A Multi-Functional Botanical Active based on Ginkgo for Anti-Aging

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Abstract

When choosing an anti-ageing active for use in skin care products there is a long list of desirable properties such as antioxidant, free radical scavenger, stimulant of cell regeneration and collagen production to name but a few. This paper describes a concentrated botanical extract derived from Ginkgo biloba leaves*, which has the advantage of being multi-functional and with independent laboratory data to support claims that it is both an effective stimulant of cell regeneration and an active free radical scavenger. In the literature Ginkgo biloba is also cited as having antioxidant, anti-inflammatory and circulatory stimulant properties and to inhibit elastases and hyaluronidases associated with ageing. It is specially developed for use in skincare in particular anti-ageing and sun care products.

1. Introduction

1a. Free radicals

Free radicals are a reactive oxygen species which can cause severe damage to biologically active molecules in cells[1,6,33]. They are unstable molecules that are seeking an electron. By removing electrons from evenly paired molecules they create more free radicals resulting in a chain reaction which eventually leads to massive degenerative changes in the cellular DNA and the immune system. These changes can result in damaged lipid membranes, an accelerated ageing process, damaged or altered DNA and a compromised immune system.

Below are examples of different free radicals :

- Superoxide Anion radical: O_2- : originates especially from enzymatic reactions.
- Hydroxyl radical: OH^- : Mainly formed under irradiation. (X - rays, UV - rays, ϒ - rays)
- O_2 molecular oxygen: (although this is no radical it acts often like a free radical). Mainly originating from photochemical activation of oxygen.
- Peroxy radicals: ROO: appear essentially with oxidation of polyunsaturated fatty acids.
- Polysaturated fatty acid radical

Free radicals can be caused by a number of different phenomena:

- Tobacco smoke
- Pollution
- Pesticides & herbicides
- Infection /disease
- UV radiation
- Alcohol
- Carcinogens
- Physical & emotional trauma

1b. Antioxidants & free radical scavengers

Free radicals can be neutralized by substances that are called antioxidants or free radical scavengers. They accomplish this by donating a free electron to the free radical which then stabilizes the molecule and prevents it doing further damage. Examples of some antioxidants are vitamins C, E & A and flavonoids.

Flavonoids

Flavonoids are polyphenolic compounds that are found in plants and which have well known antioxidant properties[1,2,3,5]. The flavonoids include phytochemical groups such as catechins, flavonols, flavones, flavanes and anthocyanidins and these different classes of flavonoids vary in their potential oxidative ability. The free radical scavenging activity of flavonoids is related to their molecular structure and the pattern of substitution on the hydroxyl groups[1,53]. The ability to scavenge free radicals plays an important part in the effectiveness of flavonoids as antioxidants[1] and many have antioxidant capacities that are higher than vitamins C & E[52]. Many plants that are high in certain flavonoids have been used medically to counteract the adverse effects of disease in which free radicals are implemented[1,51]. The intake of food high in anti-oxidants has been recommended also to ensure a healthy diet[1,14].

What role do free oxygen radicals play in skin ageing?

Skin care cosmetics and in particular anti-ageing and sun care products are developed to counteract and prevent the adverse effects that free radicals have on the skin. These adverse effects may include premature ageing, inflammation or even in the

worst case cancer of the skin. UV irradiation as well as other environmental influences (e.g. air pollution, ozone, nitrous oxides, tobacco smoke etc.) may stimulate the formation of free radicals in the skin and consequently induce skin damage.

It is therefore essential to protect the skin against deleterious effects of free radicals. In addition to sunscreens, a certain protection can be obtained by preparations containing vitamin E. Cosmetochem International research labs have developed an effective plant-based free radical scavenger. By screening a range of plant extracts a concentrated extract of Gingko biloba* was identified as having high levels of certain flavonoids. It was found that by elaborating the best extraction and purification conditions the antioxidant and free radical scavenging activities could be optimized.

1c. Ginkgo biloba

Ginkgo biloba is the only living species of the family Ginkgoaceae, which were gymnosperms that thrived 175 to 200 million years ago[5,16].

