THE SOCIETY OF COSMETIC SCIENTISTS
1999 SPRING SYMPOSIUM

Cosmeceuticals – one small step or a giant leap

Anthony C. Dweck, Consultant Dweck Data,
8 Merrifield Road, Ford, Salisbury, Wiltshire SP4 6DF.

"Proving benefits for botanical products"

Introduction

Man has been using plants for the care and repair of his body since time began. The old adage "we are what we eat" is as true today as from the moment we climbed out of the primordial swamp and began eating the vegetation about us.

It is increasingly tiresome to note the pharmaceutical industry's lack of trust and faith, when it comes to herbal or traditional medicines. Though it must be said that the more modern thinkers are beginning to realise that most of the exciting leads for the future will come from the plant kingdom. In Appendix I, there is a list of some plant-derived pharmaceuticals, which serves to remind the sceptics of their roots.

If in doubt as to the efficacy of plant materials, remember also the highly toxic species that exist around us around the world, such as the Giant Hogweed (*Heracleum sphondylium*), Curare (*Chondodendrum tomentosum*), Strychnine (*Strychnos nux-vomica*) and Hemlock (*Conium maculatum*). 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.

Plants used in cosmetics and toiletries

There are hundreds, if not thousands, of plants that have been used traditionally for the care of damaged skin and others that have been employed for the protection of healthy skin. Every continent has its own collection of favourite plants, which target specific indications and it would be impractical to attempt to mention them all here. This paper will concentrate on the European herbal remedies and on the substantiation of their benefits, when used in cosmetics and toiletries.

Claim substantiation

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

- Literature surveys
- Clinical trials
- Instrumental measurement
- Products with Pharmaceutical Licenses
- Comparison with other plants containing same active chemicals
- Comparison of benefits with related members of the same family

Literature Surveys

There exists extensive literature on the medicinal plants of most countries. These range from herbal pharmacopoeias to books on pharmaocognosy and ethnopharmacy. The World Health Organisation (WHO) has also published a number of monographs on a wide variety of species, as has the Council of Europe and the British and American Herbal Pharmacopoeias. This information has been contributed to and examined by experts from all over the world specialising in plant medicine and so may be trusted as being true.

The WHO, disappointed by the unaffordable cost to third world countries of western medicines is turning its attention to the study of local remedies for the provision of treatment to suffering patients. This is a valuable source of data and should not be ignored. Indeed, it is extremely likely that the cures to many diseases will be found from the study of plants and not from the study of synthetic molecules. Furthermore, the preoccupation of pharmacists with single active molecules may need to be reconsidered with the increasing evidence that individual plant derived molecules do not work in isolation, but do have exceptional value when used together (e.g. the active chemicals present in *Hypericum perforatum*, when used for depression).

The idea that treating a single indication with a single drug or product also seems to be strange. In the treatment of eczema, for example, the indications might include erythema (redness), scar damage, pruritis (itching) and areas where the skin has been broken. It would be logical to treat the whole condition with one topical product, possibly with an internal product that restores internal equilibrium. This is exactly the way in which the TCM (Traditional Chinese Medicine) works. Again, we can examine the components of TCM products for substantiating claims relating to skin care products.

In addition, there are extensive studies being carried out in numerous hospitals, research centres, and academic institutions to study the phytochemistry and the physiological effects of a huge variety of plants that are regularly published in numerous learned journals throughout the world.

Clinical trials

Clinical trials are very expensive, when carried out under the pharmaceutical/medical protocols. Think in terms of £200,000 for a relatively simple controlled trial. Clearly, this is not within the pocket of many (if any) skin care companies. There are a number of animal studies published, and very occasionally you will come across some very good published clinical studies relating to herbal materials. Most of the studies relate to those carried out on animals for pharmaceutical reasons and a vast number of plants have been examined in animal models over the last five years.

At a more affordable level, there are dermatological tests that are considerably less expensive, but in the most part are used to confirm the safety of a finished product, rather than to prove the efficacy of a particular component material.

At the lowest level, there are consumer (user) trials or panel tests, which will give a level of confidence that may satisfy the Trading Standards officer of a benefit.

