



## THE SOCIETY OF COSMETIC SCIENTISTS 1999 SPRING SYMPOSIUM

### Cosmeceuticals – one small step or a giant leap

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#### **“Proving benefits for botanical products”**

##### **Opening acetate**

##### **Introduction**

Good afternoon Madam Vice President, Ladies, Gentlemen and Fellow Scientists

For those of you who like to read the preprint during the presentation, please go ahead, but it will not relate to what I am going to say this afternoon, since I will be elaborating on that document.

Herbal products are now big business, not only for our industry, but also for the pharmaceutical and dietary supplement industry. The MCA or Medicines Control Agency is worried by this sudden flurry of activity and who can blame them. And yet, despite the fact that they are prepared to force you to take a product off the market as being a herbal medicine, they are exceedingly hesitant in granting that same product a Marketing Authorisation or Pharmaceutical Licence. It is a no win situation.

If in doubt as to the efficacy of plant materials, remember the highly toxic species that exist around us around the world, such as the Giant Hogweed (*Heracleum sphondylium*) and Hemlock (*Conium maculatum*), as well as the active principles such as Curare from *Chondodendrum tomentosum*, and Strychnine from *Strychnos nux-vomica* to name but a few. Careless handling of these plants will most certainly cause severe skin irritations and maybe death if ingested or absorbed through the skin.

Clearly, some plants in even relatively small concentrations will have very noticeable effects.

##### **Consultants nightmare**

As you probably realise consultants are expected to be on call 24 hours a day, we are always sitting around enjoying a quiet drink in the garden when it is sunny or watching the television when it is raining, waiting for a client to call. Ready to jump into action at the drop of a hat. Though this might be the impression we give, in reality we are usually working on a number of projects simultaneously. This can lead to very long hours and extreme tiredness. So I thought I would surf the net for some solutions. Imagine my joy when I found an advert that said “stay up all night”, this was the answer to my prayers, a herbal remedy that would act as an amphetamine. But I was wrong!

**[Acetate 2]** This was a different type of “stay up” to the one I expected!

### **Aphrodisiac preparations**

On examining the claims made for this product, purely out of professional interest you understand. I am doing a further external degree in the treatment of male erectile dysfunction using natural products. I noticed that the product contained Lola Nut, Guarana, Passion Flower, Ginseng and Damiana.

I searched for Lola Nut in my data base and could find nothing, no Latin name, no clue as to what this might be, nor did a search of the internet throw up any new information (apart from the company that was using it!).

Guarana is a tonic stimulant and full of caffeine. Despite its sexy name, passion flower is a sedative and would counteract the benefits of the guarana. Ginseng is not an aphrodisiac, it is a tonic plant and there is no mention anywhere in the serious literature that it is anything but as an alterative tonic.

**[Acetate 3]** In this next slide, another aphrodisiac preparation which this time contains Muira puama or *Liriosma ovata* (in which no active ingredient has been found that produces any effect) also contains damiana. You can rule out Smilax, which is sarsaparilla and royal jelly, because they are a source of flavour and trace minerals. If you were a bumble bee, then this product might have some benefit.

**[Slide 1 (BD4 – 12)]** Damiana is an aphrodisiac according to all the references, probably over 60 authoritative texts confirm that the active principle is damianin (a resinous compound), but there has never been an analysis on this material and nobody on the planet can tell me what it is, or if it even really exists! All the reported information says a “reputed” aphrodisiac, no clinical data exists to substantiate the claim.

So already you can begin to see, that by looking at the chemistry of the plant, by searching the literature and looking for the results of clinical trials or animal studies, you can begin to build up a picture as to whether the effect claimed is likely to be valid or not.

**[Acetate 4]** Here is an example, where major claims are being claimed for another internal herbal product:

### **Cellasene.**

A new product has recently hit the market called Cellasene.