Extracts from the dried leaves have been used in traditional Chinese medicine as remedies for a range of illnesses for over 5000 years[5,16,23,49,51,52] and are still used in modern herbal medicine for a wide range of ailments[8,16,23,24]. Ginkgo extract appears to be effective in the treatment of those diseases where free radical damage is thought to be the cause[5,8,9,11,15,16]. It has been shown to improve the mental performance of geriatric patients, where this was previously impaired[56].

Main components of Ginkgo biloba

The major components of Ginkgo biloba are the flavonoids and the terpenoids (including bilobalides and ginkgolides A,B,C,M & J)[5]. The flavonoids are the major contributors to the antioxidant activity of Ginkgo biloba[5]; in particular kaempferol and quercetin have been shown to be implemented[11,13]. The bilobalides are closely related to ginkgolides and have a protective effect on nervous tissue due to their role in motor nerve regeneration. Ginkgolides inhibit the activity of the platelet activating factor (PAF). PAF decreases inflammation by increasing the permeability of blood vessels and contracting various involuntary muscles[5,23].

The following substances are listed in the literature as actives of the plant[5,8,9,23,24,25,26,41,48]:

a. Flavonoids:
- **Flavones:** Quercetin, Isoquercetin, Isorhamnetin, Kaempferol, Myricetin, Quercetin-3-Rhamnoglucoside, Kaempferol-3-Rhamnoglucoside, Quercetin Coumaroyl Glucorhamnoside, Kaempferol Coumaroyl-Glucorhamnoside, Luteolin Glucoside.
- **Biflavones:** Bilobetin, Ginkgetin, Isoginkgetin, Sciadopytisin.

b. Catechins: Catechin, Epicatechin, Gallocatechin, Epigallocatechin.

c. Leukoanthocyanines

d. Shikimic Acid

e. Diterpenes: Ginkgolide A, B, C.

f. Sesquiterpene: Bilobalide.

g. Phytosterols: β-Sitosterol, β-Sitosterol Glucoside.

h. Aromatic Substances: Ginkgol, Bilobdol, Ginkgolic Acid.

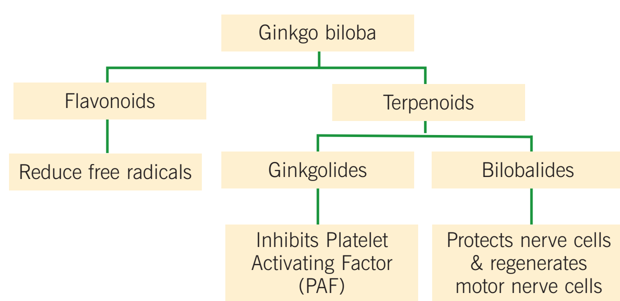

*Diagram after Chan[5]

Figure 1. Summary of effects of Ginkgo biloba

2. Efficacy of a concentrated extract of Ginkgo biloba* as a free radical scavenger

2.a. Evaluation as an effective neutralizing agent of free-radicals induced by UV rays

Method

The anti-radicular effect was assessed by means of a method which measured the cytotoxicity induced by oxygenated free radicals to human dermal fibroblasts in the presence and absence of the concentrated Ginkgo biloba extract*.

A pre-screening experiment was carried out to select extract test concentrations (i.e. 0.01%, 0.05% & 0.1%) below the IC50 i.e. the concentration which inhibits cell growth by 50% (found to be 0.84%)[34].

Treatment of cells

Human dermal fibroblasts were incubated in culture media containing, 0.01%, 0.05% & 0.1% concentrated Ginkgo biloba extract* for 48 hours before UV irradiation, during UV irradiation and until 24 hours after.

The cell treatments above were exposed to two different levels of UV irradiation (1000 mJ/cm^2 and 2000 mJ/cm^2). A negative control was also included in which no UV irradiation took place and a positive control using a UV protection standard of 0.1 g/l vitamin E plus 0.046 g/l vitamin C (maximum non-cytotoxic concentration).

MTT cell proliferation assay

Measurement of cell proliferation was made using the MTT method[54]. MTT is now a widely accepted method which uses the reduction of tetrazolium salts in the evaluation of both cell proliferation and cell death[27]. The yellow tetrazolium MTT (3-(4,5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide) is reduced by metabolically active cells, partly by the action of dehydrogenase enzymes to generate reducing equivalents of NADH and NADHP. The resulting intracellular formazan can be solubilized and quantified by spectroscopic means.

