

Australian Society of Cosmetic Chemists
Annual Congress, Hamilton Island 2003
The role of natural ingredients in anti-ageing of the skin

Anthony C. Dweck FLS FRSC FRSH

Dweck Data, 8 Merrifield Road, Ford, Salisbury, Wiltshire SP4 6DF, UK

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 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].

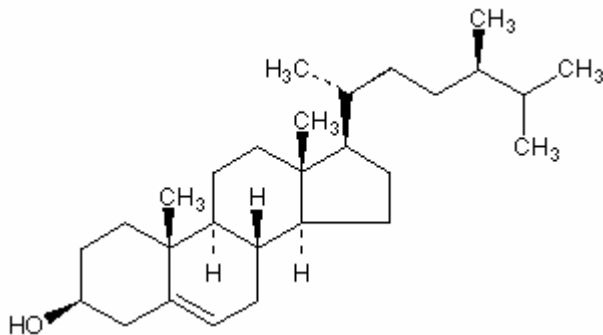
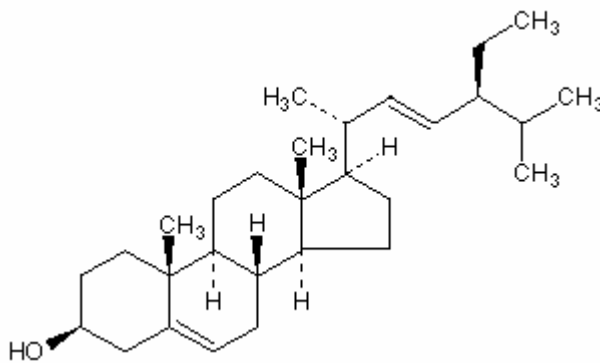


Fig.4 Campesterol

These included β -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 pruritic and erythemic conditions.

Fig.5 Stigmasterol

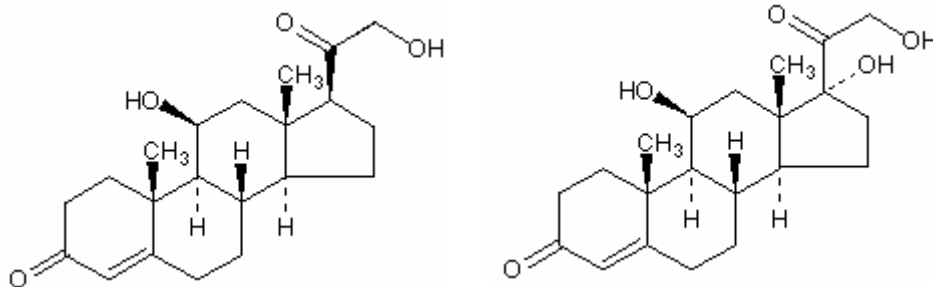


Fig.6 Corticosterone

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.

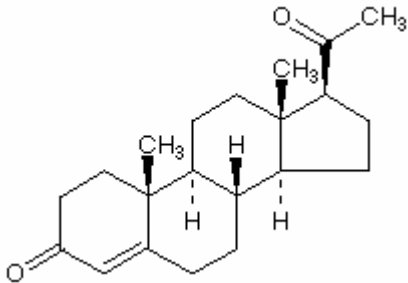


Fig.8 Progesterone

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.

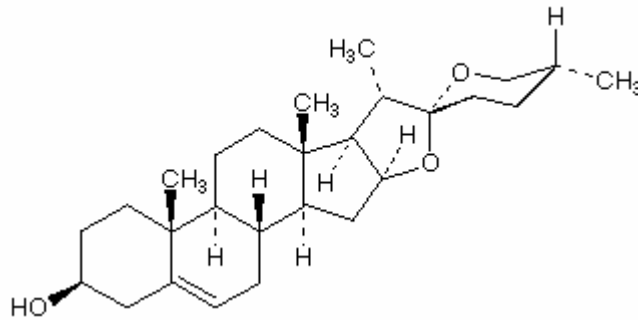


Fig.9 Diosgenin

The diosgenin was converted to progesterone. Diosgenin 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.

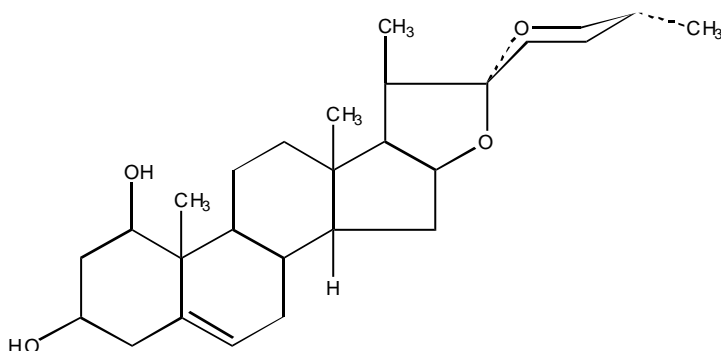
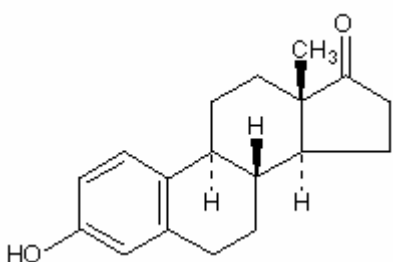


Fig. 10 Ruscogenin

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.

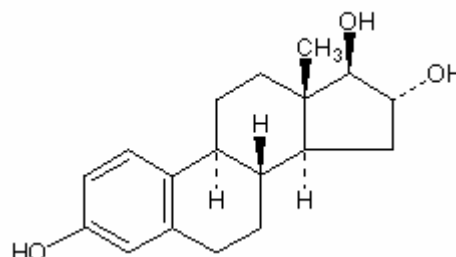
Fig.11 Estrone



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 β -sitosterol as illustrated above, but in addition contains daidzen and genistein, which are isoflavones (also anti-inflammatory and cell regenerating).

