

LECTURE TO KING'S COLLEGE LONDON

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Phytopharmaceuticals and Cosmetics

INTRODUCTION

[SLIDE T13]

Thank you for inviting me to speak to you today, I was both thrilled and honoured to accept Dr. Peter Houghton's invitation

I am a Herbal Archivist and as a hobby I collect data on plants - some people collect stamps, some collect beer mats, some collect condom packets, but I collect data. Which is rather sad isn't it! My heroes and heroines are people like Culpeper, Gerard, The Physicians of Myddvai, The Abbess Hildegard von Bingen, Philipp Theophrastus Bombastus von Hohenheim (who thankfully for us was better known as Paracelsus), Galen, Pliny the Elder, and Dioscorides to name but a few.

Today, I am going to take you through an historic trip of medicinal plants, I am going to share with you the excitement that this ancient field of science has for my industry and for me in particular. But first let me tell you a little anecdote.

THE BASIC PHILOSOPHY

[SLIDE G41]

Jivaka was an ambitious young man whose one desire was to study medicine. He made his way to the land of the five rivers in the Punjab, where he knew that Atreya, a famous physician took on candidates to learn the art of his medicinal skills. For each vacancy there were many times more students willing to fill it.

There were many trials to be completed, but the first test appeared easy, to simply go out into the jungle and bring back a plant that was medicinally useless. The three candidates went out to solve the quest. In a short time, the first candidate returned and proffered a weed, shortly afterwards, the second candidate returned with a bunch of dead prickles, after a morning, the third came back with a marsh plant. Jivaka stayed out a day, searching as he had never searched before, he stayed out another, walking and scrubbing about in the undergrowth, looking in trees, scrabbling in ditches and beside the watering holes. Eventually he came back after three days of searching, more than a little hacked off, tired, hungry, best trainers ruined and empty-handed. He could not

find a single plant that did not in some way have a healing virtue. He was, as you might have guessed, the successful candidate.

It is this story that we should all keep in mind, someone once said that there was a plant for every ill and a plant for every need. I suppose the secret is to recognise them.

HERBAL PRODUCTS

Let us now consider some products that were prescribed by some of those early herbalists and look to see if there was any scientific foundation to their endeavours, please join me in an historical trip through time and let us stop off at various points in our journey.

Pliny the Elder [1st century]

We fly back in time to the first century and to one of the earliest recorders of herbal medicine. We are in Como in northern Italy just in time to witness the birth of Caius Plinius Secundus or Pliny the Elder.

The year is A.D.23, and in A.D.79 he is destined to die during the eruption of Vesuvius, an event graphically described by his nephew and heir Pliny the Younger. I am sure that any Classics scholars amongst you will have studied Pliny as part of your course - I certainly did.

[SLIDE G33] Pliny was a huge collector of data and information, he wrote many books, but only one survives, a work of a mere 37 volumes, which was probably the first encyclopaedia ever written. The first volume was purely devoted to the contents of all the other volumes! It was called the *Historia Naturalis* and this slide shows a page from the edition held in the Victoria and Albert Museum. It was probably made in the 15th century commissioned and owned by Gregorio Lolli Piccolomini, a physician.

[SLIDE L49] We suspect this, because his coat of arms appear in one of the plates of the book, which depicts a physician bleeding his patient. A technique which, incidentally, is seriously being examined by modern medicine along with the use of medicinal leeches (*Hirudo medicinalis*) to help clear blood clots from forming under skin grafts. If anyone is interested in reading more on the subject, then I would commend to you a recent article in December 1995 *The Pharmaceutical Journal*, or speak to Professor Terence Ryan at the Churchill Hospital, Oxford.

A passage that I particularly liked was the reference to the fact that (and I quote) "a poultice is more efficacious if laid upon him by a maiden, herself fasting and naked, who at the same time has to repeat certain special words". I have no doubt that any man would feel immensely better under these conditions but I have been unable to ascertain what those words should be, I am not sure that it really matters!