After elimination of the culture medium and dissolution of the crystals by DMSO (dimethyl sulfoxide), the optical density was read at 570 nm; this reading being directly proportional to the number of live cells present.

Results

Figures 2-5 show the results of the effect of Ginkgo biloba extract* on the cell mortality of cells irradiated with UVB rays at 1000 mJ/cm^2 and 2000 mJ/cm^2. At a level as low as 0.1% Ginkgo biloba extract* reduced cell mortality between 42% and 54% compared to the unprotected control when irradiated by 2000 and 1000 mJ/cm^2 UVB rays respectively. A protective effect is already significant in the presence of 0.01% of the Ginkgo biloba extract*. The protection control containing vitamin C and E only achieved 23-26% cellular protection, approximately 50% of that of the Ginkgo biloba extract*. In addition, in the absence of UVB the growth of the human fibroblasts were stimulated by 18% by 0.1% Ginkgo biloba extract* compared to 13% for the vitamin C & E protection control.

	Concentration of Ginkgo Biloba extract* (%)				Positive control
	0	0.01	0.05	0.1	Vitamin E + C
Optical density without UVB treatment, after MTT assay	0.186 ±0.06	0.179 ±0.011	0.198 ±0.012	0.219 ±0.016	0.21 ±0.013
Cellular mortality without UVB treatment	0%	4%	-6%	-18%	-13%
Optical density after UVB treatment and MTT assay	0.093 ±0.01	0.107 ±0.011	0.134 ±0.007	0.143 ±0.013	0.118 ±0.018
Cellular mortality after UVB treatment	50%	42%	28%	23%	37%
Cellular protection in relation to control after UVB treatment in absence of Ginkgo biloba extract*	0%	16%	44%	54%	26%

Figure 2. Cellular protection provided by Gingko biloba extract to human fibroblasts exposed to UVB rays (1000 mj/cm²)

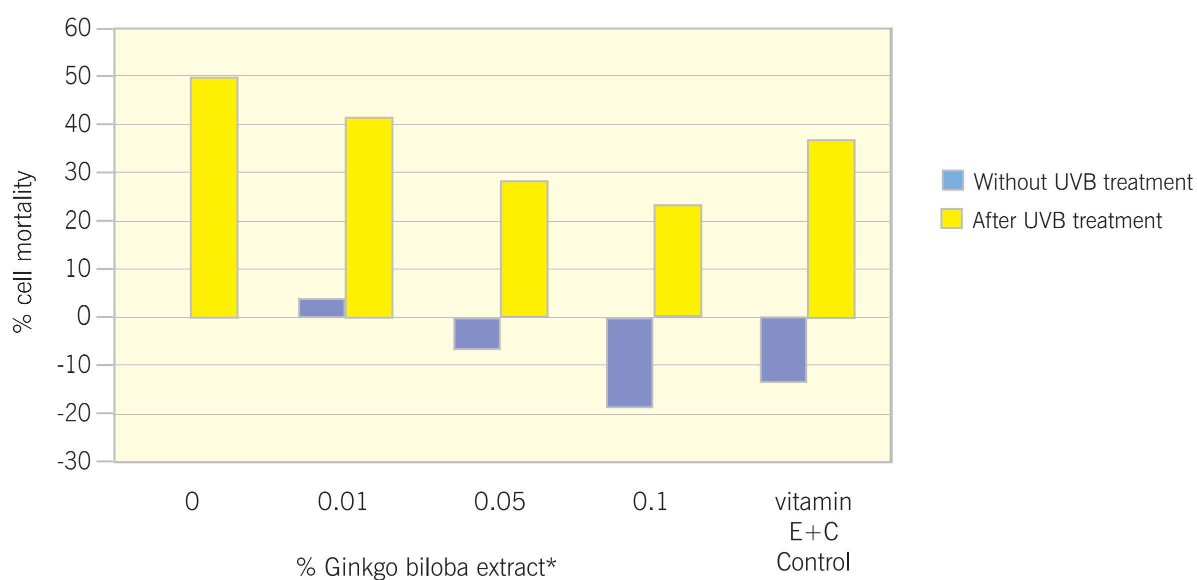

Figure 3. Effect of Ginkgo biloba extract* on cell mortality after exposure to 1000 mJ/cm2 UVB

