The role of natural ingredients in anti-ageing of the skin

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Cautionary warnings

If you think that 0.05% of a dilute botanical extract is sufficient to make claims, then think again. For there to be any chance of an effect, you have to use at least 2% of the fresh plant equivalent and levels as high as 5% are probably more realistic. A plant is a complex and sophisticated chemical factory that produces hundreds of different chemicals within its entire structure. It is essential that you are using a respectable supplier – one that knows how to carefully extract a plant in order to maximise the beneficial chemicals present. In *sophisticated* ranges it is vital to use standardised extracts where the exact level of at least one of the components is known in order to have confidence that the plant extract has activity.

Definitions

We must first define by what we mean by natural, and though this definition is not legally defined, an undisputed description would be "any material that is harvested, mined or collected, and which may have subsequently been washed, decolourised, distilled, fractionated, ground, milled, separated or concentrated in order to leave a chemical or chemicals that would be available and detectable in the original source material". As an additional consideration I would include "the modification of natural material by the action of micro-organisms, enzymes or yeasts in order to modify or increase the yield of material by this process."

The classic example is the production of alcohol by the action of yeast on sugar.

The definition of "naturally derived" would be "the use of a natural raw material as the starting point in a chemical process to produce a new chemical or chemicals that in themselves may not be available in nature or in the starting material".

An example of this would be the sulphation and ethoxylation of fatty acids obtained from coconut to produce sodium lauryl ether sulphate (CTFA Sodium laureth sulfate).

The definition of "nature identical" is "a substance that has been produced synthetically, not usually from a natural starting material, in order to produce a material that is identical to that naturally occurring in nature". An example of this would be Vitamin E from wheat as opposed to that made from a petrochemical starting point.

Another example would be the synthesis of α-bisabolol (a component naturally occurring in chamomile). The nature identical materials are considerably cheaper, and often occur as racemic mixtures, whereas the natural form is the single, optically active variety.

Sources of information

We must obtain data for all these natural materials for our PIP (Product of Information Package). In many cases the supplier data sheets are not reliable, and one cannot always trust what they say.

The use of pharmacopoeias, herbal medicinal texts, herbal pharmacopoeias, folklore, ethnobotany will provide a great deal of data, as will searching of data bases such as EMBase, and Medline.

The part of the plant to be used

There are a sequence of points that should be followed in all uses of plant material, and the grape will be used as an illustration.

- Who produced it (the Winery)
- Where was it grown, Iceland is not renowned for its vintage wines
- Which part is used for the benefit required - imagine a wine made form vine roots or leaves
- Is the fresh or dried plant used? A wine made from raisins is called sherry!
- When was it harvested? Imagine a wine fermented from immature sugarless grapes
- 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.
- 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.

Thus, be sure that you know which part of the plant is used for the purpose that you require, i.e. the leaf, flower, whole herb, stems, roots, rhizomes, fruits (seeds), the bark or the sap. Find out whether it is the aqueous or oil soluble fractions that have the beneficial ingredients. Then find out how much of the plant needs to be used in order to achieve the effect that you require. It is of no use at all to use an extract of unknown concentration and you should make it your practice to work in fresh plant equivalents. Thus if a supplier uses one part of fresh plant to one part of solvent by weight, then you may assume that when you use one gramme of that extract it will contain at least half a gramme of the plant. If the extract was made from dried plant material, then as a rule of thumb, multiply your figure by a factor of eight.

Orchestral overtures

A single plant active on its own is often worthless and the entire plant usually works far better than any of its single components. A plant may contain active chemicals that are anti-inflammatory, anti-oedema, skin calming and that encourage skin repair and reduction in erythema. The multiple effects are not caused by a single chemical instrument but by a wide collection of different molecules all acting in harmony and often in synergy.

Aesthetics

Before anything can be undertaken, establish the following:-

- How much money can you spend on the formula?
- What are the claims that you want to make?
- Can you afford the grandiose plans conceived by your marketing department on the budget that they have allocated?

Considerable costs can be saved by compromise, the more naturals you take out, the more money you will save, the more stable the product will become! Synthetics are much easier to use than botanicals.

Now that we have established some basic rules we can begin to tackle the subject matter.

Introduction

The skin ages for a number of reasons. It will naturally age with increasing loss of flexibility and ageing as collagen and elastin within the epidermis slowly cross-links and become less elastic. To a degree this is part of the genetic inheritance present within all of us, since do not seem to age at the same rate, nor share identical lifestyles.

It has been extensively proven that sunlight hastens the degradation of the skin by the bombardment of tissue with high energy photons present in UV-A and UV-B wavelengths of sunlight. This high energy has sufficient power to cleave molecules into free radicals, which are then available to react, modify and sometimes destroy healthy cellular chemistry.

Other external factors, such as the free radicals produced in vehicle exhaust gases, dirty industrial processes, and smoking can further speed the detriment of healthy skin.

Plants as skin protectants

The role of plants in the protection of the skin may be come from a number of perspectives. Plants oils may be used to form a protective emollient layer that reduces transepidermal water loss and so increase the hydration of the stratum corneum. This not only forms a lubricious layer of fatty acids on the skin but also increases the "plumping" of the tissue, so contributing to a smoothing of the wrinkles.

The presence of reactive free radicals can be 'mopped up' by the use of antioxidants and free-radical scavengers.

The use of sunscreens will also reduce the potential of solar damage.

There is an increasing body of evidence to suggest that some plants can provide a prophylactic function.

The need to tan seems to be an irrepressible desire for many people and though one can tan safely without erythema and dangerous cellular damage, it is the feeling of most dermatologists that the ageing process is accelerated by tanning, regardless of

the precautions that have been taken. The provision of cellular regeneration from plant sources is theoretically possible through the use of phytosterols and phytohormones and there are many other chemical entities within plants that can reduce erythema, reduce swelling and repair skin damage.

The chemistry of plant protectants

Plant sterols

Plant oil produced from seeds and fruit kernels are a rich source of fatty acids which provide emolliency, hydrophobicity and skin protection from the drying effects of wind and sun. As little as 2-5% of any fixed oil will provide protection to the skin and help prevent the loss of hydration for the stratum corneum and underlying tissue.

In addition to these materials one finds other materials which perhaps offer more than simple protection. These materials are *gamma*-linolenic acid (GLA), linoleic acid and other complex molecules. Theoretically, the GLA provided by Evening Primrose Oil and similar can be converted to the prostaglandin precursor dihome-GLA and might be beneficial to persons unable to metabolise cis-linoleic acid to GLA or with low dietary intake of it. The clinical uses are quoted as cardiovascular disease, cancer, rheumatoid arthritis, PMT, multiple sclerosis, atopic eczema and other diseases [Evans & Trease]. *Gamma*-linolenic acid is cited in the suppression the inflammatory process. The use of evening primrose oil (*Oenothera biennis*) seed oil [Christie] had already been reported in the literature for mastitis [Oxlade] and atopic dermatitis [Martindale] when taken internally and further information offered to show that topically it would also have a soothing and anti-inflammatory effect on the skin [Graham; Dweck, 1991]. This material is found in a number of other oils such as blackcurrant seed oil (*Ribes nigrum*), borage oil (*Borago officinalis*) sometimes called starflower oil as well as in rosehip seed oil (*Rosa* Aff *rubiginosa*).