Instrumental measurement

There are a large number of instrumental techniques employed by the cosmetic industry, which include the measurement of skin redness (chromameter), the measurement of skin circulation (Laser doppler), skin elasticity (cutometer and other techniques), skin moisturisation (corneometer) etc.

Existing Pharmaceutical License numbers

There is a danger with using the Pharmaceutical License (of Right) or PLR number as a proof of effect, as this extract from a review prepared by the World Health Organisation shows:

"*The review of herbal medicines was completed in 1990. An information sheet on the review for licence holders was published in October 1985 by the Medicines Control Agency. Herbal medicines indicated for conditions capable of self-diagnosis were granted a licence when sufficient evidence of efficacy was established, and the authority required the product label to include the statements "a herbal remedy traditionally used for the symptomatic relief of..." and "if symptoms persist consult your doctor". Combination products containing a large number of herbal ingredients or mixtures of herbal and other ingredients were not accepted, and licence holders were invited to consider to which ingredients the therapeutic claim related and to adjust the formulations.*

Thus a huge number of herbal products were allowed to continue being sold on the market, and there was no requirement to submit the very thorough proof of effect that would be required today. Indeed, it would be highly unlikely that any of these products bearing a PLR number would be able to pass the stringent criteria needed for a pharmaceutical license today (which explains the lucrative trade in these product licenses amongst the herbal product manufacturers).

Medicines which can, with reasonable safety, be sold or supplied otherwise than by or under the supervision of a pharmacist are listed in the General Sales List. The exemption from licensing for certain herbal remedies described above is modified by the Retail Sale or Supply of Herbal Remedies Order, the purpose of which is to control the use of toxic plants by removing them from the general sale list category of medicines and making them "pharmacy only", or by limiting the dose or route of administration far use outside a pharmacy setting. The plants listed in Part I of the schedule may only be sold or supplied in a registered pharmacy; those listed in Part II and Part III may be used by practitioners who sell or supply herbal remedies where they are for administration to a particular person following a personal consultation (after being requested by or on behalf of that person to use his own judgement as to treatment required), but are not for retail in circumstances other than through a pharmacy."

There is a second word of warning, when trying to copy herbal preparations that might already be on the market, which comes from the Medicines Control Agency notice MAL8: -

A product falls within this limb of the definition of a medicinal product if it has the potential to interfere with, modify, or restore a function, of the body. If it contains any ingredient(s) with a significant pharmacological effect, this will be a strong indicator that the product is medicinal by function

Thus if a product is likely to have a physiological action, then it is likely to be a medicine, and if that herbal material has already been used for a medicinal indication in a licensed product, then the next paragraph may well be quoted.

Many herbs have well-established pharmacological properties; for example, as bronchodilators (Ephedra); as respiratory stimulants (Lobelia); or as sedatives (Valerian). The presence in a product of medicinal herbs like these, (and there are many more), will be considered as strong evidence that it is intended for a medicinal purpose.

Comparison with other plants containing same active chemicals

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 would reveal that it contained

Acids. Amino acids (eg alanine, aspartic acid, glutamic acid, histidine, leucine, lysine, proline, valine), fatty acids (eg linoleic, myristic, oleic, palmitic, stearic), and other acids including ascorbic acid, caffeic acid, folic acid, salicylic acid, and succinic acid.

Alkaloids/Bases Betonicine and stachydrine (pyrrolidine), trigonelline (pyridine), betaine and choline (bases). Uncharacterised alkaloids include achiceine, achilleine, (possible synonum for L-betonicine), which is stated to yield achilletine on alkaline hydrolysis, and moscatine/moschatine, stated to be an ill-defined glucoalkaloid.

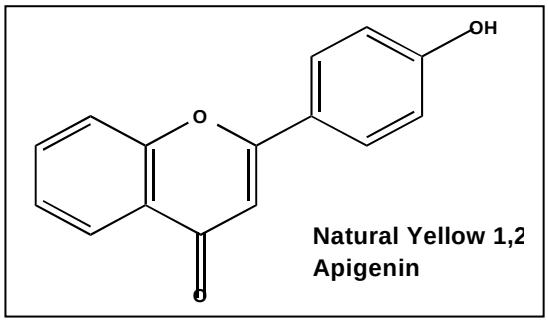
Flavonoids Predominantly flavone glycosides apigenin and luteolin-7-glycosides, with lesser quantities of artemetin, casticin, 5-hydroxy-3,6,7,4'-tetramethoxyflavone and isorhamnetin. Rutin (a flavonol glycoside).