Pliny also makes quite a profound statement for its time "The properties of all plants are weakened by habit, and they cease to be beneficial when needed if they have been in daily use". This applies as much today as it did then, and we could happily include modern synthetic medicines in this statement.

Germany: Abbess Hildegard von Bingen [12th century]

[SLIDE Q43] And so it is time to set off again and we fly north and forward in time. We arrive in the 12th century in the small German town of Bingen, [SLIDE Q44] here we find a remarkable lady, who was a mystic, stateswoman, writer of holy songs and also a phenomenal herbalist. [SLIDE Q45] Her name is the Abbess Hildegard von Bingen.

[SLIDE H20] Many of her recipes include fragrant herbal materials, in one example she mentions the use of wood betony leaves (*Stachys officinalis*) used in herb pillows. Our own [SLIDE Z2] remedy used in much the same way would be hops (*Humulus lupulus*). She says:-

"Whoever is plagued by wrong dreams should have betony leaves close by when going to sleep, and this person will see and feel fewer bad dreams".

[SLIDE AK47] She also uses another fragrant material, powdered English Geranium in a 'flu powder, which should be smelt, (she stresses) **not sniffed**, several times a day after blowing the nose. It has quite a sharp smell and is certainly less aggressive than Eucalyptus and Wintergreen oils or menthol and camphor.

[SLIDE I14] There is an interesting cure for hayfever, which is to inhale the fumes from smoking Yew-tree wood, prepared by placing the shavings of a small piece of the wood into a flower pot and then heating the pot on the stove. A flowerpot seems a strange idea, because it has a hole in the bottom, until you think about the purpose of the apparatus. The air circulates through the bottom of the pot and convects upwards carrying more vapour than a pot without the hole.

I tried this at home to see what it smelt like, it really did seem to relieve nasal congestion and was quite soothing to the eyes.

The Physicians of Myddvai [13th century]

We venture into the beauty of Wales and are headed to a small village outside of Carmarthon to visit The Physicians of Myddvai, renowned Welsh herbalists of the 13th. century. They probably had their knowledge from as early as the 6th century, not only from the Romans, but also the [SLIDE Q46] Celtic priests and the Druids of the time.

Take goat's dung, barley meal and red wine, boil together into a poultice, and apply to the part. This is the remedy, when the sore is not opened (by the forcible removal of the crust). Now I think we would all agree that barley is well respected for skin conditions as are most grains such as wheat and oat, and wine could also be explained perhaps as an astringent or mild antiseptic, but why the goat's dung? I really cannot comment.

Whatever the apprehension that I would have for this recipe, I would most certainly avoid the next one which is for application to 'proud flesh' which I interpret as another term for over-active fibroblast activity and the formation of excessive scar tissue.

[SLIDE Q49] Take a toad that can scarcely creep, beat it with a rod, till irritated, it smells, and dies. How irritated can you get? Then put it in an earthen pot, closing the same so that no smoke can come out or air enter in. Then burn it till it is reduced to ashes, and apply the same to the part. Not exactly animal friendly is it - and I could not begin to comment on this recipe from a scientific point of view!

But let's look at a recipe that they used for "any type of wounded integument".

[SLIDE F4] Take the feverfew, bruisewort....

... and here we have a problem, and at the same time, the explanation as to why we are moving to Linnean names on our ingredient declaration in the cosmetic industry. Bruisewort can apply to three herbs.....

[SLIDE H35] Daisy (*Bellis perennis*)

[SLIDE P16] Soapwort (*Saponaria officinalis*) and

[SLIDE K4] Comfrey (*Symphitum officinale*), though experience would suggest that it is the latter of the three that is used.

[SLIDE H31] also Ribwort Plantain (*Plantago lanceolata*)

[SLIDE E14] Common plantain (*Plantago officinalis*) and finally

[SLIDE B27] Sage (*Salvia officinalis*) in equal portion of each, bruise them briskly in a mortar, and boil in unsalted butter, till the butter disappears, then strain well and keep in a box. Anoint any bruise with this.