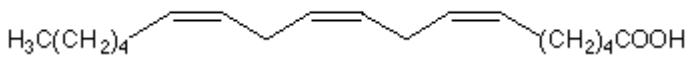
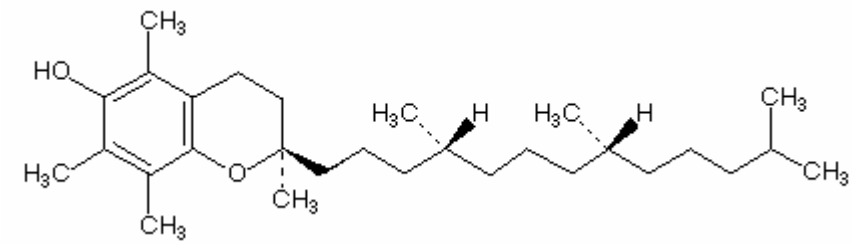


Fig.1. *Gamma*-linolenic acid

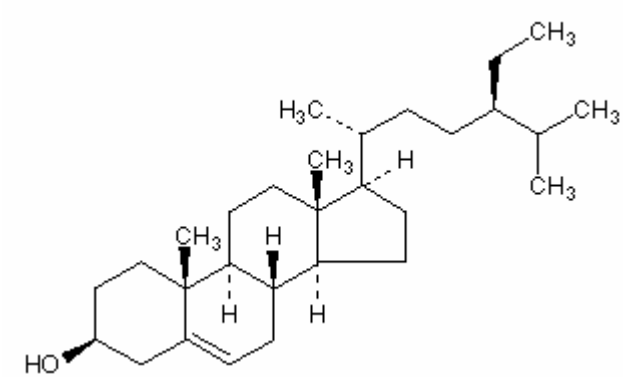
GLA may occur in some plant oils up to around 15%, so one needs to use a minimum of 5-10% if the full benefit of the active is going to be present in the final product. Clinical trials were carried out at anything from around 5% all the way up to 100% in the case of rosehip oil.

Fig.2 Tocopherol



Rosehip seed oil has been the subject of considerable clinical research and shown exceptional cicatrising and

vulnerary properties [Valladares *et al*.; Camacho *et al*.; Moreno *et al.*; Marchini *et al*.]. This plant seed oil has also shown exceptional effect in reducing the hyperpigmentation of scars and reducing their profile. For a long time this remained a mystery, until a search of the literature uncovered the presence of retin A or retinoic acid, discovered by a researcher looking for a quick drying varnish oil [Pareja; Siber Hegner].



There still remains a great deal of doubt over this research, since a study carried out by King's College London failed to find any trace of this vitamin in the oil samples they examined. Yet the effectiveness of this oil remains undisputed.

Fig.3 ß-sitosterol

Plant sterols or phytosterols

Another oil, Avocado (*Persea gratissima*), has also shown excellent effect on the skin, particularly for the soothing, repairing and calming effect it exhibited. The analysis of the unsaponified components within this oil identified some phytosterols as the likely reason for this materials success on the skin as well as many other derivatives [Leung].

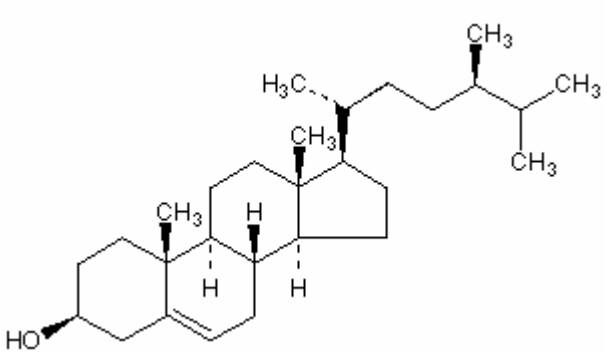
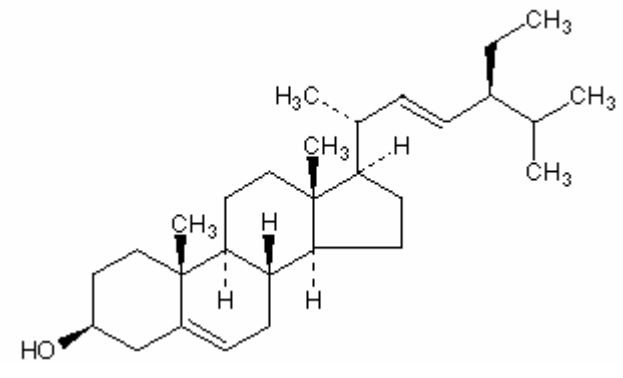


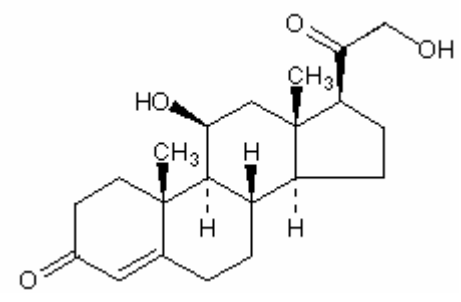
Fig.4 Campesterol

These included ß-sitosterol, campesterol, stigmasterol, brassicasterol, delta5-avenasterol, tocopherols and other unidentified sterols [Crodarom].



These naturally occurring sterols bear a tremendous similarity to synthetic materials, those synthetic materials like corticosterone and hydrocortisone, traditionally used in allopathic medicine for their anti-inflammatory effects and particularly for skin eruptions, eczema and other pruritc and erythemic conditions.

Fig.5 Stigmasterol



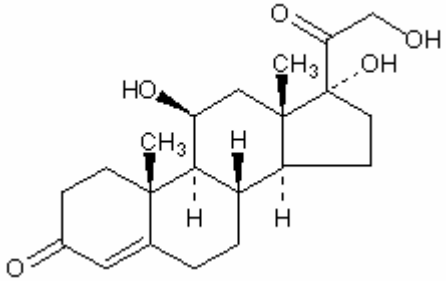


Fig.6 Corticosterone **Fig.7 Hydrocortisone**

Interestingly, the use of hydrocortisone or corticosteroids may ablate the symptoms of a distressing skin condition but not tackle the underlying reason for the skin reaction that underlies that condition. [Burden & Beck] Indeed, extended use of high levels of hydrocortisone can drastically alter the ratio between dermis, epidermis and stratum corneum and compromise the integrity of the skin to leave it with a thin topical fragility and visual transparency [Zachariae; Guin]. The answer to this apparent conundrum may lie within the chemistry, since though the structure bears an uncanny resemblance to the naturally occurring sterol materials, the exact configuration is never found in nature. The skin may be "fooled" into reacting to the drug, because the synthetic steroid has a skeletal configuration or key that fits the lock.

Plant hormones

In the old days (up until circa 1975) the cosmetic and toiletry industry were using oestrogen in products for mature skin until the pharmaceutical industry raised concerns that pure oestrogen was a pharmaceutical and it was subsequently banned. This material's disappearance from the cosmetic ingredient inventory led to an outcry from the skin care manufacturers, but an even larger cry from the mature consumer who had discovered and proven for themselves the benefits of topical hormonal preparations. The use levels of these hormonal materials appears to be very low and as little as 0.1% of the active may be effective. The percentage of active present in the final plant preparation will vary from supplier to supplier and from plant source to plant source and so one is dependant on the supplier to provide the active content of the plant.