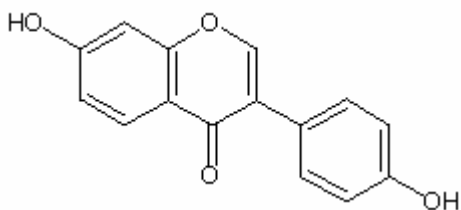


Fig.13 Daidzein

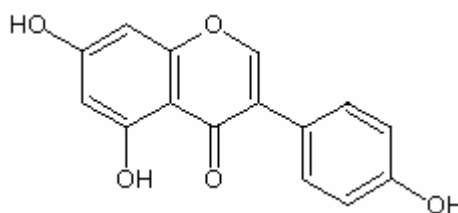


Fig.14 Genistein

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.

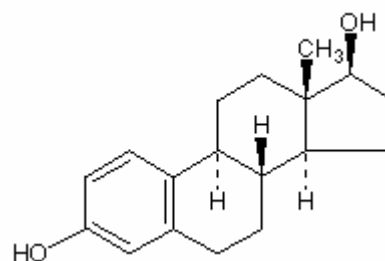


Fig.15 Estradiol

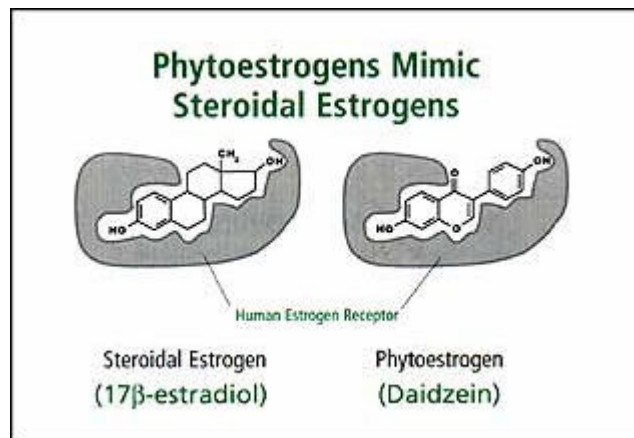
Proof of the steroidal nature of this Thai plant comes from its promotion as a bust developing preparation when taken internally. The supporting data is not conclusive, but shows some promise to its validity. Clearly this root would also have a topical application and benefit.

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].

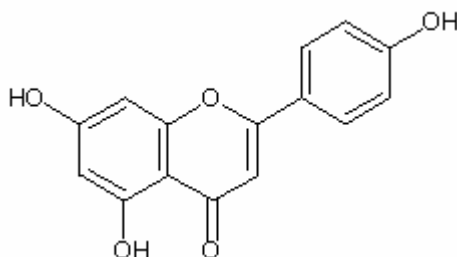


Fig.16 Apigenin

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.

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.

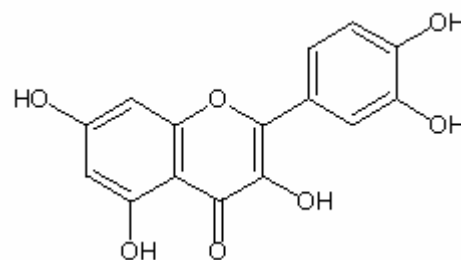


Fig.17 Quercetin

The iso-flavones have a phenyl group attached to the 3-position as opposed to the 2-position 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.

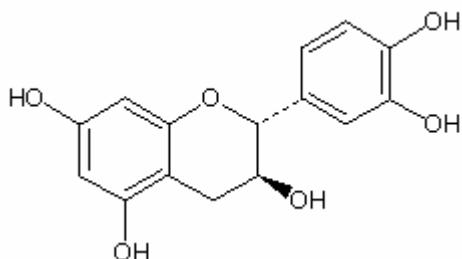
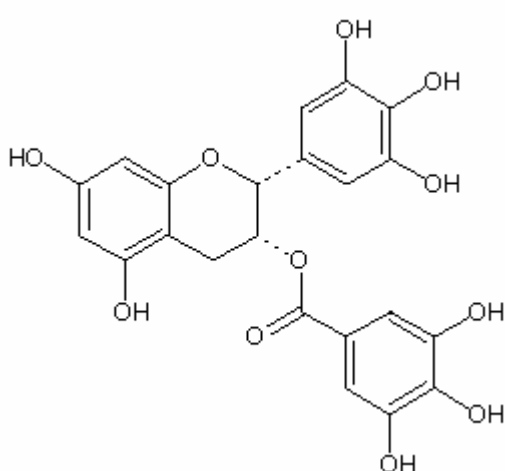


Fig. 18 Catechin

Catechins lack the carbonyl group at the 4-position.



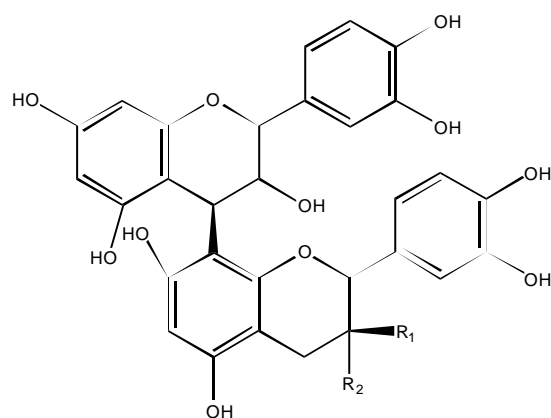
The formation of a powerful dimer called epigallocatechin-3-O-gallate occurs via the hydroxyl group and is found in materials like green tea (*Camelia sinensis*) and more recently in the stronger preparation white tea that is produced from the newly forming buds of that plant.

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.