A modern herbalist would not be at all uncomfortable with this product and most of these herbs are well cited for the treatment of problem skin conditions. Comfrey contains one of the richest natural sources of allantoin, which is described in Merck as a topical vulnerary and skin ulcer therapy. Both Ribwort Plantain and Common Plantain are well cited in the literature for their beneficial effect on sores, treatment of wounds, bruises and insect bites. They contain a high mucilage content rich in polysaccharides as well as a number of alkaloids (such as aucubin, indicaine, plantagonine etc.). Sage is another well-respected herb for problematic skin conditions, and the oil most certainly possesses antiseptic action. Some of the beneficial properties may be attributed to the tannins, which give the plant its astringency, and flavonoids which would account for some of the vulnerary virtues. A quotation from the Salerno Medical School in the 11th century reads “Why should a man die if sage grows in his garden”, at the end of the treatise it says “Sage, thou healer, Nature’s mediatrix”.

Gilbertus Anglicus [15th century]

In the early 15th century, there existed a gentleman by the name of Gilbertus Anglicus, who developed and marketed a salve. The formula is as follows.

[SLIDE G12] Take a very fat puppy dog and skin him; then take the juice of cucumber, rue and pellitory; berries of ivy and juniper; fat of vulture, fox and bear in equal parts; stuff the puppy therewith and boil him. Add wax to the grease that floats on the surface and make therefrom an ointment.

This is a tricky recipe, because it is difficult to obtain some of the ingredients, especially the berries of [SLIDE AC31] *Hedera helix* and [SLIDE I32] *Juniperus communis*, which are only available for a limited time during the year. Joking apart, the recipe contains animal fats which would be excellent emollients on the skin, cucumber which is traditionally used as a soothing component in eye gels, ivy which is used in prevention of oedema and the treatment of cellulite, juniper has antiseptic properties and is used in cases of eczema, acne and other skin problems. [SLIDE Z48] Rue or *Ruta graveolens* is a rather powerful herb and a photosensitiser, but it has been used in the past for varicose veins and for its anti-cellulite properties.

THE DOCTRINE OF SIGNATURES

Paracelsus [16th century]

Let us consider Paracelsus, born in 1493, he was one of the first to lecture in German as opposed to the traditional Latin, and proposed a philosophy known as the Doctrine of Signatures.

"The mind need not concern itself with the physical constitution of the plants and roots. It recognises their powers and virtues intuitively thanks to the signatures they carry".

This is probably best explained with a few examples.

[SLIDE AL12] Let us look at Heartsease or Wild Pansy, *Viola tricolor*. The lower leaves are heart shaped, and so the Doctrine stated that this plant should be good for the heart. In fact it is a heart tonic, and has been used in cases of heart failure. There is no clinical data that supports this effect, but the chemical constituents responsible could be anything from the salicylates to the unusual glycosides present.

[SLIDE H45] Self Heal or *Prunella vulgaris*, is also known as the Carpenters' herb, because the corolla is shaped like a bill hook. The doctrine said that this plant should be good for wounds caused by scythes or similar implements, and it is a proven vulnerary (or wound healer) and helps stop bleeding. Again, we are not certain of the responsible actives in this plant, but one might speculate that it is the pentacyclic triterpenes present that are giving this effect such as ursolic acid.

[SLIDE AL7] Celandine or *Chelidonium majus* has a bright yellow juice and so should be good for biliary conditions and jaundice. Examination of its properties shows it to be an antispasmodic, reducing inflammation of the biliary ducts and has been used successfully for the treatment of jaundice. It is very likely one of the alkaloids present in the plant, chelidonine, chelerythrine or sanguinarin that are responsible for this effect.

