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Cosmetic Utilization of Phospholipids-*Panax ginseng* Saponins in Phytosoma Form

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Abstract

The cosmetic effects of epicutaneous treatment with extracts of *Panax ginseng* C.A. Meyer have been poorly investigated. The little published data found in cosmetic literature emphasize the activating effects on sagging and wrinkled skin and some favorable activities on dry and/or greasy skin. Earlier observations have shown the excellent skin tolerability of some liposomal ginseng extract preparations. No moisturizing and seboregulatory effects were demonstrated, but eutrophic effects on subjects with aging skin have been observed. The present study concerned the preparation of a special extract derivative obtained by Physical-chemical interactions of ginseng saponins and some phospholipids, which we have called "fitosoma." These complexes have been characterized by NMR spectroscopy and electron microscopy. Furthermore, these complexes are new, stable, and water microdispersible, forming liposomal structures in water. The cosmetic activities of these compounds have been examined by means of corneometry and elastometry to study their influence on aging skin, on skin layer hydration, and to determine skin elasticity.

Introuduction

For thousands of years, extracts of *Panax ginseng* C. A. Mayer have been administered systematically for the prevention and treatment of a variety of pathological conditions frequently associated with aging. Pharmacological and clinical data which have been accumulating during the last few years on this extract and on pure substances isolated thereof have provided an explanation for many of the virtues ascribed to this plant and have documented its excellent tolerability as well as its lack of toxicity at reasonable dosages. To date, however, ginseng extracts have found little application in functional cosmetics (1) except for occasional attempts with formulations developed on the basis of commercial interest rather than on a serious evaluation of appropriate dosages. Rovesti (2) investigated along these lines some not clearly defined extracts and reproted a certain activating action on sagging and wrinkled skin as well as on, dry, greasy and acneic skin. More recently, Chang (3) proposed the use of ginseng extracts in bubble baths, lotions, creams and detergents for intimate higiene ; these formulations have shown a stimulating action on the superficial blood circulation, which appears to be mediated by arteriolar and capillary dilatation and results in improved delivery of water and nutrients to the cutaneous layers. Apart from their cosmetic properties, these formulations have been reported to exert therapeutic effects on sprains, rheumatism, blood circulatory disorders and leukorrhea. Kim, Yang and Lee (4) studied the effects of ginseng saponins on the structure and mechanical properties of hair and reported an increased distensibility as well as a 60% increase in resistance to breakage ; the mechanism underlying this effect has been ascribed to the formation of hydrogen bonds between the polar groups of the saponins and the polipeptidic constituents of the hair. On the basis of the results obtained in parallel investigations (5,6), indicating that certain classes of substances show a high affinity interaction with phospholipids, resulting in the generation of new chemical entities, with improved biological action, we designed a special study to evaluate whether the active principles of ginseng also exhibit this kind of interaction and whether the newly generated products have any relevant biological activities.

As mentioned above, previous investigations had demonstrated that phospholipids show a high affinity for certain flavonoidic and terpenic molecules, with which they react leading to the formation of new chemical entities with physical-chemical and spectroscopic properties different from those of the components in free form. Highly polar molecules such as flavonoids, which in free and glucosidated form are insoluble in aprotic solvents such as aromatic hydrocarbons, become readily soluble in these solvents when bound in the complex. This polarity change is associated with marked changes of the spectroscopic properties as indicated by inspection of the ^{1}H-NMR, ^{13}C-NMR and ^{31}P-NMR spectra. Analysis of these spectra provides evidence that the product of the interaction is a real complex generated by the reaction of the polar head (choline and glyceric moiety) of the phospholipid with the polar centres of the principles bound in the complex. From a biological point of view, these complexes have shown in animals and in man an improved bioavailability after epicutaneous application, with a clear cut increment of the biological activity of the principle bound in the complex (5, 8). Systematic studies with the preparation of these complexes using various classes of substances have indicated that among the several saponins examined those of ginseng exhibit a particularly high affinity for phospholipides. During the course of studies on the biological activity of the ginseng extract after topical application in the dermatologic and cosmetic fields, it was possible to demonstrate that the extract exhibits a moderate antiinflammatory activity in the carrageenin-induced oedema and in the UV-induced dermatitis models in experimental animals (unpublished data).

In preliminary researches in man, liposomal suspensions prepared according to the technique described by Curri

(9) have shown a perfect tolerability as well as a favourable action (10, 11) on the hydratation and elasticity characteristics of the aging skin. These general observations suggested that ginseng extracts or purified, standardized fractions of these extracts could be usefully employed in dermatology and cosmetics. Based on these data, complexes of individual ginsenosides (or their natural mixtures) with natural and synthetic phospholipids were prepared and tested to assess their pharmacological properties in animals and their cosmetic / dermatologic activities in man. Cosmetic functionality was evaluated by assessing preliminarily vasomotor and corneometric effects in the aging skin: the promising results obtained in these studies will be described below.