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 B₁ and B₂

R₁ = OH; R₂ = H for Procyanidin B₁
R₁ = H; R₂ = OH for Procyanidin B₂

Fig.21 Procyanidin B₃ and B₄

R₁ = OH; R₂ = H for Procyanidin B₁

R₁ = H; R₂ = OH for Procyanidin B₂

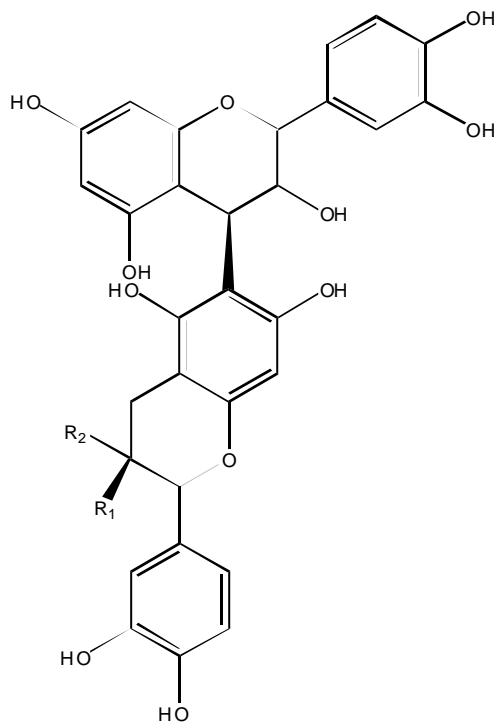


Fig.22 Procyanidin B₅ and B₇

R₁ = OH; R₂ = H for Procyanidin B₁

R₁ = H; R₂ = OH for Procyanidin B₂

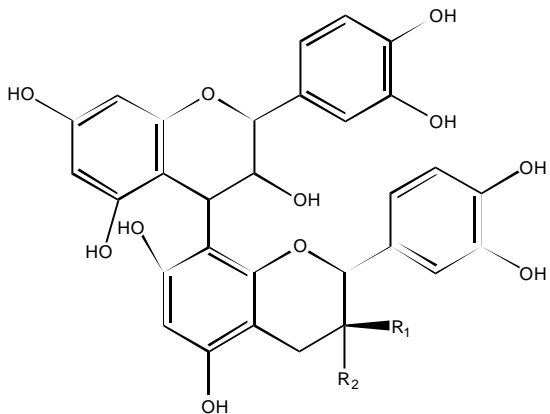
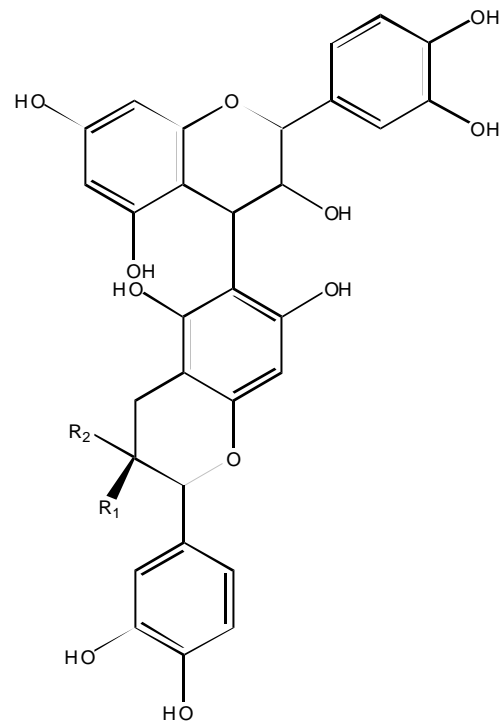


Fig.21 Procyanidin B₆ and B₈

R₁ = OH; R₂ = H for Procyanidin B₁

R₁ = H; R₂ = OH for Procyanidin B₂



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 Bombastus 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.

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).

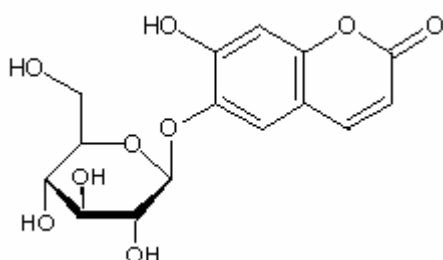
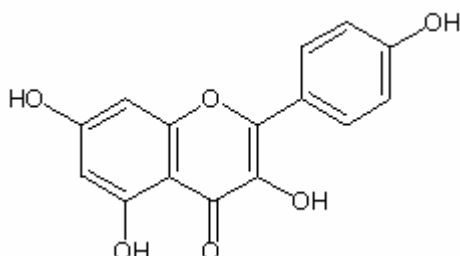


Fig 23 Esculin

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*), Marigold (*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.

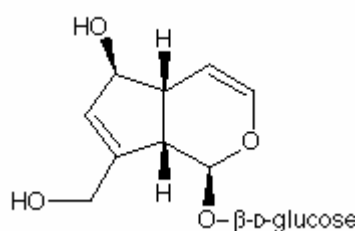
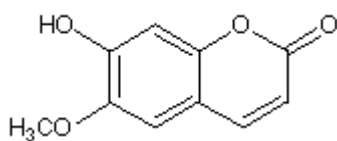


Fig 25. Aucubin

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

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*).

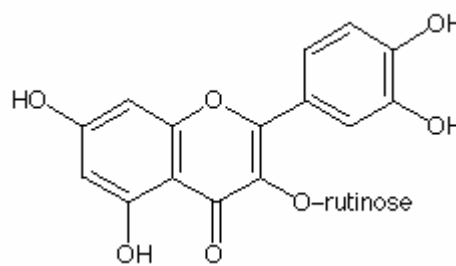
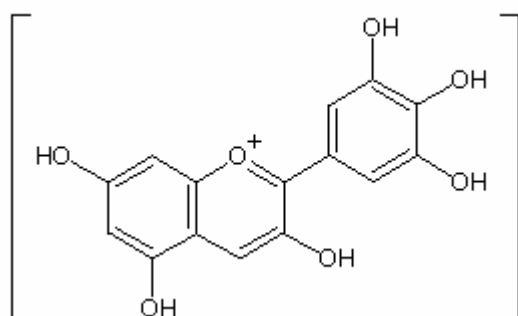


Fig 27. Rutin (Rutoside)

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].