*“Cellasene contains carefully selected herb extracts in a formulation designed to tackle ‘orange peel skin’ and to help keep legs smooth. This is the original Cellasene, which received enormous media coverage when it was launched in Australia. In Italy the product has been successful for the last 3 years with its popularity growing due to recommendations made by its delighted users.”*

Additional information:

*“The herbs in Cellasene have been chosen for their recognised ability to support the capillary network that runs throughout all the tissues of the body including subcutaneous fat deposits. A healthy capillary network is needed to ensure that tissues are kept supplied with nutrients and that any fat stored in the tissues is able to be mobilised when required.”*

*Cellasene has been tested in studies at a University in Italy. The studies were designed to investigate if the product could reduce the ‘dimpling’ of the skin that commonly occurs on women’s thighs, sometimes referred to as ‘orange peel skin’. The studies produced statistically significant results against a number of measurements. For most women the effect was noticeable. However, the results show that Cellasene does not work for everyone.*

The carton lists the primary ingredients as Evening Primrose oil, *Fucus vesiculosus* (a seaweed called Bladderwrack), *Melilotus officinalis* (Melilot of Yellow Sweet Clover), *Ginkgo biloba* and various other excipients, (which would probably have no effect on oedema or cellulite). For completeness these are gelatine, fish oil, glycerin, soya oil, lecithin, fatty acids and colour.

**[Slide 2]** In ingredient order, Evening Primrose is a useful dietary supplement, but would have no effect on oedema, though it is good for atopic eczema, mastitis and contains EFAs (essential fatty acids) and PUFAs (polyunsaturated fatty acids), which are good for protection of the coronary artery and its associated diseases. The oil is also a rich source of GLA (gamma-linolenic acid), which is a good anticoagulant and precursor to prostaglandin.

**[Slide 3 ]** *Fucus vesiculosus* is a product, where derivatives have been used for the treatment of cellulite. It is cited for its antihypothyroid, anti-obesic, anti-rheumatic properties. Traditionally it has also been used for lymphadenoid goitre and myxoedema, and this is probably an additional key to the effect of the product.

**[Slide 4 K6]** *Melilotus officinalis* is also cited for anti-oedema and as a venous astringent. It has been cited for the treatment of complaints caused by chronic venous insufficiency, such as pain and heaviness of the legs, treatment of thrombophlebitis, lymphostasis and obstructive oedema. Clearly, this material is the work horse of the formula.

**[Slide 5 ]** *Ginkgo biloba* is capillary dilating and stimulates the circulation in deep-seated arteries. It is very much an herbal material that improves blood flow, which is why it is used in cases of dementia, to improve blood flow to the brain. In this product the ingredients would be expected to improve the transport of waste products from the site of oedema to the lymph drainage system. It is, if you like, the last link in the distribution chain!

Does it really work? No idea. It probably works for a number of women, probably women in the early stages of cellulitis.

**Plants used in cosmetics and toiletries**

I apologise for having concentrated for such a long time on the oral products, and now I would like to move on to those products, which are used topically.

### **The level of plant material to be used**

But before I do, let us just remind ourselves of a few important factors relating to the selection of a particular plant extracts. I will use grape juice as my illustration.

- **[Slide 6 AR1]** Who produced it (the Mondavi Winery)
- **[Slide 7 AR2]** Where was it grown, Iceland is not renowned for its vintage wines
- **[Slide 8 P22]** Which part is used for the benefit required - Imagine a wine made from vine roots or leaves
- Is the fresh or dried plant used? A wine made from raisins is called sherry!
- **[Slide 9 T15]** When was it harvested? Imagine a wine fermented from immature sugarless grapes
- **[Slide 10 AR3]** How was it harvested? Suppose that the grapes were slashed out together with the leaves and stems using a combine harvester, so that the extracted grape contained leaf and woody materials as well.
- **[Slide 11 T27]** How was it processed? What sort of wine would you obtain by using a hydroglycolic extraction to replace the traditional method of pressing
- How much of the plant was used to produce the final product. It is an easy question in wine making, since 100% grape juice makes the wine, but suppose that the pressed juice was diluted with other solvent materials.
- How was it stored? Wine stored in open vats exposed to large volumes of air would quickly turn vinaigre - fine for fish and chips, but not for drinking.

Clearly, the amount of plant material that is used is going to have a bearing on whether the product is likely to work or not. If you use 0.05% of a dilute extract and expect this to have any effect in your product's delivered performance, then clearly you are totally and utterly bonkers!

### **Claim substantiation**

The proof of benefit may come from a number of sources: -

- Literature surveys
- Clinical trials
- Instrumental measurement
- Copying products with Pharmaceutical Licenses (a dangerous route to take!)
- Comparison with other plants containing same active chemicals
- Comparison of benefits with related members of the same family

### **Comparison with other plants containing same active chemicals**

**[Slide 12 ]** So lets look at a few easy examples. Suppose that we were looking at Yarrow (*Achillea millefolium* and other closely related species) and we were not too sure of the claims made for the properties of this plant mentioned in the folkloric uses.