Experimental

Substances and methods: *Panax ginseng* C.A. Mayer pure ginsenosides, total saponins and their complexes with phospholipids were produced by Indena S.p.A., Milan, Italy. Distearoyl-phosphatidylcholine was purchase from Sigma, St. Louis, U.S.A.; soybean phospholipids were purchased from Lipoid KG, Papenburg, Federal Republic of Germany. All other reagents and solvents were of analytical grade and were purchased from Merck.

Preparation of complexes: The complexes of ginseng saponins were prepared by allowing the saponins to react with the phospholipid in a molar ratio and in aprotic solvents according to the procedure described in Patent Application t. 19496 A/87. The total ginseng saponins were prepared according to Patent Application No. GB. 1 574 806. 1977, whereas the pure ginsenosides were prepared by using normal chromagraphic procedures well described in the literature.

Characterization of the complexes: The formation of the complexes was checked by using a Varian VXR 300 MHz spectrometer. The behaviour of such complexes in water was analysed by Stereoscan 250 scanning electron microscope, Cambridge Scientific Instr. Ltd. Cambridge, U.K.; these complexes when treated with water give rise to lipophilic micelles. The sample for the determination of the shape of the micelles was obtained by suspending the complex at an approximately 1% concentration by using ultrasounds for two hours. The sample was then frozen in liquid nitrogen at -180°C, pulverized and liophylized. After gold metallization, the sample was irradiated and photographs were taken at different magnifications.

Results

To evaluate the interaction of ginseng saponins with phospholipids, the model compounds used were Ginsenoside Rg1 and Ginsenoside Rb1 for the saponinic moiety and di-stearoylphosphatidycholine for the phospholipidic component. Subsequently, the results obtained with individual compounds were applied to the study of the complex of total ginseng saponins with soybean phospholipids. For the preparation of the complexes, the pure saponins suspended in aprotic solvents were allowed to react with 1 mole of the phospholipid dissolved in the same solvent. The saponins, which are initially insoluble, become progressively more soluble as the reaction proceedes. When all reagents are completely solubilized, the complex can be isolated by distillation or by precipitation in non solvents, such as hexane or petroleum ether, in which the complex is insoluble whereas any excess phospholipid is freely soluble. The product of the reaction can be considered as a novel compound on the basis of the following observations:

- the reaction product is a solid substance with a melting point often well defined and different from that of the individual components;
- formation of the complex takes place according to simple molecular ratios;
- the end product is lipophilic and soluble in apolar solvents in which the hydrophilic moiety is insoluble;
- the ^{1}H-NMR, ^{13}C-NMR and ^{31}P-NMR spectra of the complex show marked changes without any summation of the signals typical of the individual components.

When the solubility in benzene is sufficiently high (100 mg/ml at 5°C) it is possible to measure the molecular weight. The latter, determined by a cryoscopic method, corresponds to 1:1 complex between the two original molecules. Confirmation of a molecular complex can be achieved in any case by spectroscopic analysis with NMR techniques (^{1}H-NMR, ^{13}C-NMR and ^{31}P-NMR). In non polar solvents there is a marked change of the NMR signals originating from the atoms involved in the generation of the complex.

In the ^{1}H-NMR spectra (Fig.1), the signals from the

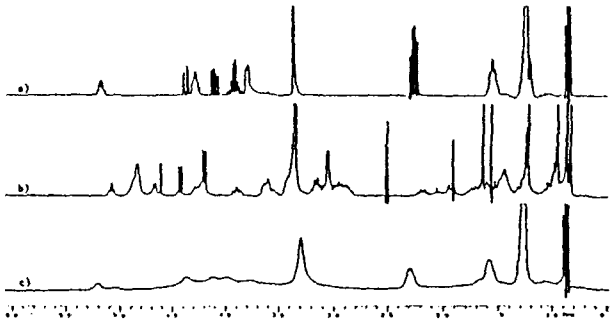

Fig 1. Formation of Ginsenoside Rg1/distearoylphosphatidylcholine complex: ^{1}H-NMR spectra

a) Distearoylphosphatidylcholine in $CDCl_3$
b) Ginsenoside Rg1 in DMSO-d_6
c) 1:1 Molar complex Rg1/phosphatidylcholine in $CDCl_3$