[SLIDE I30] Eyebright or *Euphrasia officinale* has spots on the flowers that look like blood-shot eyes. This is a superb plant for conjunctivitis and sore or inflamed eyes and it makes an excellent eye wash. To my knowledge, there have been no studies carried out on this plant to determine the active component responsible for this effect, but one might hazard a guess that it is the glycoside aucubine.

[SLIDE L42] Willow or *Salix alba* grows in damp places, because of this it was assigned under the Doctrine to be valuable for conditions caused by the damp, for example rheumatism. The willow bark was prescribed and worked. Modern technology investigating the reasons for the success found a glucoside called salicin from which salicylic acid or aspirin was derived. Other plants which have also been helpful in rheumatism have also been found to contain salicin (for example wintergreen, birch bark and other members of the *Spiraea* family). As we know, the prescribing of aspirin as an analgesic in rheumatic and sciatic conditions is well documented.

[SLIDE D12] Walnut or *Juglans regia* looks like a brain and so should be good for headaches or mental disturbances. We discover that the walnut is one of the foods rich in manganese, important for nerves, brain and cartilage. Nutritionally, the Missouri Black walnut is of the highest manganese content. But perhaps I am trying to make this plant fit the case.

MODERN HERBAL MATERIALS

That is probably enough of the historical anecdotes, let me now look at some of the more interesting modern materials that are being examined. I intend to concentrate primarily on topical drugs intended for the skin and related mucosa, since that is my main area of interest. However, I would like to remind you of just a few of the medicinal plants that have been of key importance in recent times.

[SLIDE I15] The yew (*Taxus baccata*) has already been mentioned earlier in a recipe from the Abbess Hildegard von Bingen, but today we would think of yew (particularly the Pacific Yew, *Taxus brevifolia*) for its taxol content, which is being used very successfully as a chemotherapy treatment for breast and ovarian cancer. This drug is being marketed by Smith Klein Beecham, if my memory serves me correctly.

[SLIDE A6] Another plant that has recently made the headlines is Bluebell or *Endymion nonscriptus*, which contains lectins that can bind to sugars, and specifically to the glycoprotein gp120, the characteristic surface glycoprotein of HIV.

[SLIDE AC29] While we are thinking of spring flowers, we should spare a thought for the Snowdrop or *Galanthus nivalis*, which is a rich source of galanthamine. This plant drug has been investigated by Shire Pharmaceuticals

for Chronic Fatigue Syndrome and may have some benefit to patients suffering from Alzheimer's Disease.

[SLIDE AA35] On the subject of this very distressing disease, it has been clinically proven that Tobacco or *Nicotiana tabacum* can help these patients, especially in the partial restoration of the brain's organisational ability. The nicotine interferes with the tyrosinase pathway?

[SLIDE W13] Another plant that has been heavily promoted for improving mental acuity is that of the Maidenhair tree or *Ginkgo biloba*, where the ginkgolides seem to have their effect by improving cerebral blood flow. A study was being conducted at Reading University, but I do not know the results. There is a Commission E monograph in Germany for this plant.

TOPICAL MEDICINAL PLANTS

Obviously, I could carry on with this list until dinner time, but I must now concentrate on those topical plants that I promised - and I have to say that the number of potential materials is absolutely huge. Well over a thousand plants come up on my data base, which are suitable for the treatment of skin diseases.

The areas in which I am particularly interested are the medical conditions of eczema, psoriasis, skin ulcers, burns and acne. However I am also interested in cosmetic conditions, such as, freckles, age spots and wrinkles. The condition that falls between the two stools is that of cicatrisation - is the treatment of scar tissue a cosmetic function, or are there physiological factors involved which make it a medical function? I think the answer is probably medical.

Forgive me if this next fundamental statement is so obvious that it does not need stating, but I really do not know my audience that well! Many 'plant based' trials fail, because the people setting up the trial do not know their botany, phytochemistry or their pharmacognosy. The collection of the right species, the right part of the plant, at the right time of year, from the right growing conditions, having the right climate, using the right harvesting and storage techniques as well as ensuring that the right extraction procedures are used, are absolutely vital. You might agree that wine made by boiling dried vine leaves in propylene glycol would be a treat worth avoiding.