Fig.8 Progesterone

The pharmaceutical use that led to the ban was based on progesterone (one of the first female contraceptives), the raw material source was originally from Wild Yam (*Dioscorea villosa*) in the form of diosgenin.

Fig.9 Diosgenin

The diosgenin was converted to progesterone. Disogenin is most certainly physiologically active and this can be seen by looking at molecule that is a close relative called ruscogenin (1-β-hydroxydiosgenin) and is found in Butcher's Broom (*Ruscus aculeatus*) and used for the inflammatory conditions of oedema and associated erythema. It is also a useful material for the treatment of varicose veins and haemorrhoids.

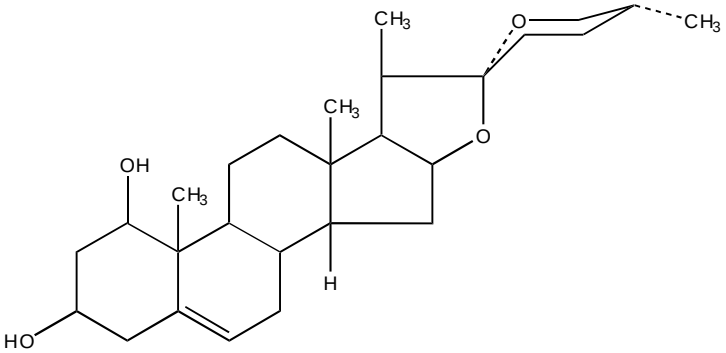
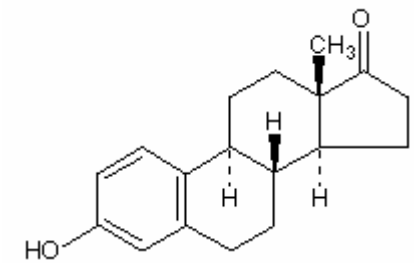


Fig. 10 Ruscogenin

Eventually the stocks of Wild Yam fell to such low levels that industry was finding it hard to support the demand and so the much more widely available material Fenugreek (*Trigonella foenum*-graecum) was used as an alternative source of diosgenin. However the diosgenin by this time was being converted to another hormonal steroid, namely estrone.

Fig.11 Estrone



The use of plant materials as a source of these steroids faded as the products became produced synthetically. However, the relevance of plant steroids as a soothing and therapeutic source of active material is too irresistible to ignore.

A literature survey suggested that Ginseng (*Panax ginseng*) might be a source of estriol. This would be useful for the industry because there are very few papers published on the benefits of ginseng topically, because its main use is an alterative tonic taken internally.

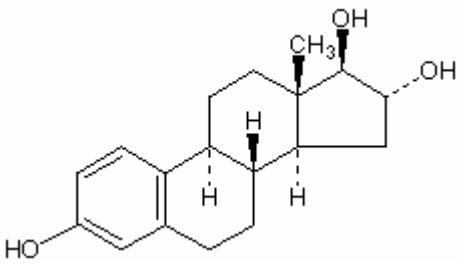


Fig.12 Estriol

Another plant material that was enjoying a great revival, until the issue of genetic modification spoilt the image, was soya (*Glycine max*). This material also contains ß-sitosterol as illustrated above, but in addition contains daidzen and genistein, which are isoflavones (also anti-inflammatory and cell regenerating).

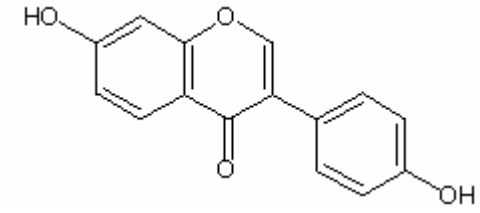


Fig.13 Daidzein

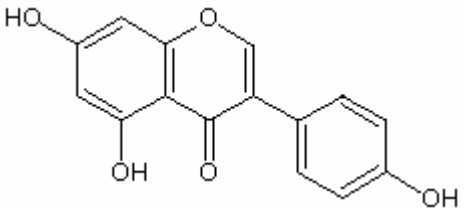


Fig.14 Genistein

The excitement of discovery grew immensely when we came to review a paper on *Pueraria mirifica* and discovered that this root also contained daidzein and genistein along with some other fascinating steroids and hormonal materials. In this case the steroidal material was estradiol and this offered an opportunity to offer another new steroidal derivative to our collection.

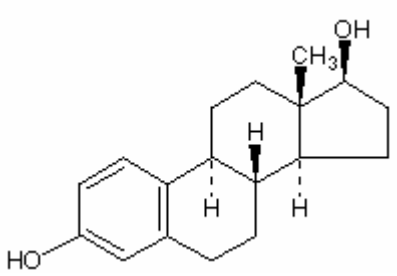


Fig.15 Estradiol

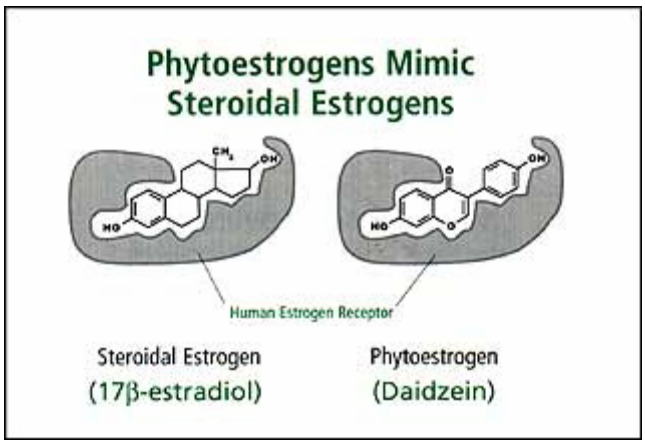
Proof of the steroidal nature of this Thai plant comes from its promotion as a bust developing preparation when taken internally. The supporting data is not conclusive, but shows some promise to its validity. Clearly this root would also have a topical application and benefit.

Plant isoflavones

Isoflavones differ from flavones, because the phenyl group is attached to the 3-position, compared to flavones where the phenyl group is attached to the 2-position. The isoflavones occur naturally mainly within the Leguminosae (beans, soybeans, lentils, chick peas, etc).

Well-known examples of isoflavones are genistein (4',5,7-trihydroxyisoflavone) and daidzein (4',7-dihydroxyisoflavone). Daidzein and genistein are phyto-estrogens. They are also named phenolic estrogens, to distinguish them from steroidal estrogens.

The geometrical structure of daidzein compares to 17-β-estradiol and is therefore able to mimic its spatial structure [our thanks to Dr. Hans Brand for the use of his illustration]. Phyto-estrogens are much weaker in activity than steroidal estrogens, varying from 0.005 - 2%.



Diag.1 molecular spatial representation

The estrogenic properties are by no means suitable to replace steroidal estrogens, but they do have significant interactions with the organism to enable to reduce the effects of ageing and include the improvement of the quality of the skin [Brand-Garnys].

A closely related chemical group are the flavones, which include chemicals such as apigenin, luteolin and flavonols (which have an additional hydroxyl group in the 3-position) for example in quercetin.