Tannins Condensed and hydrolysable, with glucose as the carbohydrate component of the latter.

Volatile oils Numerous identified components include borneol, bornyl acetate (trace) camphor, 1,8-cineole, eucalyptol, limonene, sabinene, terpinen-4-ol, terpineol and α-thujone (monoterpenes), caryophyllene (a sesquiterpene), chillicin, achillin, millefin and millefolide (sesquiterpene lactones), azulene and chamazulene (sesquiterpene lactone-derived) and isoartemisia ketone. The relative composition of the components varies greatly between *Achillea* species, especially the azulene content. Azulene has been reported as the major component. However, true yarrow (*A. millefolium*) is thought to be hexaploid and azulene-free, whereas closely related species, such as *Achillea lanulose* Nutt. and *A. collina* Becker are tetraploid and contain up to 50% azulene in their volatile oil. The tetraploid species may be supplied for *A.. millefolium*. The azulenes are not present in the fresh herb; they are formed as artefacts during steam distillation of the oil, from unstable precursors called proazulenes (eg achillin and achillicin), via equally unstable azulene-carboxylic acid intermediates.

Other constituents Unknown cyanogenetic compound, sugars including arabinose, galactose, dextrose, dulcitol, glucose, inositol, maltose, mannitol, sucrose.

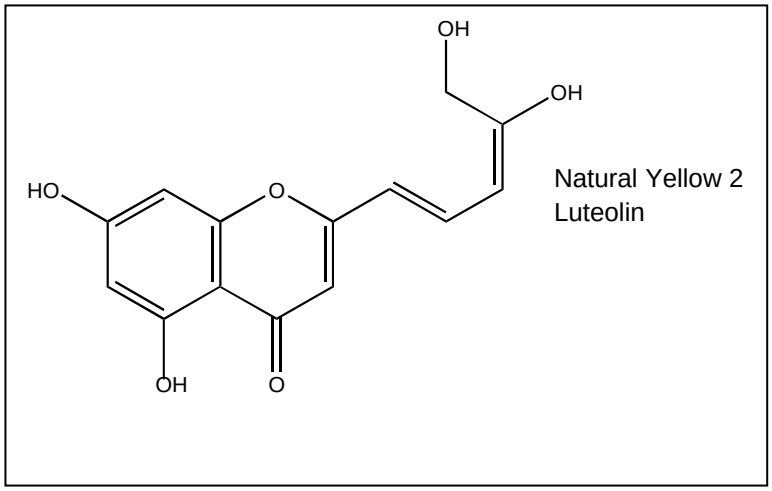
The similarity between these components and those of German Chamomile (*Matricaria recutita*) would suggest that yarrow would possess similar properties. This is confirmed by the historic uses of the plant, which is defined as being excellent for skin eruptions, chapped hands, sore or inflamed skin.



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.

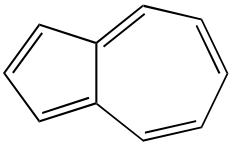
The occurrence of apigenin and luteolin in nature is quite common, and it comes as no surprise to discover that many of the "soothing" plants such as Plantain (*Plantago major*) and Milk Thistle (*Silybum marianum*) also contain significant quantites of apigenin. Indeed, in one report, it was shown that the apigenin present in Milk Thistle was more effective than indomethacin as an anti-inflammatory agent.



Natural Yellow 2
Luteolin

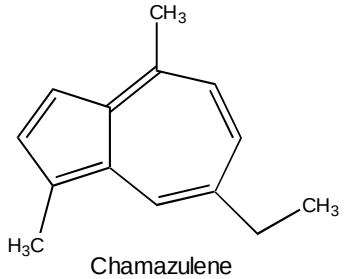
Luteolin is also quite abundant in nature, especially in Roman Chamomile (*Anthemis nobilis*), which has properties that are very similar to German Chamomile, despite being different species.

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



Azulene

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 Nu Chen or *Ligustrum lucidum*, 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.



Chamazulene

Comparison of benefits with related members of the same family

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 individual irritation by this material.