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 xanthenes such as mesuaxanthone B and calophyllin B are obtained [Govindachari, *et al*;1968].

Fig 29. Mesuaxanthone-B

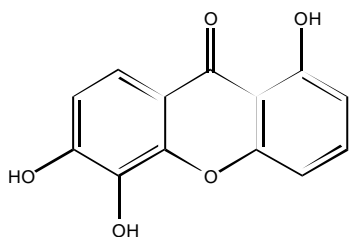
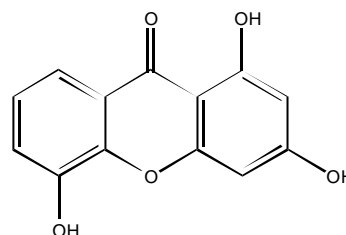


Fig 30. Mesuaxanthone-A



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

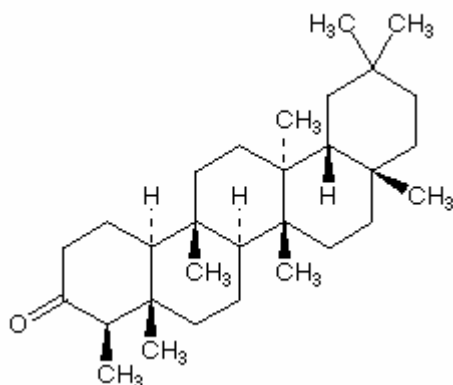


Fig 31. Friedelin

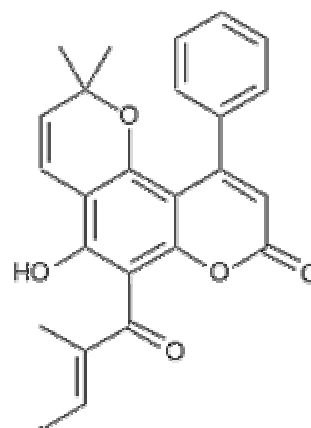
Friedelin has been identified. [Merck, 1996]

Calophyllolide, isolated from the nuts [Rastogi *et al*, 1998; Bhalla]. ED₅₀ was 140 mg/kg orally. Showed anti-inflammatory 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.

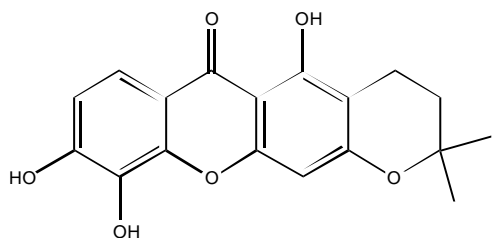
Fig. 32 Calophyllolide

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 xanthenes 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



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).

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

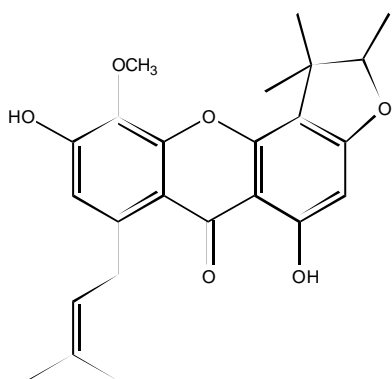
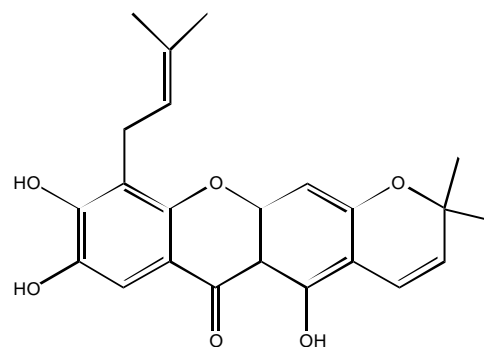


Fig 35. Caloxanthone B

Fig 34. Caloxanthone A

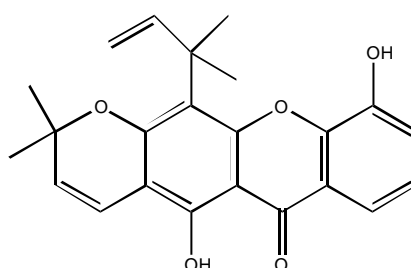


Fig 36. Caloxanthone C

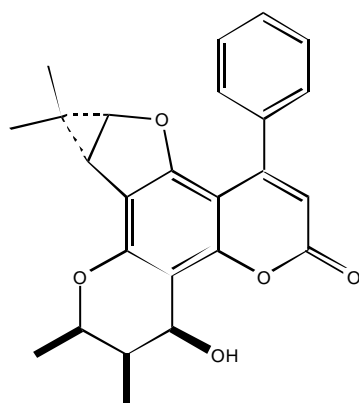


Fig 37. Inophyllum G-1

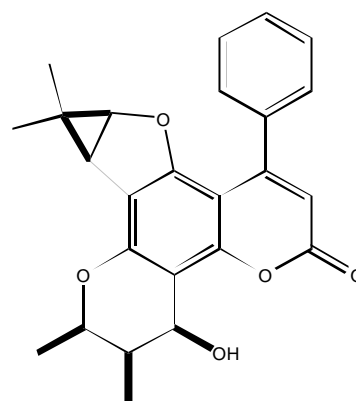
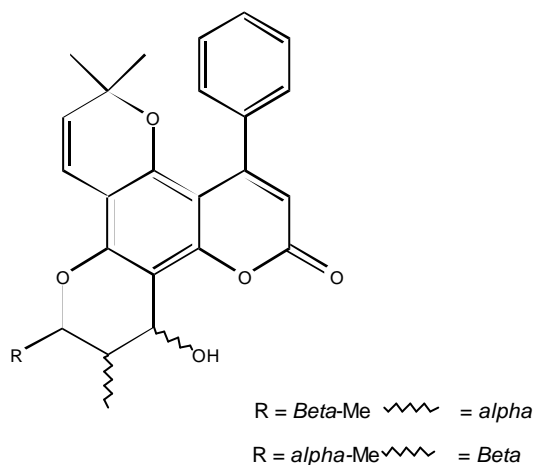