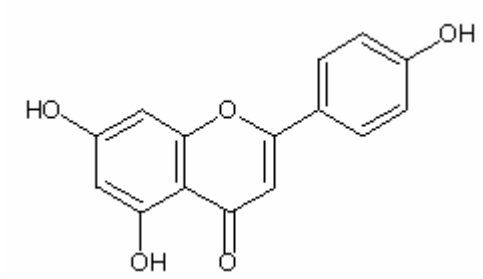
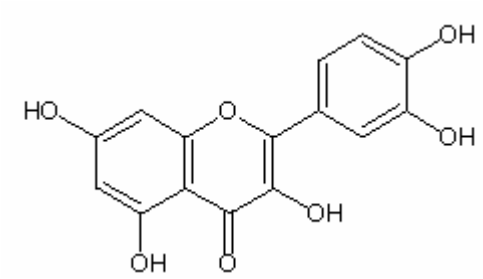


Fig.16 Apigenin

The flavones, which are normally coloured [Dweck, 2002] also possess anti-inflammatory properties and are found in a variety of plants renowned for their soothing and healing properties. The effect seems to occur at very low levels and anything from 0.05% might be expected to be effective.

Fig.17 Quercetin



The iso-flavones have a phenyl group attached to the 3-position as opposed to the 2-postion found in flavones. An example of an iso-flavone would be the genistein and daidzen already mentioned above.

These flavonoids have another important subgroup called the catechins, which have another remarkable property within plants and that is to be able to bind together in various configurations in order to form a powerful new complex group called procyanidins, which are free-radical scavengers and anti-oxidants.

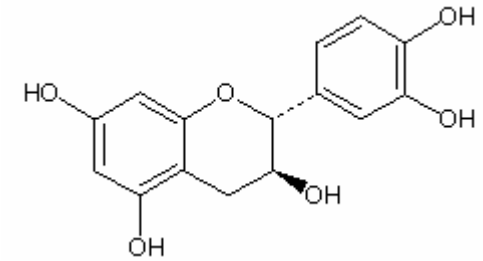
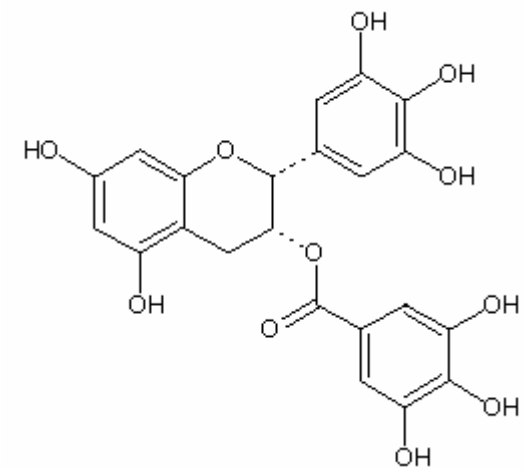


Fig. 18 Catechin

Catechins lack the carbonyl group at the 4-position.



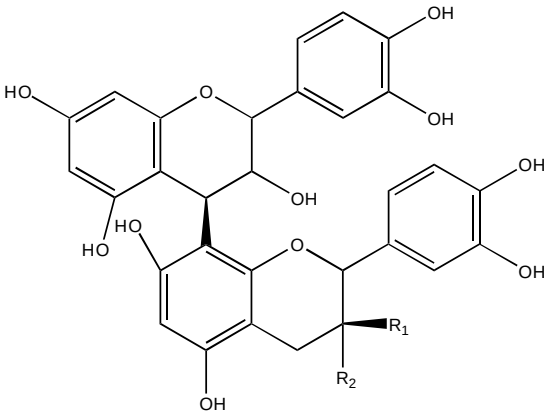
The formation of a powerful dimer called epigallocatechin-3-O-gallate occurs via the hydroxyl group and is found in materials like green tea (*Camelia sinensis*) and more recently in the stronger preparation white tea that is produced from the newly forming buds of that plant.

These materials (catechin and epicatechin) have also been extracted from the seeds of apples (*Pyrus malus*).

Fig. 19 Epigallocatechin-3-O-gallate

The wide distribution of these chemical moieties in nature suggests that the future will show a great opportunity for natural producers to extract and provide an even greater variety of these materials from ever more diverse sources. As with all of these antioxidants or free radical scavengers, the safest way to determine the effective concentration is to demand proof of effect and activity from the supplier of that material.

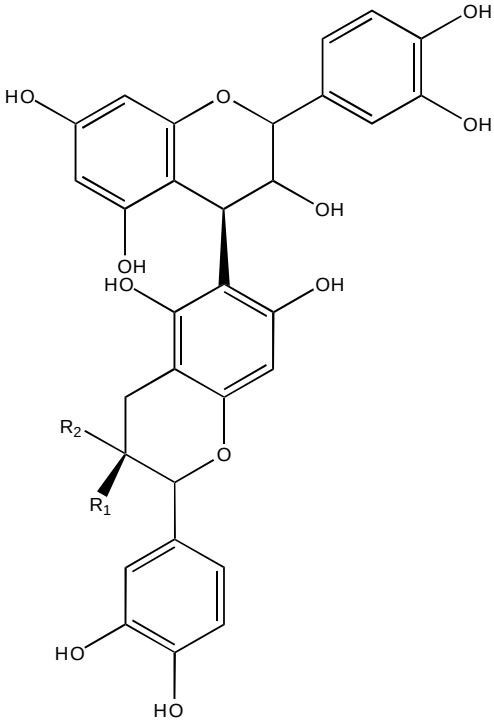
Plant procyanidins



The classic source for the procyanidins has been the grape seed (*Vitis vinifera*), although a source was produced from marine pine and soya, that found its way into dietary supplements under the name pycnogenol (a name often used incorrectly for procyanidins) [Passwater and Kandaswami]

Fig.20 Procyanidin B_1 and B_2
R_1 = OH; R_2 = H for Procyanidin B_1
R_1 = H; R_2 = OH for Procyanidin B_2

Fig.21 Procyanidin B_3 and B_4
R_1 = OH; R_2 = H for Procyanidin B_1
R_1 = H; R_2 = OH for Procyanidin B_2



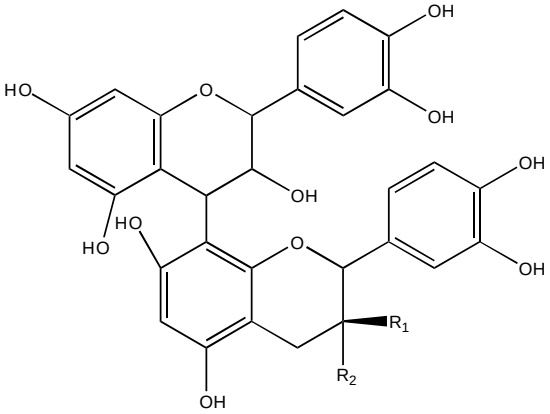


Fig.21 Procyanidin B_6 and B_8
R_1 = OH; R_2 = H for Procyanidin B_1
R_1 = H; R_2 = OH for Procyanidin B_2