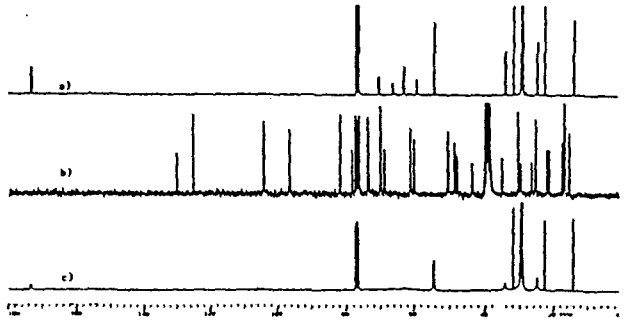

Fig 2. Formation of Ginsenoside Rg1/distearoylphosphatidylcholine complex: ^{13}C-NMR spectra

a) Distearoylphatidylcholine in $CDCl_3$
b) Ginsenoside Rg1 in DMSO-d_6
c) 1:1 Molar complex Rg1/phosphatidylcholine in $CDCl_3$

protons belonging to the saponin moieties are so broadened that their protons cannot be revealed. As far as the phospholipids concerned, there is a broadening of all the signals while the singlet corresponding to the N-$(CH_3)_3$ of choline undergoes an appreciable upfield shift.

In the ^{13}C-NMR spectra (Fig.2) recorded in C6D6 at room temperature all the saponin carbons are practically invisible; the signals corresponding to the glycerol and choline portions of the lipid are broadened and some are shifted, while most of the resonances of the fatty acid chains retain their original lineshape. After heating at 60°C all the signals belonging to the saponin moiety appear, even though they are still very broad and partially overlapping. The ^{1}H-decoupled ^{31}P-NMR spectrum (Fig.3) of the pure lipid displays a singlet at - 0.169 with a linewidth of 3.38 Hz which in the complex is shifted at - 0.151 and broadened until 8.9 Hz.

All the above mentioned physical and physical-chemical features suggest that a rather strong interaction takes place in solution between the saponin molecule and the polar part of the phospholipid, with the two long aliphatic chains "wrapped" around them and producing a lipophilic envelope which allows the complex to dissolve in low polarity solvents.

Inspection of the molecular models, as shown in Fig. 4, supports this hypothesis. The complexes are broken down to their individual components by solvents with high dielectric constant such as demethylsulfoxide, formamide, alcohols, and to a different extent by chlorinated solvents; if such solvents are used for the NMR analysis, all the signals are present in the spectrum but depending on the dielectric strength may be broadened or may give rise to summation of the signals of the complex (Figs. 5, 6).

The complexes are stable in water, due to their lipophilic character which makes them insoluble in this

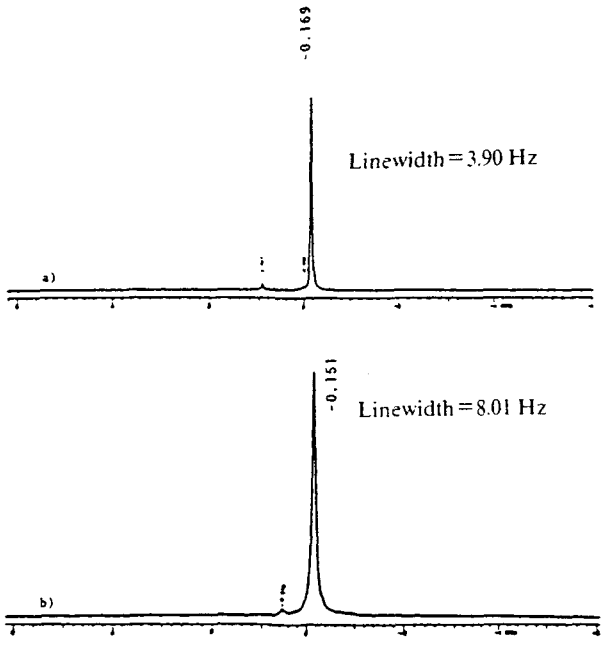

Fig 3. Formation of Ginsenoside Rg1/distearoylphosphatidylcholine complex: ^{31}P-NMR spectra

a) Distearoylphosphatidylcholine in $CDCl_3$
c) 1:1 Molar complex Rg1/phosphatidylcholine in $CDCl_3$

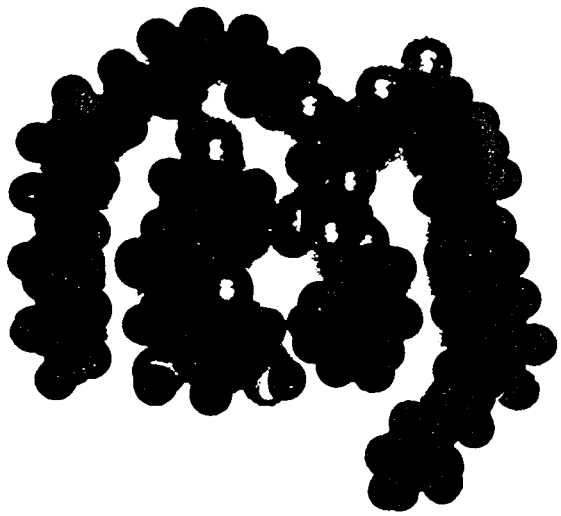

Fig 4. Molecular models : Example of wrapping of molecules by the fatty acid chains of distearoylphosphatidylcholine. The length of the polar head of phospholipid is about 13A°, the length of flavonoids, terpenes is nearly the same.