Examination of the constituents in the aqueous extract would reveal that it contained predominantly, the flavone glycosides apigenin and luteolin-7-glycosides, and tannins. In the oil one would find an azulene derivative.

**[Slide 13 ]** The similarity between these components and those of German Chamomile (*Matricaria recutita*) would suggest that yarrow would possess similar properties.

**[Slide 14 ]** Here is the apigenin present in *Matricaria* extract

**[Slide 15 ]** Here is the chamazulene

This is confirmed by the historic uses of the plant, which is defined as being excellent for skin eruptions, chapped hands, sore or inflamed skin.

The anti-inflammatory action of the aqueous extract can easily be explained from the presence of the flavonoid apigenin and the other related flavonoid glycosides of rutin and luteolin.

The knowledge that yarrow is also a member of the Compositae family (Asteraceae) and that many of these daisies have similar properties is quite reassuring.

The occurrence of apigenin and luteolin in nature is quite common, and it comes as no surprise to discover that many of the “soothing” plants such as

**[Slide 16 ]** Plantain (*Plantago major*) and

**[Slide 17 ]** Milk Thistle (*Silybum marianum*) also contain significant quantities of apigenin. Indeed, in one report, it was shown that the apigenin present in Milk Thistle was more effective than indomethacin as an anti-inflammatory agent.

Luteolin is also quite abundant in nature, especially in

**[Slide 18 ]** Roman Chamomile (*Anthemis nobilis*), which has properties that are very similar to German Chamomile, despite being different species.

The oil also has anti-inflammatory activity according to the folklore and on examination of the literature one can find reference to the presence of azulene or its precursors. Azulene is found in both of the chamomiles already mentioned and in addition can be found in another member of the Compositae family, namely

**[Slide 19 ]** *Inula helenium* or Elecampane, which has been reported to have antispasmodic and antipruritic activity.

It is therefore quite reasonable to assign these properties to the substantiation of the claims made for the aromatic oil from yarrow, which is said to be healing and good for itching skin.

Further substantiation can be found from looking at a traditional Chinese medicinal plant

**[Slide 20 ]** Nu Chen or *Ligustrum lucidum* the Japanese Chastity Flower, which also contains azulene and is a soothing anti-inflammatory. There are many other plants that also contain this phytochemical and possess the same properties.

On a less positive note, it should be remembered that most of the Compositae family contain pyrrolizidine alkaloids and that in very rare cases, there may be a possibility of rare individuals experiencing irritation by this material.

Continuing with the Compositae family we could turn our attention to bisabolol, [Slide 21 ] which is another anti-inflammatory agent present in this family. This material is reported in *Anthodium chamomillae*, *Anthemis nobilis*, *Matricaria recutita*, *Eremanthus elaeagus*, *Lychnophora* spp, *Vanillosmopsis* spp, and *Vernonia* spp, which are all of the Compositae family. Coincidentally, it is also found in *Sideritis mugronensis* (Lamiaceae), *Populus deltoides* (Salicaceae), and *Myoporum crassifolium* (Myoporaceae) to name but a few.

### **Comparison of benefits with related members of the same family**

Clearly, members of the same family of plants show striking similarities in many cases, though it would be a dangerous assumption to assume that this is always the case. The potato (*Solanum tuberosum*) would appear to have little in common with [Slide 22 ] Jimsonweed or *Datura stramonium*, [Slide 23 ] Angels' Trumpet or *Brugmansia versicolor* Bittersweet (*Solanum dulcamara*) or [Slide 24 ] Deadly Nightshade (*Atropa belladonna*). [Slide 25 ] Tomato or *Lycopersicon esculentum*.

However, they all have varying concentrations of toxic solanine-like alkaloids, which in the potato are present in the green shoots of the tuber, in the tomato can be found at low concentrations in the leaves and stems.