	Concentration of Ginkgo Biloba extract* (%)				Positive control
	0	0.01	0.05	0.1	Vitamin E + C
Optical density without UVB treatment, after MTT assay	0.206 ±0.007	0.205 ±0.021	0.219 ±0.017	0.238 ±0.012	0.225 ±0.023
Cellular mortality without UVB treatment	0%	0%	-6%	-16%	-9%
Optical density after UVB treatment and MTT assay	0.075 ±0.01	0.083 ±0.011	0.110 ±0.007	0.130 ±0.013	0.105 ±0.020
Cellular mortality after UVB treatment	64%	60%	47%	37%	49%
Cellular protection in relation to control after UVB treatment in absence of Ginkgo biloba extract*	0%	6%	27%	42%	23%

Figure 4. Cellular protection provided by Gingko biloba extract* to human fibroblasts exposed to UVB rays (2000 mj/cm^2)

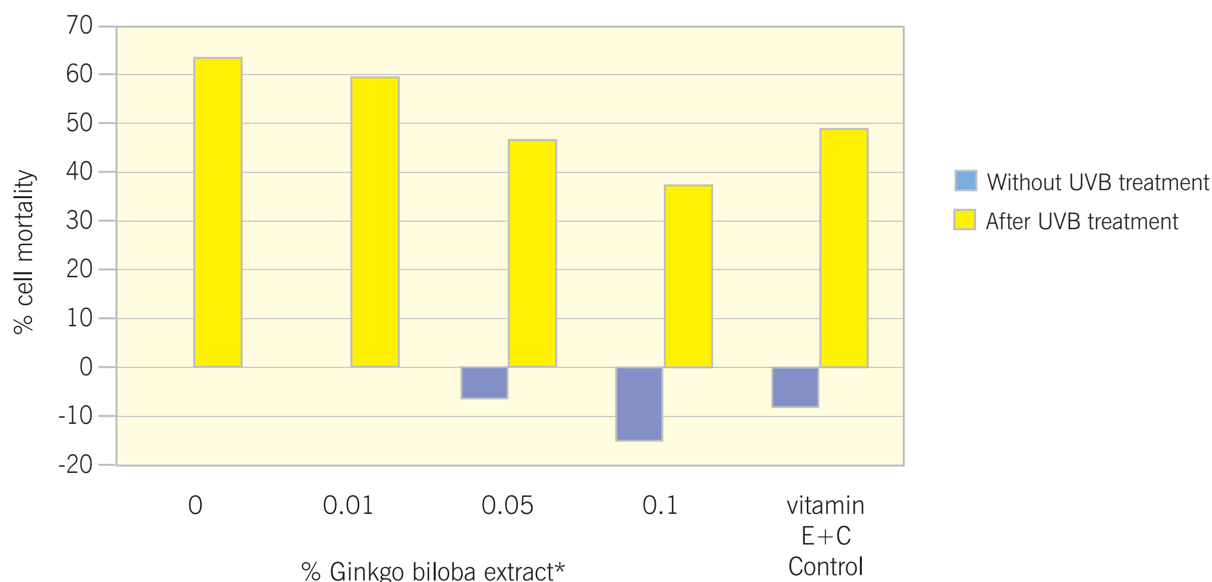

Figure 5. Effect of Ginkgo biloba extract* on cell mortality after exposure to 2000 mJ/cm2 UVB

2.b. Determination of MDA (malondialdehyde) formation from deoxyribose in the presence or absence of Ginkgo biloba extract*

The action of xanthine oxidase on hypoxanthine in the presence of iron results in the formation of oxygenated free radicals able to degrade deoxyribose to produce malondialdehyde (MDA). The study described below used this method to measure the formation of MDA in the presence and absence of Ginkgo biloba extract* to determine its efficacy as a free radical scavenger.