Fig 38. Inophyllum G-2

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]

Fig 39. Inophyllum P

The following active principles have been found in the oil:
- calophyllolide (C₂₅H₂₂O₅) the molecule of which contains a lactonic

and a methoxyl group.

- calophyllic acid (C₂₅H₂₄O₆), which results from the saponification of the calophyllolide.

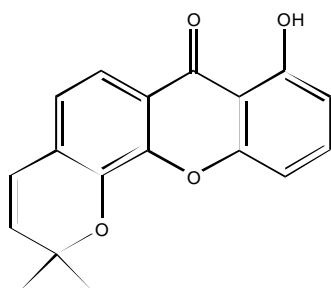


Fig 40. Dehydrocycloguanandin

These active principles are coumarin derivatives [Muller].
Composition of the oil :

- * Free fatty acids, glycerides, Sterols
- * Terpenoids & steroids (canophyllal, canophyllol, calophyllic 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).

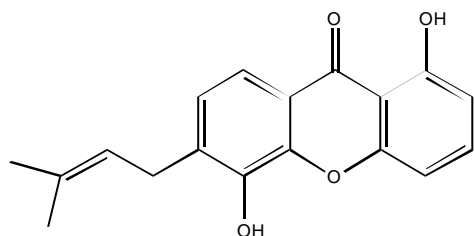


Fig 41. Calaphyllin-B

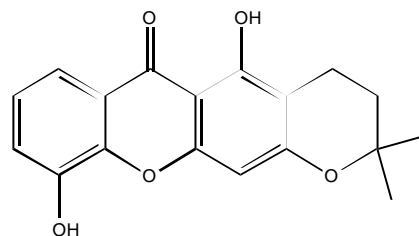


Fig 42. 6-desoxyjacareubin

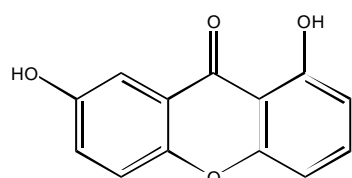
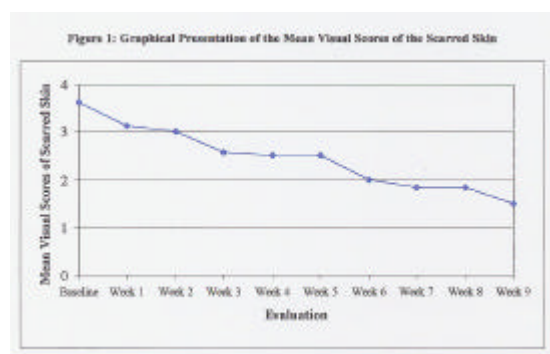
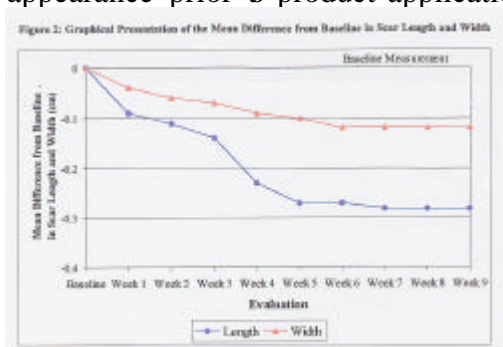


Fig 43. Euxanthone

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



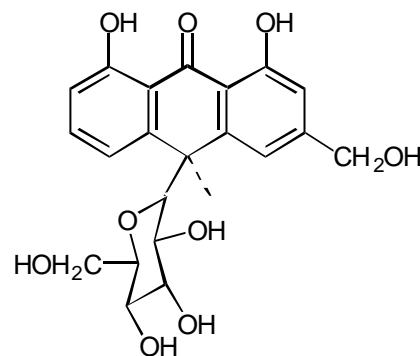
(baseline) and again at the end of week nine (9). The subjects also completed a product questionnaire that assessed their likes and dislikes of the product.

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 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

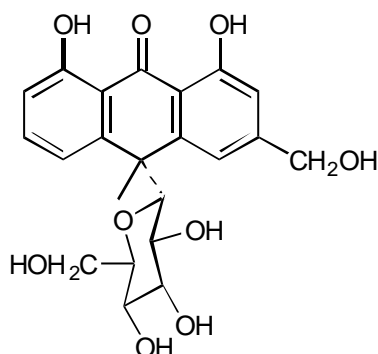


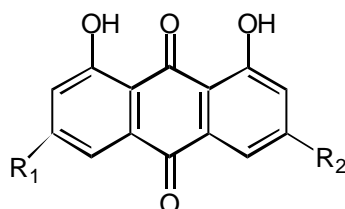
Fig 45. 10-(1',5'-anhydroglucosyl)-aloe-emodin-9-anthrone

These two chemicals are present as a mixture of:

10-C-β-L-glucosyldiastereo isomer of aloe-emodin anthrone and

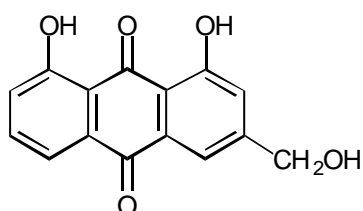
10-C-β-D-glucosyldiastereo isomer of aloe-emodin anthrone

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 ₂ OH	ALOE-EMODOL
H	COOH	RHEINE
H	CH ₃	EMODOL

Fig 46. Anthraquinone derivatives



3-Hydroxymethyl anthraquinone

1,8-dihydroxy-3-hydroxymethyl-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.)