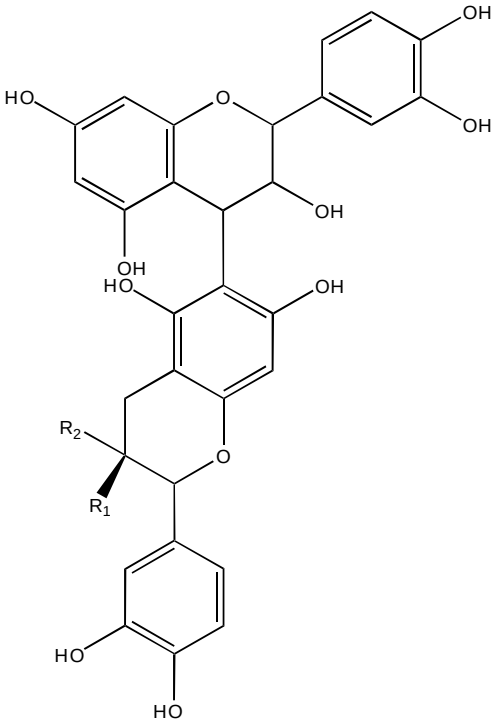


Fig.22 Procyanidin B_5 and B_7
R_1 = OH; R_2 = H for Procyanidin B_1
R_1 = H; R_2 = OH for Procyanidin B_2

Orchestral plants

Up until now we have talked of single chemical species being responsible for the care and protection of the skin, in reality this is rarely the case in herbal medicine. Plants are not single chemical entities and do not give their maximum benefit when the single active molecule is extracted. The effect is not caused by a single instrument but more likely by an orchestra of different chemicals that work synergistically and in concert.

Two examples will be shown as a demonstration of this proposal.

Self Heal (*Prunella vulgaris*)

Consider Self Heal (*Prunella vulgaris*) mentioned as long ago as around 1500AD by Theophrastus Bombastsus von Hohenheim (better known to us as Paracelsus) in his *Doctrine of Signatures*.

It is a wound healing plant, used for swellings, pruritis and the treatment of cuts and abrasions. It has also been used by nursing mothers for sore and cracked nipples and is reputed to help stop the bleeding in wounds as an anti-haemorrhagic.

The chemical portfolio is quite remarkable and we find quercetin, esculin, delphinidin, rutin, aucubin, kaempferol and scopoletin. A perfect example of orchestral harmony, where the lead players have been seen playing in other orchestras!

One has to look at the root of the chemical name in order to gain a clue as to its original discovery and we find that esculin was originally called aesculin (and still is in some texts).

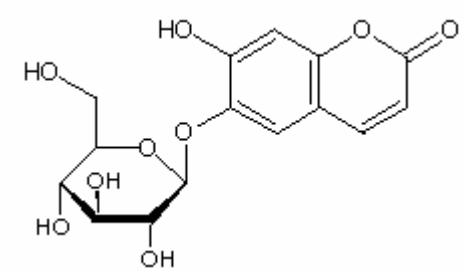
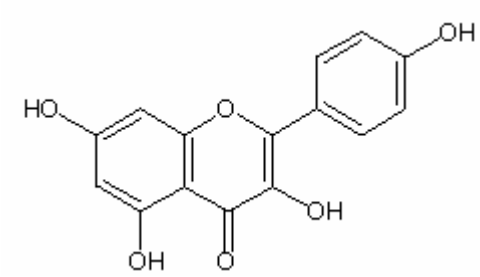


Fig 23 Esculin

The root of the name aesculin is *Aesculus hippocastanum* or Horse Chestnut, which is well-known for its treatment of oedema and other inflammatory conditions [Fluck]. The esculin and related esculoside are attributed to with the properties of anti-oedema and anti-inflammatory effects [Weiss]. We can therefore make a guess that the esculin will exhibit similar properties in this plant.



We have already mentioned quercetin which is a flavonol (see Fig.13) and this is a well-respected soothing and healing agent, again with anti-inflammatory properties.

Fig 24. Kaempferol

Another flavonol present is kaempferol. This occurs widely in the plant world (often present with quercetin) and is found in a huge variety of plants that include Horse Chestnut (*Aesculus hippocastanum*), Arnica (*Arnica Montana*), Marigiold (*Calendula officinalis*), Indian Pennywort (*Centella asiatica*) [Dweck, 1996] and Purple Coneflower (*Echinacea purpurea*) to name but a few. The plants have the same property in common - they are all renowned for their skin healing effect.

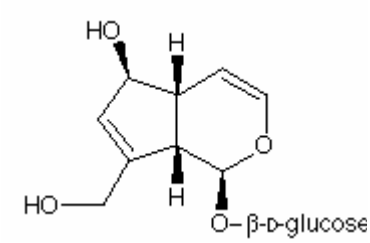


Fig 25. Aucubin

The root of this chemical would seem to come from *Aucuba japonica* – a Japanese variegated Laurel and chemically it is an iridoid glycoside. Aucubin is quite a difficult chemical to find data on. It is found in Eyebright (*Euphrasia officinalis*), Common Plantain (*Plantago officinalis*) and *Eucommia ulmoides*. The effects seem to be indicated as anti-viral and also to increase skin cell turnover, but these properties are far from being accurately defined.

The derivative of the chemical name scopoletin – an hydroxycoumarin - comes from the *Scopolia japonica* and the chemical is found in plants like Wormwood (*Artemisa annua*), Helichrysum picardii [Puerta], Horse Chestnut (*Aesculus hippocastanum*) [Komissarenko], Borage or Starflower (*Borago officinalis*) [Gudej] and Mallow (*Malva sylvestris*) [Tosi] where the plant is cited for its anti-inflammatory activity.

The exact function of scopoletin is hard to determine, some references lead towards it being a diuretic, while others lead to the reduction in PAF (Platelet Aggregation Factor). The likely action is anti-inflammatory from the studies on a variant of Cotton Lavender (*Santolina oblongifolia*) [Silvan] and also the antiinflammatory activity study of *Lomatia hirsuta* leaves (radal), a plant used in Chilean traditional medicine for bronchial troubles and asthma, which was evaluated in guinea pigs by the carrageenan-induced paw oedema method [Erazo].

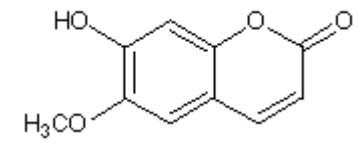
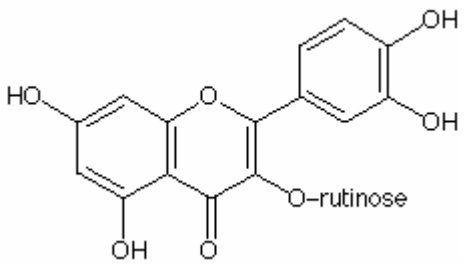


Fig 26. Scopoletin

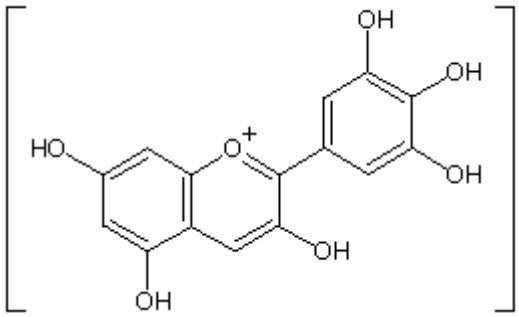
Fig 27. Rutin (Rutoside)



Rutin is found in the Graminae family and in products like Buckwheat (*Fagopyrum esculentum*) [Dabrowska-Zamojcin], *Anthriscus sylvestris* [Milovanovic] and

Ginkgo biloba [Joyeux] where the effect appears to be antioxidant and protects cells against lipo-peroxidation.