Method

Generation of oxygenated free radicals : Iron, deoxyribose, EDTA, hypoxanthine, 0.1% Ginkgo biloba extract* phosphate buffer and xanthine oxidase were mixed in borosilicated glass tubes with screw caps. The mixture was incubated for 1 hour at 37°C.

The following controls were included:

- **Product control:** 0.1% Ginkgo biloba extract without deoxyribose – to verify that the product is not degraded by MDA

- **Negative control:** Mixture without xanthine oxidase
- **Degradation control:** Mixture with no Ginkgo biloba extract* protection
- **Protection control:** Mixture where 230mM of vitamin E & 500mM of vitamin C replaces Ginkgo biloba extract*.

All tests were carried out in triplicate.

Measurement of MDA formation: After incubation the tubes were centrifuged and the concentration of thiobarbituric acid reactive substances (TBARS), of which MDA is the main representative, were determined in the different test supernatants. Each supernatent, with thiobarbituric acid, perchloric acid & BHT (butylated hydroxytoluene) added, was incubated at 95°C for 1 hour and then extracted with butanol. A standard range was set up with dilutions of MDA solution instead of the test supernatants. The MDA concentration was determined in each butanolic extract by spectrofluorimetry (excitation : 532 nm & emission : 553 nm).

Results

Figures 7 & 8 show the results of the analyses of MDA in the test product compared to the controls. A low level of MDA indicates an effective free radical scavenger (Fig. 6). 0.1% Ginkgo biloba extract* inhibited the formation of free

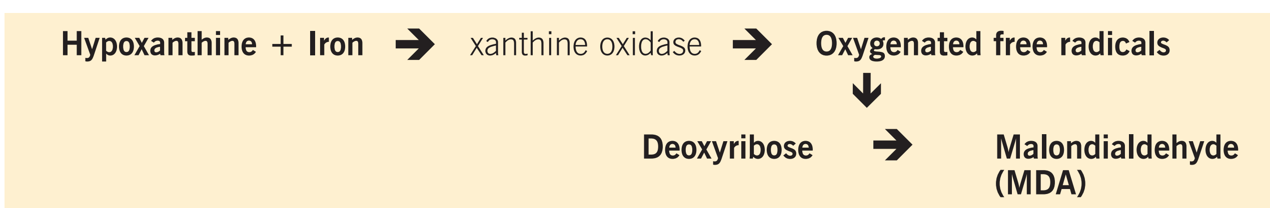

Figure 6. Mechanism for the measurement of an effective free radical scavenger

Treatment	Concentration of Ginkgo Biloba extract* (%)		Positive control
	0	0.1	Vitamin E + C
Product control: MDA (n moles) generated in absence of deoxyribose	-	0	0
MDA (n moles) generated in the presence of deoxyribose	16.5 ±1.2	0.13 ±0.08	3.69
MDA (n moles) generated from deoxyribose	16.5	0.13	3.69
Inhibition of MDA formation (%)	0	99	78

Figure 7. Determination of MDA (malondialdehyde) formation fron deoxyribose in the presence and absence of Ginkgo biloba extract*

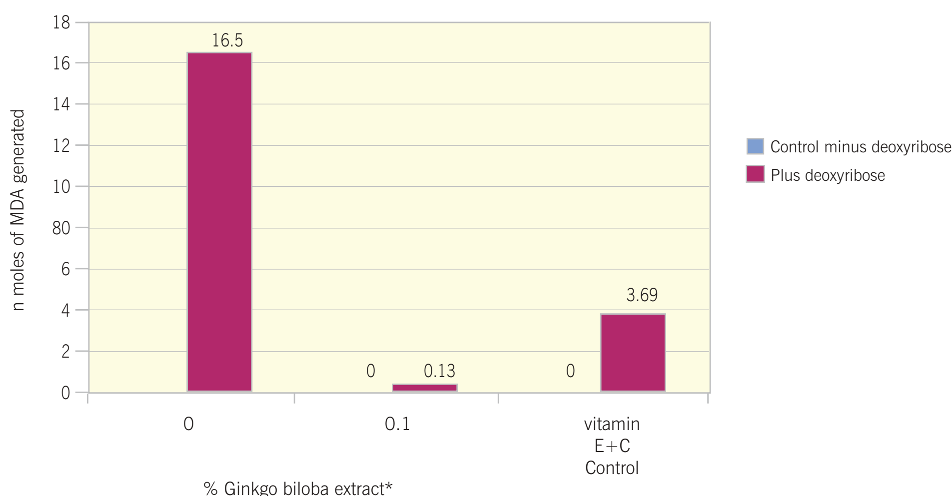

Figure 8. Determination of MDA formation from deoxyribose in the presence & absence of Ginkgo biloba extract*

radicals by 99% compared to 78% by the protection control containing the mixture of vitamins C & E.