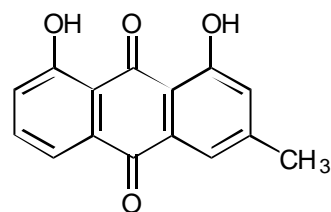
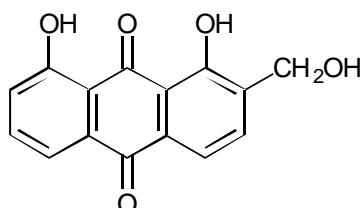
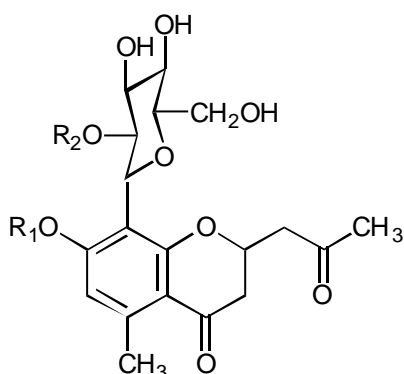


Fig. 49 Aloetic acid

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	<i>p</i> -coumaroyl	ALOERESIN A
H	H	ALOERESIN B
Glucosyl	<i>p</i> -coumaroyl	ALOERESIN C

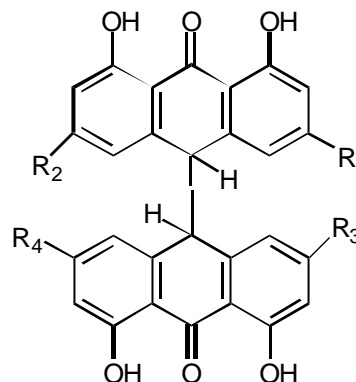
Fig 50. Aloeresin A, Aloeresin B and Aloeresin C
 Aloeresin A is 2-*p*-coumaroyl aloeresin
 Aloeresin B is 8-C-glucosylchromone aloeresin B
 Aloeresin C is 7-O-β-D-glucoside of aloeresin

Aloesone

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

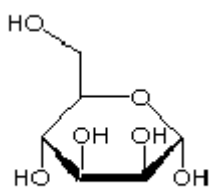
Homodianthrones

Fig 51. Sennidin A and B



R ₁	R ₂	R ₃	R ₄	Chemical Name
COOH	H	COOH	H	SENNIDIN A, B
CH ₂ OH	H	COOH	H	SENNIDIN C, D

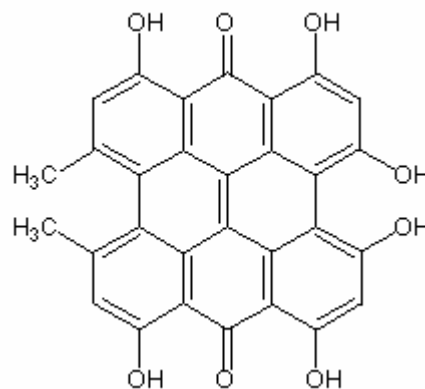
The above are the trace components, the major constituent is mannose-6-phosphate and it is this material which is attributed with the beneficial effects of the aloe vera. However, it is unlikely that this sugar derivative alone could give all the properties found for aloe in the scientific literature.



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.

References

Bezakova, L., Psenak, M., Kartnig, T. Effect of dianthrones and their precursors from *Hypericum perforatum* L. on lipoxygenase activity. *Pharmazie* 1999, 54, 9, 711 .
Department of Cell and Molecular, Biology of Drugs, Odbojarov 10, 83232 Bratislava, Slovakia.

Bhalla, TN, Saxena, RC, Nigam, SK, Misra, G., Bhargava, K.P.: Calaphyllolide – a new non-steroidal anti-inflammatory agent. *Indian J. Med. Res* 1980, **72**, pp 762-5

Brand-Garnys, E, Dansic van, Paul, Brand, Hans M.: Flavonoids: looking in the face of cosmeceuticals. *SÖFW*, 127(1/2), 8, (2001).

Burden, A.D.; Beck, M.H.: Contact hypersensitivity to topical corticosteroids. In: *Br J Dermatol* (1992 Nov) 127(5):497-500

Burkill, H.M.: The useful plants of West Tropical Africa. Edition 2. Vol. 2. Families E-I. Royal Botanic Gardens Kew. 1994. ISBN No. 0-947643-56-7.

Camacho F.; Institution: Departamento de Dermatologia Medico, Facultad de Medicina, Universidad de Sevilla, Sevilla; Spain. Treatment of acne scars with musk rose oil. *Medicina Cutanea Ibero-Latino-Americana*. Vol 22(3) (pp 137-142), 1994.

Christie, William W.: The analysis of evening primrose oil. *Industrial Crops and Products* 10 (1999) 73–83. Scottish Crop Research Institute ,In6ergowrie,Dundee DD25DA,Scotland,UK

Crodarom Avocadin data sheet and brochure

Dabrowska-Zamojcin, E; Katdonska, M; Tustanowski, S. Effect of buckwheat extract on free radical generation in rabbits administered a high-fat diet. *Phytotherapy Research* (1995) 9(5): 323-326. [Department of Pathophysiology, Medical Academy, Powstancow Wlkp. 72, 70-111 Szczecin, Poland.]