Continuing with the Compositae family we could turn our attention to bisabolol, 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.

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 Jimsonweed (*Datura stramonium*), Bittersweet (*Solanum dulcamara*) or Black

Nightshade (*Solanum nigrum*). However, they all have varying concentrations of toxic solanine-like alkaloids, which in the potato are present in the green shoots of the tuber.

If, however, the species within the *Mentha* group (Labiatae) were to be considered, then in every case one would expect to find that the essential oils from these plants would have a typically minty fragrance and would in almost every case have carminative, digestive and flavouring qualities. Topically, one would also expect them all to have a cooling effect followed by a longer term rubefacient activity.

Likewise, many of the *Salvia* species would possess typically sage-like qualities both in their essential oils and in their aqueous extracts.

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, no active material will confer any benefit to your product, if it is used at a trivial level.

APPENDIX I

The Phytochemical basis of modern medicine:

Although many modern drugs are chemically produced to be clean and of a single entity, many of them owe their origins to plants and some still only employ *materia medica.*

Drug or Compound	Example or Note	Main action	Plant Origin
Alginic Acid / Sodium reflux		- Gaviscon	Raft former vs brown seaweeds
Alginate	- Gastrocote	of gastric acids	*Laminaria s*pecies.
Analgesics	- The majority of opiates have there origin from *Papaver somniferum*		
Antibiotics	- Many are obtained extracted by bacterial or fungal fermentation		
Arachis Oil	- via enema	- Faecal Softener	Obtained from *Arachis*
	- Oilatum	- Dry skin cream,	*hypogaea*, Peanut oil
Aspirin	- Original idea gained from the use of willow bark *Filipendula ulmaria*		
Atopine Sulphate	- Lomotil	Anti-spasmodic First line treatment for M.I. Used in eye diagnostics	*Atropa belladonna* "Deadly Nightshade"
Carbenoxolone	- Pyrogastrone	Ulcer-healing	*Glycyrrhiza glabra*
Cocaine		Local anaethetic	*Erythroxylum coca*
Codeine			*Papaver somniferum*
Cytoxic antibiotics	- Extracted from the *streptomycese* fungi species		
Digoxin	Lanoxin	Cardiac glycoside	*Digitalis purpurea*, "Fox glove"
Ephedrine		Decongestant	*Ephedra hydra* *Ephedra sinica* *Ephedra gerardiana*

Hyoscine	Buscopan	Anti-spasmodic	*Hyoscyamus Leaf*
Ipecac *ipecacuanha*			*Psychotria*
Ipecacuanha *ipecacuanha*		Emetic	*Cephaelis*
Ispagula Husk	Regulan	Bulk laxative	*Plantago Ovata*
Liquorice	Caved S	Ulcer-healing	*Glycyrrhiza glabra*
Peppermint Oil	Colpermin	Anti-spasmodic	*Mentha piprita*
Physostigmine *venenosum*		Anti-cholinesterase	*Physostigma*
Pilocarpine *jaborandi*			*Pilocarpus*
Podophyllin *hexandrum*			*Podophyllum*
Quinidine	Kinidin	Anti-arrythmic	*Cinchona* bark
Quinine *bubescens* bark		Anti-malarial	*Cinchona*
Reserpine *serpentina*			*Rauwolfia*
Scopolamine *stramonium*			*Datura*
Senna senna	Senokot	Laxative	*Cassia senna,* Alexandrian
Simvastatin *terreus*	Zocor	HMG CO-A Reductase Inhibitor	*Aspergilus*
Steroids Oral contraceptives	- First derived and then modified from the South American wild yam,		*Dioscorea villosa*
Taxol	- Paclitaxel	Ovarian malignancy	Yew Tree *Taxus bacata*

Theophylline			*Camellia sinensis*
Tubocurrarine	- Jexin	Neuro-muscular blocker	*Chondodendron tomentosum*
Vinca Alkaloids	- Oncovin	solid tumours, leukaemias	*Vinca rosea,*
Vinblastine			*Catharanthus roseus*
Vitamins	- Some are produced by fungal fermentation		
Warfarin	-	Anticoagulant	Related to coumarin
			Alkaloids
Xanthine		- Respiratory Stimulant	*Coffea arabica*