Conclusions

At a concentration as low as 0.1% Ginkgo biloba extract* was shown to:

- Provide good protection against UVB irradiation and to exhibit better protection than the vitamin C + E control
- Be an effective scavenger of free radicals
- Stimulate cell growth
- Be safe[35,36,37]

These results are supported by other research which has showed that standardized extracts of flavonoids of Ginkgo biloba have been shown to exhibit strong antioxidant[7,18,19,20,21] and anti-radicular[6,40] activity and to be more effective as antioxidants than vitamins C & E[15,54]. Ginkgo biloba extracts have also been shown to be more effective at protecting lipids from oxidative degradation than proteins[5]. A possible reason for the differences in antioxidant activity between different sources of Ginkgo biloba extracts found by other workers could be due to differences in manufacturing processes[10].

The results presented here in addition to those properties previously documented in the literature for Ginkgo biloba (Fig. 9) make Ginkgo biloba Extract* an ideal candidate as an anti-ageing active for skin care products.

Properties	Suggested cosmetic applications
• Free radical scavenger[4,5,6,11,12,22,23,40,43,44,45] • Antioxidant[4,5,6,7,10,13,15,18,19,20,21,23,42,44,45,46] • Inhibits elastases & hyaluronidases associated with ageing[48] • Good treatment for dry skin[38]. • Stimulates collagen production & skin regeneration[46] • Inhibits lipid peroxidation of membranes & helps to maintain integrity & permability of cell walls[40,42] • Circulatory stimulant[8,23,24,41,42,44,49,52] • Stimulant[41] • Tonic[41,47] • Anti-inflammatory[5,6,9,42,49,50,52] • Antibacterial[39,44,47]	• Skin care especially: • Anti-ageing products and products for mature skins • Sun & after sun care products

Figure 9. Cosmetic related activities of Ginkgo biloba extracted from the literature

*** The concentrated Ginkgo extract used in this study is sold under the Cosmetochem trade name : Flavonoid Complex SC**

References

1. Amic, D. et al. (2003). Structure-radical scavenging activity relationships of flavonoids. Croat. Chem. Acta 76 (1) : 55-61.

2. Hollman, P.C.H. & Arts, I.C.W (2000). J. Sci. Food Agric. 80, 1081-93.

3. Aherne,S.A. & O'Brien N.M. (2002). Nutrition 18, 75-81.

4. Louajri, A. et al. (2001). The effect of Ginkgo biloba extract on free radical production in hypoxic rats. Biol. Pharm. Bull. 24 (6) : 710-12.

5. Tan, E & Chan, P (2003). Ginkgo biloba. Disease mechanism IV : Free Radical Damage. http://cgi.stanford.edu/group

6. Hibatallah, J., Carduner, C. & Poelman M.C: (1997). Protective effect of a flavonoidic extract from Ginkgo biloba against free radical injury. Proceedings of the 19th IFSCC Congress, Sydney.

7. Huang, P. et al. (2004). Effect of Ginkgo biloba leaves on oxidation of human low density lipoproteins in vitro. Wei Sheng Yan Jiu. 33 (4) : 453-54.

8. Hoffmann, D. (). Ginkgo biloba. American Botanical Council- Herbal Materia Medica.

9. Ilieva, I. et al. (2004). The effects of Ginkgo biloba extract on lipopolysaccharide-induced inflammation in vitro and in vivo. Exp. Eye Res. 79 (2) : 181-87.

10. Mantle, D., Wilkins, R.M. & Gok, M.A. (2003). Comparison of antioxidant activity in commercial Ginkgo biloba preparations. J. Altern. Complement. Med. 9 (5) : 625-29.