In some cases, it is the hydrophobic part of the plants composition in which we are interested, in others it is the hydrophilic part that interests us. The extraction may be of the leaves, flowers, seeds or fruits, stems, rhizomes, roots or bark. In some cases it may be the fungus or wax that forms on the plant, or it may be the work of insects that we are looking to harvest (e.g. shellac).

HYDROPHOBIC EXTRACTS

Tea Tree oil

Let us first look at the family of *Melaleuca*. This is a very useful family, which includes [SLIDE AL46] Niaouli (the Paper Bark Tea Tree) or *Melaleuca quinquenervia* synonym *Melaleuca viridifolia* - an important perfumery oil, Cajuput (the Swamp Tea Tree) or *Melaleuca leucadendron*, which is another perfumery oil. However, the one about which I am going to talk is [SLIDE AN15] *Melaleuca alternifolia* which is the Tea Tree and used as an antiseptic.

The aborigines knew about this plant three thousand years before we did, some fresh water lakes were considered sacred, because they would cure a number of skin diseases.

[SLIDE AM27] The water of these lakes was tinged a brown colour, from the tannins it contained, [SLIDE AM28] and these tannins came from the tea trees that grew around the lake margin.

Never dismiss the folk lore or ethnobotanical use of plants, in most cases the traditional use of these trusted remedies can stand up to technical scrutiny and clinical trial.

I talked a little earlier about the importance of getting all the parameters just right, so let us look now at how this plant is grown, harvested and processed. Though the aqueous extract of tea tree is effective, the oil is even more potent.

[SLIDE AM36] First the sappling is planted using this ingenious piece of equipment.

[SLIDE AM41] When the plant is this tall it needs to be harvested

[SLIDE AN11] This is done by cutting the plant down and macerating it with this piece of kit

[SLIDE AN12] This is what's left after cutting, and the root stock can be harvested for another 6 years

[SLIDE AN13] The macerated plant is then fed directly into the distillation bins

[SLIDE AN6] From the bins it is taken into the distillation plant, where it is steam distilled

[SLIDE AM48] The oil comes over with the condensed steam and is separated off

[SLIDE AN5] The final oil is separated into pharmaceutical and cosmetic grades and stored in stainless steel drums

So just how powerful is tea tree as an antiseptic? If one uses the Rideal Walker test, then one finds that it is about 11 times more potent than phenol, but without the potential to produce skin burns. The chloroxylenol in Dettol has a value of about 60 compared to phenol. It is the complex blend of terpenes, sesquiterpenes and their corresponding alcohols that give tea tree these properties.

A 5% tea tree oil cream was tested against a similar cream containing 5% benzoyl peroxide in a single blind randomised trial. The tea tree performed as well as the benzoyl peroxide, and though the effect was slower, the patients using tea tree experienced less side effects. The action is more than likely due to its ability to knock out *Propionibacterium acnes*.

The oil has also been tested for vaginal candidiasis, topical skin infections (such as athlete's foot) and clearing of *Staphylococcus* infections.

Chamomile oil and extract

[SLIDE AD2] Another plant, which I have been looking at for the last five years or more is *Matricaria recutita* or German Chamomile, which is already used in a licensed product in Germany called Kamillo-san.

[SLIDE AE12] A product with the same name is marketed by Norgene in the UK, however, the plant used in this product is *Anthemis nobilis* or Roman Chamomile. The German product is standardised against chamazulene, whereas the UK product is standardised against (-)- α -bisabolol.

Both products rely solely on the essential oil obtained from the flower heads of the respective chamomiles (which are both members of the Compositae family). However, folk lore also mentions the use of the hydrophilic part of the flower extract. This extract is rich in flavonoids, particularly in apigenin and apigenin-7-glucoside.