Davis, R.H.; Leitner, M.G.; Russo, J.M.; Byrne, M.E.: Wound healing. Oral and topical activity of Aloe vera. *J Am Podiatr Med Assoc*. 1989 Nov; 79(11): 559-62. ISSN: 8750-7315.

Dweck, A.C.: "Evening Primrose Oil.". *Soap, Perfumery and Cosmetics*. November (1991).

Dweck, A.C.: Soap, Perfumery and Cosmetics Asia "On the *Centella asiatica* trail." October/November (1996), **1**, 1, 41-42.

Dweck, A.C.: Natural Ingredients for colouring and styling. International Journal of Cosmetic Science **24**, 5, p.287-302, (2002).

Dweck, A.C.: *Calophyllum inophyllum* – Tamanu oil the African, Asian, Polynesian and Pacific Panacea. International Journal of Cosmetic Science **24**, 6, 1-8 (2002).

Fluck, Hans: Medicinal Plants, 1988 W.Foulsham & Co. Ltd. ISBN 0-572-00996-8.

Fulton, J.E. Jr: The stimulation of postdermabrasion wound healing with stabilized aloe vera gel-polyethylene oxide dressing. Acne Research Institute, Newport Beach, CA 92663. J Dermatol Surg Oncol. 1990 May; 16(5): 460-7. ISSN: 0148-0812.

Gopalakrishnan, C., Shankaranarayanan, D., Nazimudeen, S.K., Viswanathan, S., and Kameswaran, L.: Anti-inflammatory and C.N.S. depressant activities of xanthenes from *Calophyllum inophyllum* and *Mesua ferrea*. Ind. J. Pharmac., 12 (3), 181-191 (1980)

Govindachari, TR *et al.* Chemical components of the heartwood of *Calophyllum inophyllum*. Part 1. Isolation mesuaxanthone B and a new xanthone, calophyllin B. Indian Journal of Chemistry 6: 57 (1968).

Graham, J.: Evening Primrose oil, its remarkable properties and its use in the treatment of a wide range of conditions. 1984. Thorsons. ISBN No. 0-7225-1749-1.

Gudej, J; Tomczyk, M. Chromatographic analysis of polyphenolic compounds from the herbs of *Borago officinalis* (L.). [Badania chromatograficzne zwiaskow polifenolowych w zielu *Borago officinalis* (L.).] Vth Conference on the application of chromatographic methods in phytochemical and biomedical research, Lublin, Poland, 21-22 June, 1995. Herba Polonica (1996) 42(4): 252-256. [Zaklad Farmakognozji Akademii Medycznej, ul. Mickiewicza 2a, 15-230 Bialystok, Poland.]

Erazo, S., Garcia, R., Backhouse, N., Lemus, I., Delporte, C., Andrade, C. Phytochemical and biological study of radical *Lomatia hirsuta* (Proteaceae). Journal of Ethnopharmacology 1997 57 2 81-83 Chile. Department of Pharmacological and Toxicological Chemistry, Faculty of Pharmaceutical and Chemical Sciences, University of Chile, P.O. Box 233, Santiago-1, Chile.

Evans, W.C.: Trease and Evans, Pharmacognosy. 13th edition. 1989. Balliere Tindall ISBN 0-7020-1357-9.

Govindachari TR Viswanathan N Pai BR Rao R Srinivasan M: Triterpenes of *Calophyllum inophyllum* Linn. Tetrahedron (1967 Apr) 23(4):1901-10. ISSN: 0040-4020

Govindachari, TR *et al.* Chemical components of the heartwood of *Calophyllum inophyllum*. Part I Isolation mesuaxanthone B and a new xanthone, calophyllin B. Indian Journal of Chemistry 6: 57 (1968).

- Guin, J.D.: Complications of topical hydrocortisone. In: J Am Acad Dermatol (1981 pr) 4(4):417-22
- Iena, I.M.: [The therapeutic properties of aloe]. Vrach-Delo. 1993 Feb-Mar(2-3): 142-5. ISSN: 0049-6804
- Jayaweera, D.M.A.: Medicinal Plants used in Ceylon Part 3. National Science Council of Sri Lanka. Colombo 1981.
- Joshi, S. P. Chemical constituents and biological activity of Aloe barbadensis - a review. Journal of Medicinal and Aromatic Plant Sciences 1998, 20, 3 768-773 India. National Chemical Laboratory, Pune 411 008, Maharashtra, India.
- Joyeux, M; Lobstein, A; Anton, R; Mortier, F. Comparative antilipoperoxidant, antinecrotic and scavenging properties of terpenes and biflavones from Ginkgo and some flavonoids. Planta Medica (1995) 61(2): 126-129. [En, 15 ref.] [CEREPHA, 22 Rue Dupont des Loges, F-57000 Metz, France.]
- Komissarenko, NF; Derkach, AI; Komissarenko, AN; Chermeneva, GV; Spiridonov, VN. Coumarins of Aesculus hippocastanum L. Rastitel'nye Resursy (1994) 30(3): 53-59. [Ru, 18 ref.] [Gosudarstvennyi Nauchnyi Tsentr Lekarstvennykh Sredstv Ukraina, Khar'kov, Ukraine.]
- Leung, A.Y.: Encyclopedia of Common Natural Ingredients used in food, drugs and cosmetics. 1st. edition. John Wiley 1980 ISBN No. 0-471-04954-9.
- Marchini FB. Martins DM. de Teves DC. Simoes M de J.: [Effect of Rosa rubiginosa oil on the healing of open wounds (letter)]. [Portuguese]. Original Title: Efeito do oleo de rosa mosqueta na cicatrizacao de feridas abertas. Revista Paulista de Medicina. 106(6):356, 1988 Nov-Dec.
- Martindale. The Extra Pharmacopoeia. 29th. Edition. 1989. The Pharmaceutical Press. ISBN. No.0-85369-210-6.
- Merck. The Merck Index. 12th edition. Merck & Co. Inc. 1996 Whitehouse Station, NJ, USA. ISBN No. 0911910-12-3.
- Milovanovic, M; Picuric-Jovanovic, K; Vucelic-Radovic, B. Flavonoids of Anthriscus sylvestris. Fitoterapia (1994) 65(4): 376. [En, 7 ref.] [Faculty of Agriculture, Department of Food Technology, University of Belgrade, Nemanjina 6, PO Box 127, YU-11081 Zemun, Yugoslavia.]
- Moreno Gimenez JC. Bueno J. Navas J. Camacho F.: Institution: Departamento de Dermatologia Medico-Quirurgica y Venereologia, Facultad de Medicina, Universidad de Sevilla. [Treatment of skin ulcer using oil of mosqueta rose]. [Spanish]. Original Title: Tratamiento de las ulceras cutaneas con aceite de rosa de mosqueta. Medicina Cutanea Ibero-Latino-Americana. 18(1):63-6, 1990.
- Muller, Alban - The Pacific Ocean Oils (L'Ami Sept. 1993, No.5).