### **Synthetic copies of naturally occurring ingredients**

Sometimes we can draw on a synthetic material which is “nature identical”, and I could think of no better example than [Slide 26 ] allantoin, which is listed in Merck. This is primarily associated with the plant

[Slide 27 ] Comfrey or *Symphitum officinale* but is also found in

[Slide 28 ] Lungwort or *Pulmonaria officinalis*

[Slide 29 ] Corn Silk or *Zea mays*

[Slide 30 ] Greater Plantain or *Plantago major*

[Slide 31 ] Bearberry or *Arctostaphylos uva-ursi*

[Slide 32 ] Borage leaves or *Borago officinalis*. All of these plants are associated with having a soothing action on inflamed tissues and improve healing rates. It is also excreted by maggots and was found to be a good way to cure battle wounds in the trenches of World War One. In fact you stood a better chance of not getting gangrene if you avoided a visit to the field hospital!

### **Less well known compounds**

What do we do in the case of a slightly more obscure compound? Certainly [Slide 33 ] aucubin is a less well known material and not quite as well documented as the others I have mentioned, so what can we learn about this material? Well it occurs in quite a few plants, such as

[Slide 34 ] Speedwell or *Veronica officinalis*

[Slide 35 ] Eyebright or *Euphrasia officinalis*

[Slide 36 ] Vervain or *Verbena officinalis*

[Slide 37 ] Cleavers or *Galium aparine*

[Slide 38 ] Self heal or *Prunella vulgaris*. By comparing all these plants and noting their properties using tick boxes, one discovers that all of these plants have ticks under anti-inflammatory and skin healing properties and most are ticked for their soothing effect and elimination of skin blemishes. None of the usual sources ascribed a specific topical function to aucubin.

### Comparison of similar molecules

[Acetate 5] Sometimes one can make a guess as to the function of an ingredient by simply looking at the structure of the molecule. In the example that I have chosen, both of the ingredients are well known for their anti-oedema effect. The first is 1-hydroxydiosgenin or ruscogenin the active principle from

[Slide 39 ] *Ruscus aculeatus* or Butchers Broom, whereas the second is hederagenin from

[Slide 40 ] *Hedera helix* or Ivy

Diosgenin is the precursor to the synthesis of hydrocortisone, which as we all know is another anti-inflammatory drug. Most of the steroidal saponins exhibit the same effect.

[Acetate 6] In my last example I am going to look at another two molecules, the first is naringenin, which is the active material in

[Slide 41 ] Grapefruit seed extract or *Citrus paradisi* and is the flavonoid responsible for the antibacterial activity. The second material is found in

[Slide 42 ] Lemon or *Citrus limonum* and is called hesperitin. One might expect this material to have antibacterial activity and indeed it does. You might be thinking that this is not so unexpected, since both plants are citrus fruits. However, hesperetin is also found in Shepherd's Purse (*Capsella bursa-pastoris*), Cleavers (which I showed earlier), Hyssop or *Hyssopus officinale*, and Linden or *Tilia europeae*, while naringenin is found in plants like

[Slide 43 ] Hops or *Humulus lupulus*, Liquorice or *Glycyrrhiza uralensis* and certain

[Slide 44 ] *Epimedium* species. All of these plants show mild antibacterial activity, probably mild, because the content of these materials is not as high as it is in citrus species.

### Conclusions

There are many ways in which the benefit and efficacy of a botanical species can be proven. It is hoped that this paper has demonstrated a rich and varied source of further information that could be explored to offer alternative methods to satisfying the Trading Standards office, that the plant in your product does perform a useful function. Clearly, as I have said before, no active material will confer any benefit to your product, if it is used at a trivial level.

In the preprint I mentioned that there are many excellent texts that can be consulted, these include the British Pharmacopoeia, the World Health Organisation monographs, the Council of Europe monographs and any good volume on pharmacognosy will provide reliable data. The older pharmacopoeias, such as the

[Slide 45 ] British Pharmacopoeia the

[Slide 46 ] United States Dispensatory, Merck, Martindale, and other Materia Medica will provide valuable and valid data.

Modern academic volumes that examine the ethnopharmacy of third world countries will invariably provide solid information and will be totally reliable. All I would say is that you avoid those books written by crackpots and wishful amateurs, because the information they give does not stack up against the scientific facts or the plant's phytochemistry.

I hope that in the short time available, that I have been able to demonstrate that plants are prolific producers of novel and active chemicals, which undoubtedly have a function and a role to play in cosmetics and toiletries. I know that this is the last lecture of the day and many of you will be eager to beat a hasty retreat to the comfort of your own homes. However, if there are any questions, then I would be delighted to answer them.

Thank you for your kind attention.