It is also found in plants like fennel (*Foeniculum vulgare*) and Aniseed (*Pimpinella anisum).*



Rutin or rutoside is shown as a capillary protectant [Merck]

The final material in this orchestra is a natural colour called delphinidin and closely related to flavones and flavanols.

Fig 28 Delphinidin

Its name is derived from the plant in which it was first found, namely delphinium and comes from the chemical family called anthocyanidins which coincidentally is another class of natural colourants [Dweck, 2002].

Another plant worthy of mention, that has recently come to attention is Tamanu oil or *Calophyllum inophyllum*. This has an extremely complex portfolio of chemistry that is hard to explain and decipher

Tamanu (*Calophyllum inophyllum*)

It is a member of the mangosteen family and the dried seeds produce a fixed oil. The full paper is published [Dweck, 2002;2]

Calophyllic acid and a lactone endowed with antibiotic properties are said to be at the origin of the oil's amazing cicatrising power. The dark-yellow oil extracted from the seeds contains a poisonous resin, which has a parsley-like odour. The resin is not dissimilar to myrrh and is alcohol-soluble.

The bark contains tannin [Burkill] and exudes an oleoresin which contains benzoic acids [Jayaweera]. The oleoresin is officinal in the Mexican and Spanish Pharmacopoeias [Quisumbing].

Fig 29. Mesuazanthone-B

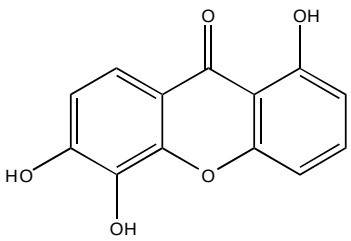
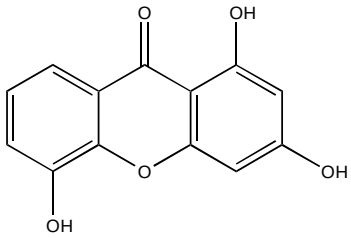


Fig 30. Mesuazanthone-A



The leaves of *Calophyllum inophyllum* contain friedelin and triterpenes of the friedelin group, namely canophyllal, canophyllol and canophyllic acid, [Govindachari, *et al*;1967] and from the heartwood xanthones such as mesuaxanthone B and calophyllin B are obtained [Govindachari, *et al*;1968].

Interestingly, many of these substances i.e. canophyllal and friedelin are also found is *Syzigium* species.

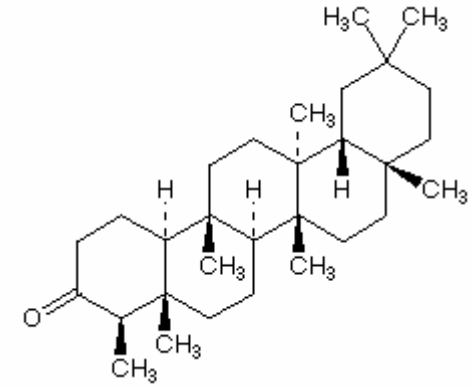


Fig 31. Friedelin

Friedelin has been identified. [Merck, 1996]

Calophyllolide, isolated from the nuts [Rastogi *et al*, 1998; Bhalla]. ED_{50} was 140 mg/kg orally. Showed anti-inflammatopry and anti-arthritic activity in formaldehyde-induced arthritis and adjuvant arthritis in rats. LD50 2.5 g/kg p.o. It was devoid of ulcerogenic activity up to twice the ED50 dose.

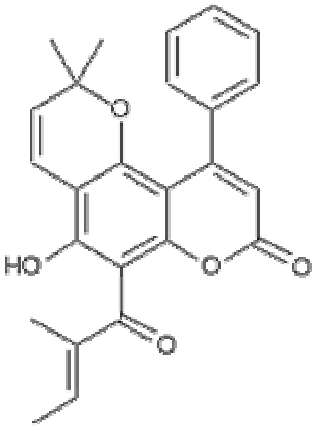
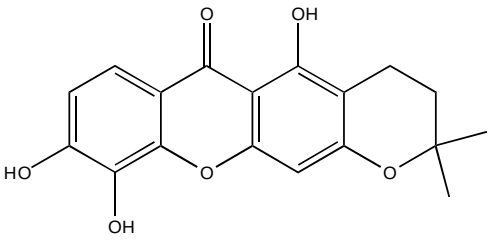


Fig. 32 Calophyllolide

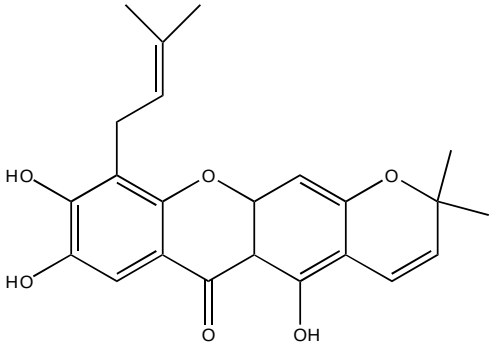
De-hydrocycloguanindin, calophyllin-B, jacareubin and 6-deoxyjacareubin, produced varying degrees of CNS depression, characterised by ptosis, sedation, decreased spontaneous motor activity, loss of muscle tone, potentiation of phenobarbitone sleeping time and ether anaesthesia in mice and rats. All the xanthones exhibited anti-inflammatory activity by both i.p. and oral routes in rats. Jacareubin and 6- deoxyjacareubin also showed anti-ulcer activity in rats [Gopalakrishnan *et al*].

Fig. 33 Jacareubin



Calophyllolide, isolated from the seeds [Oliver-Bever], reduced histamine inflammation and carrageenan-induced tissue swelling in rats.

Together with inophyllide reduced oedema by 60.7% and 29.8% respectively (compared to hydrocortisone, which reduced inflammation by about 44%). The safety margin of calophyllolide is very similar to that of oxyphenbutazone (21.4 mg/kg and 25 mg/kg respectively).