Oliver-Bever, Bep. Medicinal Plants in Tropical West Africa. Cambridge University Press 1986

Oxlade, L: Chemistry in Britain, 27, 1, 1991, p.9-10. Evening Primrose oil has recently yielded a new approach to the management of breast pain.

Pareja B. Kehl H.: Contribution to the identification of the active principles of *Rosa aff Rubiginosa* L. Anales de la Real Academia de Farmacia; Instituto de Espana. Vol 56(2) (pp 283-294), 1990. Institution: Departamento Farmacotecnia, U.N.M. de S.M. Lima, Lima; Peru.

Passwater, Richard A. and Kandaswami, Chithan: Pycnogenol - the super "protector" nutrient. Keats Publishing. 1994. ISBN No. 0-87983-648-2.

Puerta, R de la; Garcia, MD; Saenz, MT. Phenolics from *Helichrysum picardii*. Fitoterapia (1994) 65(4): 375. [En, 6 ref.]. [Laboratory of Pharmacognosy, Faculty of Pharmacy, University of Sevilla, 41012 Seville, Spain.]

Quisumbing, Eduardo. Medicinal Plants of the Philippines. Manila: Dept of Agriculture and natural Resources, Bureau of Printing, 1951.

Rastogi, Ram P., Mehrotra, B.N.: Compendium of Indian Medicinal Plants. Vol.3. 1980-1984. Central Drug Research Institute, Lucknow & Publications and Information Directorate, New Dehli. 1993. ISBN No. 81-85042-11-X.

Rastogi, Ram P., Mehrotra B.N.: Compendium of Indian Medicinal Plants. Vol.5. 1990-1994. Central Drug Research Institute, Lucknow & Publications and Information Directorate, New Dehli. 1998. ISBN No. 81-85042-14-4.

Reynolds, T.; Dweck, A.C.: Aloe vera leaf gel - a review update. Journal of Ethnopharmacology, **68** (1999) 3-37. Elsevier Publishers

Sato, Y; Ohta, S; Shinoda, M: Studies on chemical protectors against radiation. XXXI. Protection effects of *Aloe arborescens* on skin injury induced by X-irradiation. M. Shinoda, Faculty of Pharmaceutical Sciences, Hoshi University, 2-4-41, Ebara, Shinagawa-ku, Tokyo 142, Japan. Yakugaku Zasshi = Journal of the Pharmaceutical Society of Japan. 1990, 110: 11, 876-884

Siber Hegner of an analysis of "Aceite de Rosa mosqueta Lote 107" by SGS Chile Ltda. We read that this batch of Rosehip seed oil contained 0.83 mg of *trans*-retinoic acid/100 g of oil. The certificate was dated 10th September 1993 and numbered No. 450101R. SGS Chile Ltda. 1, Valdivieso 2409 (S. Joaquin), Santiago de Chile.

Silvan, AM; Abad, MJ; Bermejo, P; Sollhuber, M; Villar, A.: Antiinflammatory activity of coumarins from *Santolina oblongifolia*. Journal of Natural Products (1996) 59(12): 1183-1185. [English, 23 ref.] [Department of Pharmacology, Faculty of Pharmacy, University Complutense, 28040 Madrid, Spain.]

Strickland, F.M.; Pelley, R.P.; Kripke, M.L. : Prevention of ultraviolet radiation-induced suppression of contact and delayed hypersensitivity by *Aloe barbadensis* gel

extract. Department of Immunology, University of Texas M.D. Anderson Cancer Center, Houston 77030. *J Invest Dermatol.* 1994 Feb; 102(2): 197-204

Tosi, B; Tirillini, B; Donini, A; Bruni, A. Presence of scopoletin in *Malva sylvestris*. *International Journal of Pharmacognosy* (1995) 33(4): 353-355. [English, 11 ref.] [Institute of Botany, University of Ferrara, 2, Cso., Porta Mare, 44100 Ferrara, Italy.]

Valladares J. Palma M. Sandoval C. Carvajal F.: Institution: Universidad de Concepcion, Concepcion; Chile. Cream of rosehip oil (*Rosa aff. rubiginosa*). I. Formulation, preparation and first results in regeneration of damaged tissues. *Anales de la Real Academia de Farmacia; Instituto de Espana.* Vol 51(2) (pp 327-332), 1985.

Weiss, R.F.: *Herbal Medicine.* (translated from the 6th. German edition of *Lehrbuch der Phytotherapie* by A.R.Meuss). The Bath Press. 1986. ISBN 0-906584-19-1.

Zachariae L. Deleterious effects of corticosteroids administered topically, in particular intra-articularly. In: *Acta Orthop Scand* (1965) 36(2):127-36.