11. Smith, J.V. & Luo, Y. (2003). Elevation of oxidative free radicals in Alzheimer's disease models can be attenuated by Ginkgo biloba extract EGb 761. J. Alzheimer's Dis. 5 (4) : 287-300.

12. Zhang, Y., Wu, X.Q. & Yu, Z.Y. (2002). Comparison study on total flavonoid content and anti-free radical activity of the leaves of bamboo, Phyllostachys nigra and Ginkgo biloba. Zhonngguo Zhong Yao Za Zhi. 27 (4) : 254-57.

13. Bedir, E. et al. (2002). Biologically active secondary metabolites from Ginkgo biloba. J. Agric. Food Chem. 50 (11) : 3150-55.

14. Gohil, K. & Packer, L. (2002). Bioflavonoid-rich botanical extracts show antioxidant and gene regulatory activity. Ann. N.Y. Acad. Sci. 957 , 70-77.

15. Horakova, L. et al. (2003). Standardized extracts of flavonoids increase the viability of PC12 cells treated with hydrogen peroxide : effects on oxidative injury. Arch. Toxicol. 77 (1): 22-29.

16. Gaby, A.R. (1996). Ginkgo biloba extract : A review. Altern. Med. Rev. 1 (4) : 236-42

17. Ginkgo biloba Monograph. (1998). Altern.Med. Rev. 3 (1) : 54-57.

18. Rong, Y., Geng, Z. & Lau, B.H. (1996). Ginkgo biloba attenuates oxidative stress in macrophages and endothelial cells. Free Radic. Biol. Med. 20 : 121-27.

19. Yan, I.J. , Droy-Lefaix, M.T. & Packer, L. (1995). Ginkgo biloba extract (EGb 761) protects human low density lipoproteins against oxidative modification mediated by copper. Biochem. Biophys. Res. Commun. 212 : 360-66.

20. Shen, J.G. & Zhou, D.Y. (1995). Efficiency of Ginkgo biloba extract (EGb 761) in antioxidant protection against myocardial ischemia and reperfusion injury. Biochem. Mol. Biol. Int. 35 ,125-34.

21. Marcocci, L. et al. (1994). Antioxidant action of Ginkgo biloba extract EGb 761. Methods Enzymol. 234 , 462-75.

22. Maitra, I. et al. (1995). Peroxyl radical scavenging activity of Ginkgo biloba extract Egb 761. Biochem. Pharmacol. 49 , 1649-55.

23. Carr, D. , Bartoleti, R.M. & D'Angela, A. (1997). Medical attributes of Ginkgo biloba–The Maidenhair Tree. Paper developed as part of the Medical Botany course at Wilkes University.

24. Stromgaard, K. & Nakanishi, K. (2004). Chemistry and biology of terpene trilactones from Ginkgo biloba. Angew. Chem. Int. Ed. Engl. 43 (13) : 1640-58.

25. van Beek, T.A. (2002). Chemical analysis of Ginkgo biloba extracts. J. Chromatogr. A. 967 (1) : 21-55.

26. Deng, F. & Zito S.W. (2003). Development and validation of a gas chromatographic-mass spectrometric method for simultaneous identification and quantification of marker compounds including bilobalide, ginkgolides and flavonoids in Ginkgo biloba L. extract and pharmaceutical preparations. J. Chromatogr. A. 986 (1) : 121-27.

27. Mossmann, T. (1983). Rapid colorimetric assay for cellular growth and survival : application to proliferation and cytotoxicity assays. Immunol. Methods, 65 . 55-63.

28. Torel, J. , Cillard, J. and Cillard, P. (1986). Antioxidant activity of flavonoids and reactivity with peroxy radical " Phytochemistry, 25 (2) : 383-385.

29. Corungiu, F. et al. (1986). Lipid peroxidation and molecular damage to polyunsaturated fatty acids in rat liver. Recognition of two classes of hydroperoxides formed under conditions in vivo Chem. Biol. Interactions, 59, 147-55.

30. Corongiu, F. et al. (Antioxidant activity of a-tocopherol against lipid peroxidation in rat liver microsomes. IRL Press Limited, Oxford, (England), 81-86.