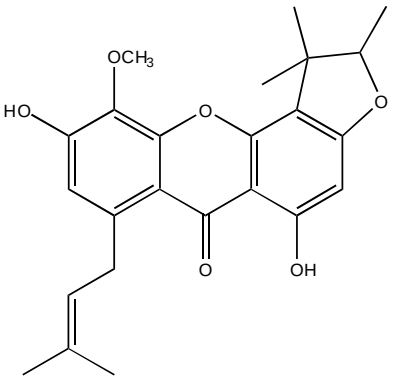


Fig 34. Caloxanthone A

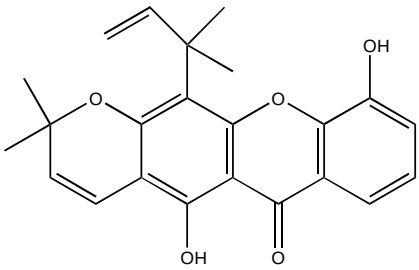


Fig 35. Caloxanthone B

Fig 36. Caloxanthone C

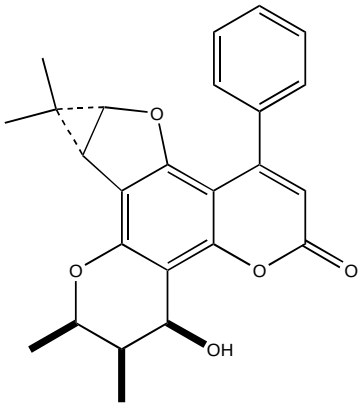


Fig 37. Inophyllum G-1

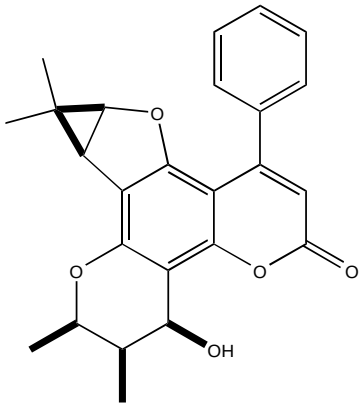
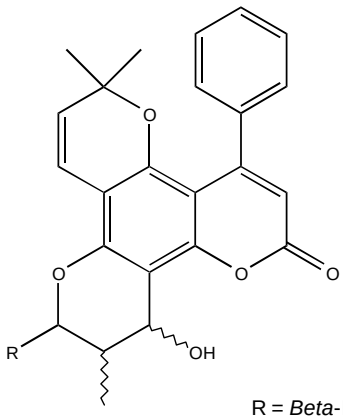


Fig 38. Inophyllum G-2

Inophyllums B and P inhibited HIV reverse transcriptase (IC50 38 and 130 nm respectively). [Rastogi *et al*, 1998]

Tamanu oil contains terpenic essences, benzoic and oxi-benzoic acids. Small amounts of vitamin F and phospho-amino-lipids come along with glycerides and saturated fatty acids.

The plant contains 4-phenylcoumarins that have anti-tumour activity [Itoigawa]



R = *Beta*-Me ~~~ = *alpha*

R = *alpha*-Me ~~~ = *Beta*

Fig 39. Inophyllum P

The following active principles have been found in the oil:
- calophyllolide ($C_{25}H_{22}O_5$) the molecule of which contains a lactonic and a methoxyl group.

- calophyllic acid ($C_{25}H_{24}O_6$), which results from the saponification of the calophyllolide.

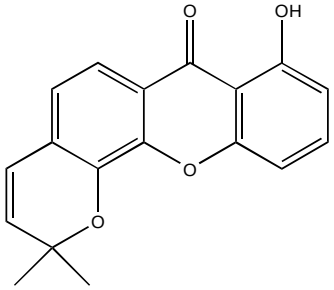


Fig 40. Dehydrocycloguanandin

These active principles are coumarine derivatives [Muller].
Composition of the oil :
* Free fatty acids, glycerides, Sterols
* Terpenoids & steroids (canophyllal, canophyllol, canophyllic acid)
Coumarinic derivatives : Calophyllolids (natural neo-flavonoids with antibacterial, anti-inflammatory and anti-blood coagulation properties), Inophyllolids (natural neo-flavonoids with anti-viral properties), calophyllic acid (natural neo-flavonoid with anti-molluscidal and healing activities).

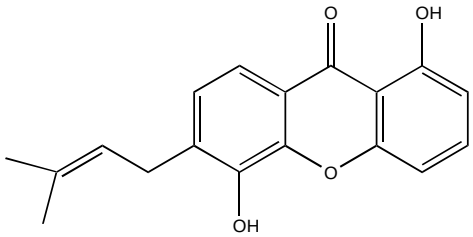


Fig 41. Calaphyllin-B

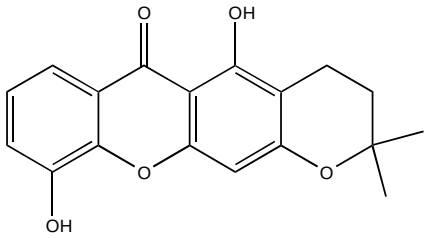


Fig 42. 6-desoxyjacareubin

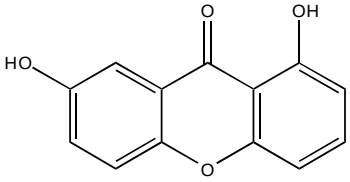


Fig 43. Euxanthone

This study evaluated the ability of one (1) test product to improve the appearance of scars. Six (6) subjects with visually obvious, aged scars (1 year or more) were utilized for the study. The subjects were restricted from using any moisturizing products on the scarred area for a seven (7)-day pre-test period and throughout the nine (9) week test period. *0.5* mL aliquots of the product were applied to the scarred area twice a day for nine (9) consecutive weeks. Product applications were performed by the subjects and recorded on a product application tracking form provided to them.

The subjects were evaluated prior to product application (baseline) and each week for nine (9) weeks at the testing facility. Visual ratings of scar appearance (color, roughness, and degree of difference from surrounding normal skin) and scar size measurements (length and width) were performed.

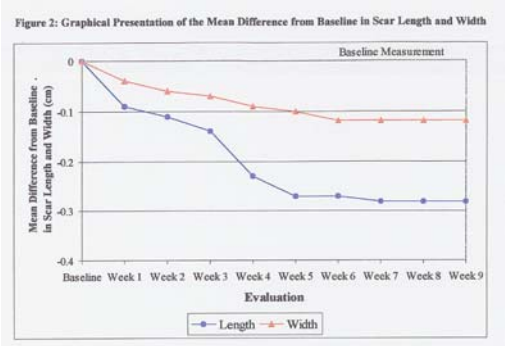
Quantitative measurements of skin color for melanin (darkness) and hemoglobin (redness) were made on the scarred and adjacent normal skin areas using a Mexameter MX 18. Quantitative measurements of skin hydration were also performed on the same sites. Digital photographs of the scar were taken prior to product application (baseline) and again at the end of week nine (9). The subjects completed a self-evaluation questionnaire regarding their scar's appearance prior to

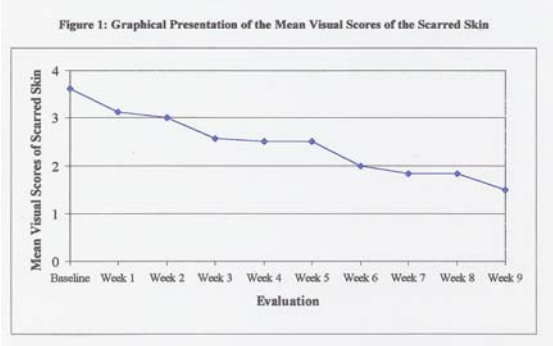
product application (baseline) and again at the end of week nine (9). The subjects also completed a product questionnaire that assessed their likes and dislikes of the product.

A significant improvement in the appearance of scars after six (6) weeks of Tamanu Oil use was observed visually. This improvement continued through to Week 9 of the study. The overall size of the scars consistently decreased throughout the study. The length of scars was reduced by an average of 0.28 cm, and the width by an average of 0.12 cm [Beausoleil].

Plants with prophylactic activity

There is one plant that can most certainly protect the skin against radiation be it thermal [Fulton; Davis], solar [Strickland] or high energy radiowaves [Sato; Iena]. A review of the literature shows that the Aloe vera (*Aloe barbadensis*) can fulfil this promise [Reynolds & Dweck]. The use level has to be a minimum of 50% (5% of





10:1) and the author routinely uses 100% in his recommendations to clients.