All of these active components, the bisabolol, the chamazulene and the apigenin explain the plant's reputation for being anti-inflammatory, antipruritic and granulating to damaged tissue. There are many clinical trials that have been successfully completed to substantiate these effects, but time does not allow me to go into detail. I am more than happy to let anyone who is interested to have this data after I have finished my paper.

Aloe vera gel

[SLIDE W17] Most pharmacists will be familiar with the dried aloes or *Aloe ferox*, which is a dried extract of the whole plant used as a rather drastic purgative. However, this is not the species of plant in which I am interested.

[SLIDE AL19] The plant most renowned for its skin care properties is *Aloe barbadensis* Miller, where only the inner gel obtained from the inner, colourless, mucilaginous parynchema (or tubular leaf cells) is used. We take every precaution to ensure that only the gel is taken, since the outer leaf contains anthraquinones, such as aloin and barbaloin, which are known skin irritants.

It was folklore that first came to the attention of many researchers. The gel was used for the severe Roentgen burns experienced by some of the early researchers investigating x-rays. Later, after the dropping of the atomic bombs on Hiroshima and Nagasaki, the plant was dispensed as a treatment for severe radiation burns.

The plant then came to be investigated for other sources of burns, and anecdotal evidence exists for the treatment of animals which suffered severe thermal burns, that otherwise would have perished had it not been for the intervention with aloe vera gel.

Today, we are looking at aloe vera gel for prophylactic use in patients undergoing radiotherapy treatment to ablate the skin reactions that can occur during radiotherapy at day 3 (a primary 'sun burn-like' erythema) and then at day 10 (when a secondary erythema can develop). Professor Sato in Japan has successfully carried out two animal trials in this area, and we are about to enter into clinical trials at Christie Hospital Manchester. Further work has been published by Strickland at the Anderson Cancer Centre in Texas, who examined the prophylactic effect of aloe vera gel in UV-induced erythema.

The chemical entities responsible for this effect are still being defined, however, in all likelihood it is the complex polysaccharides, mannose-6-phosphate, and sugars that are the key agents. We are also looking at the possibility that it is the presence of gibberelline (a hormone growth regulator) that is in part responsible

for some of the beneficial properties. In reality, it is very likely the entire combination that is important.

CONCLUSIONS

Time does not permit me to cover any more of the plants that we are investigating, such as [SLIDE J10] Burdock or *Arctium lappa*, Liquorice or *Glycyrrhiza glabra* and *Glycyrrhiza uralensis*, which contains the exciting compound glycyrrhetic acid and 18- β -glycyrrhetic acid. Nor do I have time to speak about a number of fixed oils such as Rosehip oil or *Rosa rubiginosa* and Sea Buckthorn oil or *Hippophae rhamnoides*. I know that Peter has spent a great deal of time investigating the chemistry of these last two oils, and we are actively looking at the clinical effects on the skin. On the rosehip oil, I still believe that this is a potential source of Retin A, despite the fact that the samples that this department examined did not show its presence. That is not a criticism of the analytical chemistry, but it is a criticism of my sourcing of the oils, and the age and condition of those oils.

I did say that I was going to discuss the use of plant extracts in skin care and cosmetics, we do use them, but usually at low levels, and then only for their protective action. To have really high levels would likely induce a physiological benefit, which would mean that we would infringe the criteria laid down in the Medicines Act.

My conclusions are simple, plants most certainly provide drugs, some of which are extremely potent.

[SLIDE AK21] We only have to look at digitalis from *Digitalis purpurea*
[SLIDE X14] aconite from *Aconitum napellus*, [SLIDE AE5] opiates from *Papaver somniferum* to see just how powerful these drugs can be.

Never ignore the ethnopharmacy, very often the proof is easy to find. There is a fortune to be made in this field. [SLIDE G11] This is me back at work. Thank you for inviting me to speak to you and thank you for your attention.

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