31. Situnayake, R.D. et al. (1990). Lipid peroxidation and hepatic antioxidants in alcoholic liver disease. Gut, 31, 1311-17.

32. Rafat Husain S., Cillard. J. & Cillard, P. (1987). Hydroxyl radical scavenging activity of flavonoids. Phytochemistry, 26, 2489-91.

33. Miiyachi,Y., Horio, T. & Imamura, S.J. (1983). Clin. Exp. Dermatol. 8, 305-310.

34. EVIC-CEBA Laboratoire de Recherche et d'Expérimentation, France. Test Report N° B228/3255 . Assessment of the effect of Flavonoid Complex SC on the cytotoxicity of oxygenated free radicals induced by UVB rays.

35. Test report (IC 94.51) Primary Skin irritation BIOGIR S.A.F-33611 GAZINET (France) February 1994.

36. Test report (IO 94.51) Occular irritation BIOGIR S.A.F-33611 GAZINET (France) February 1994

37. Test report (INR 94.51) Acute, single oral dose BIOGIR S.A.F-33611 GAZINET (France) February 1994

38. Rovesti, P. (1974) Riv. Ital. Ess. Prov., 56, 13-17 .

39. Mourey, M., Mortier, F. & Mourey, A. (1985). Plantes Méd. Phytothér., 19, 270-76.

40. Pincemail, C. & Deby, C. (1986). Presse Méd., 15, 1475-1479.

41. Plants in Cosmetics, Volume 1 : Prepared by the Committee of Experts on Cosmetic Products with the collaboration of Prof. Anton Robert, Dr Franco Patri & Prof. Vittorio Silano. , Council of Europe Publishing, 2001.

42. Leung, A.Y. & Foster, S. (1996). Encyclopedia of Common Natural Ingredients used in Food and Cosmetics

43. Krishnakanatha, T.P. & Lokesh, B.R. (1993). Scavenging of superoxide anions by spice priciples. Indian J. Biochem.Biophys, 30 (2) . 133-4.

44. Stephen Foster : Botanical Booklet Series – American Botanical Council Site. Ginkgo : http://www.herbalgram.org/botanicalbooks/ginkgo.html

45. Lin, S.Y. & Chang, H.P.(1997). Induction of superoxide dimutase and catalase activity in different tissues and protection from UVB radiation after topical application of Ginkgo biloba extracts. Methods Find. Exp. Clin.Pharmacol., 19 (6) : 367-71.

46. Kim, S.J. et al. (1997). Effects of flavonoids of Ginkgo biloba on proliferation of human skin fibroblasts. Skin Pharmacol. 10 (4) : 200-05.

47. Ody, P.(2000) The Complete Guide Medicinal Herbal, publ. Dorling Kindersley, 2nd edn.

48. Brand-Garnys, E. et al. (2001). Flavonoids : looking at the face of pharmaceuticals (part 2), p.93. Cosmetic and Toiletry Manufacture Worldwide, pub. Aston Publishing Group.

49. Wren, R.C. (1988). Potter's New Encyclopedia of Botanical Drugs & Preparations, publ. Daniel Co. Ltd.

50. Castelli, D. et al. (1998). Pretreatment of skin with a Ginkgo biloba extract / sodium carboxymethly-b-1,3-glucan formulation appears to inhibit the elictation of allergic contact dermatitis in man. Contact Dermatitis, 39 (5) : 274.

51. Middleton Jr, E., Kandaswarmi, T.C. & Theoharides, C. (2000). For review. Pharmacol. Rev. 52, 673-751.

52. Prior, R.L. & Cao, G. (2000). J. AOAC Int. 83, 950-56.

53. Rice-Evans, C. Miller, N.J. & Paganga, G. (1996). Free Radical Biol. Med.20, 933-56.

54. www.trevigen.com

55. EVIC-CEBA Laboratoire de Recherche et d'Expérimentation, France. Test Report N° B229/3255. Assessment of the effect of Flavonoid Complex SC on the deoxyribose degradatiomnof oxygenated free radicals induced by the action of xanthine oxidase on hypoxanthine.

56. LeBar et al. (1997), A placebo-controlled double blind, randomised trial of extract of Ginkgo biloba for dementia. JAMA, 278 (16). 1327-32.

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