuss the concerns expressed by scientists and try to decide which side of the argument is most credible. Students can evaluate the quality of science in the news by looking at the difference between facts and opinions, discussing the results of actual experiments and the validation of the work of one particular research group by other scientists working in the field. Finally students can decide whether the approval of Sativex was a decision they would endorse.