The chemistry is complex and the arguments still rage as to which component is responsible. The debate may never be resolved if researchers continue to look for just a single component responsible for the activity.

Barbaloin or Aloin A

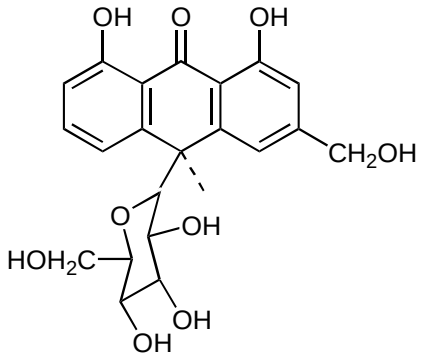


Fig 44. 10-(1',5'-anhydroglucosyl)-aloe-emodin-9-anthrone

Isobarbaloin or Aloin B

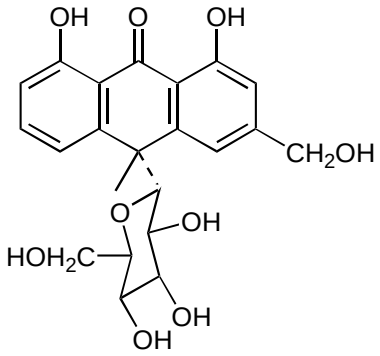
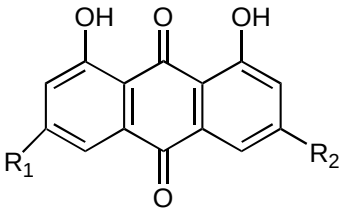


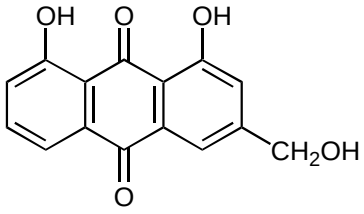
Fig 45. 10-(1',5'-anhydroglucosyl)-aloe-emodin-9-anthrone

These two chemicals are present as a mixture of:
10-C-ß-L-glucosyldiastereo isomer of aloe-emodin anthrone and
10-C-ß-D-glucosyldiastereo isomer of aloe-emodin anthrone
They are present at 25-40% or 500mg/100g in the prepared aloe vera gel.



R_1	R_2	Chemical Name
H	CH_3	CHRYSOPHANOL
H	CH_2OH	ALOE-EMODOL
H	COOH	RHEINE
H	CH_3	EMODOL

Fig 46. Anthraquinone derivatives



3-Hydroxymethyl anthraquinone
1,8-dihydroxy-3-hydroxymethy-9,10-anthracenedione
Typically present at 2.05-2.2% in the aloe vera gel.

Fig 47. Aloe-emodin or Aloe-emodol

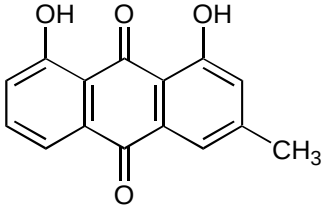


Fig 48. Chrysophanol or Chrysarobin
(Sometimes referred to Chrysophanic acid, which is a misnomer.)

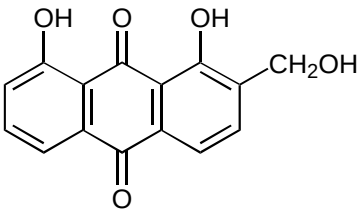
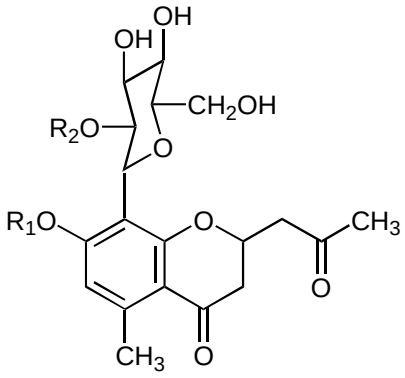


Fig. 49 Aloetic acid
Also mentioned is aloetic acid, which has a similar structure, but is not widely mentioned in the literature.
2-Hydroxymethylanthroquinone

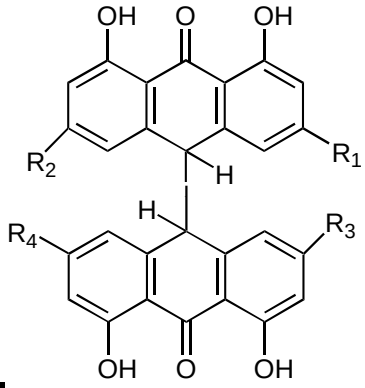
Chromone derivatives - Aloe resins



R_1	R_2	Chemical Name
H	ρ-coumaroyl	ALOERESIN A
H	H	ALOERESIN B
Glucosyl	ρ-coumaroyl	ALOERESIN C

Fig 50. Aloeresin A, Aloeresin B and Aloeresin C
Aloeresin A is 2-*p*-coumaroyl aloeresin
Aloeresin B is 8-C-glucosylchromone aloeresin B
Aloeresin C is 7-O-ß-D-glucoside of aloeresin

Aloesone
The aglycone of aloeresins A, B and C. This is only present in trace amounts.

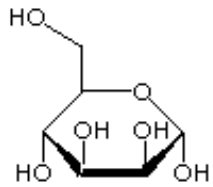


Homodianthrones

Fig 51. Sennidin A and B

R_1	R_2	R_3	R_4	Chemical Name
COOH	H	COOH	H	SENNIDIN A, B
CH_2OH	H	COOH	H	SENNIDIN C, D

The above are the trace components, the major constituent is mannose-6-phosphate and it is this material which is attributed with the beneficial effects of the aloe vera. However, it is unlikely that this sugar derivative alone could give all the properties found for aloe in the scientific literature.



α-D-Mannose

The anthrones must play a part in the scenario a view perhaps shared by other authors [Joshi] who mention the chromones and anthracenes present possibly contributing to the action of the plant.

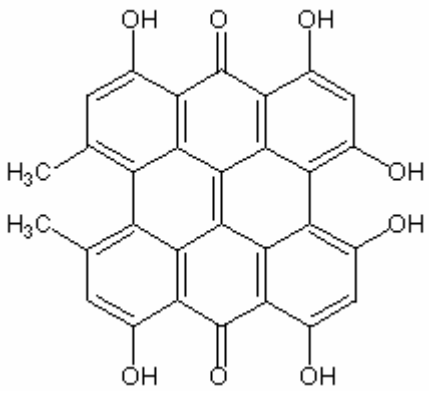


Fig 52. Hypericin

The clue may come from research into other medicinal plants, where it was proposed that the anthrone, anthraquinone, emodin, hypericin and pseudohypericin, isolated from St, John's Wort (*Hypericum perforatum*) may be involved in the anti-inflammatory effects [Bezakova]. The similarity between the structures of hypericin and sennidin (Fig.51) is too close to ignore.

Conclusions

We have endeavoured to make a case for the protection of the skin using phytochemicals present in medicinal plants and have also speculated that the use of phytosterols and phytohormones would be beneficial to damaged and ageing skin. We examined those chemicals (from the published scientific literature) to the beneficial effects reported and were encouraged that the comparisons showed agreement.

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