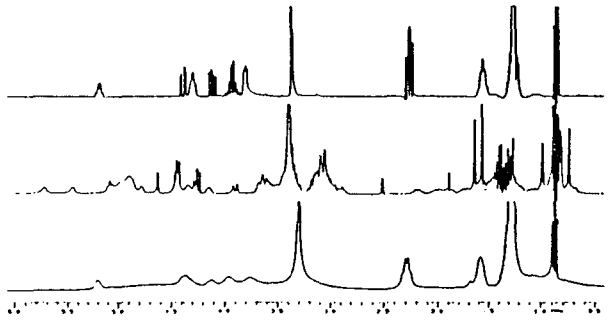

Fig. 5. Formation of Ginsenoside Rg1/distearoylphosphatidylcholine complex: ^{1}H-NMR spectra

a) Distearoylphosphatidylcholine in $CDCl_3$
b) Ginsenoside Rb1 in DMSO-d_6
c) 1:1 Molar complex Rb1/phosphatidylcholine in $CDCl_3$

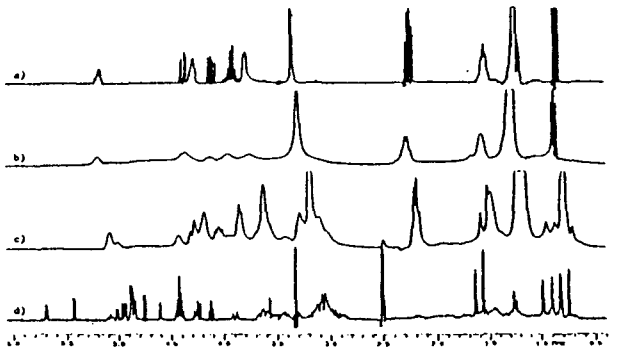

Fig 6. Behaviour of lineshapes and chemical shift in ^{1}H-NMR spectra of Ginsenoside Rb1/distearoylphosphatidylcholine complex.

a) Distearoylphosphatidylcholine in $CDCl_3$
b) Rb1/phosphatidylcholine complex in $CDCl_3$
c) Rb1/phosphatidylcholine complex in 1:1 mixture $CDCl_3$/DMSO-d_6
d) Rb1/phosphatidylcholine complex in DMSO-d_6 (distearoylphosphatidylcholine is insoluble in this solvent).

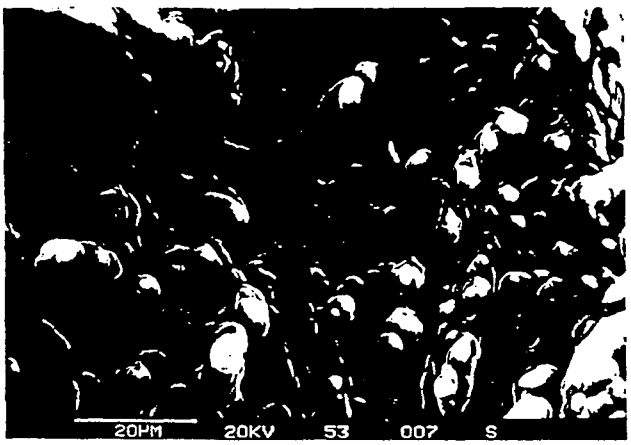

Fig 7. Electron-microscopic examination of lyophilized microdispersion of Ginseng total saponins/Soybean phospholipids complex microdispersion 0.1% in water. Magnification 1 × 4000.

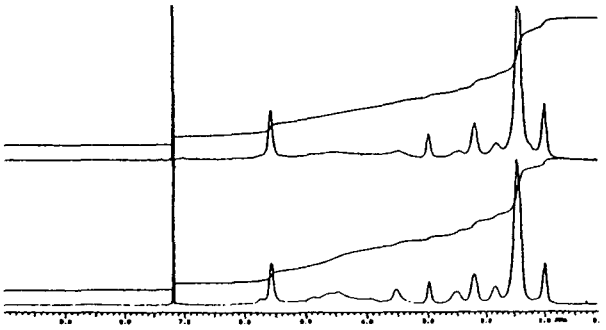

Fig 8. Formation of Ginseng total saponin/soybean phospholipids complex: ^{1}H-NMR-spectra

a) Soybean phospholipids (96%) in C_6D_6
b) Ginseng saponin soybean phospholipids complex : only the enbroadened signals of phospholipids are present in C_6D_6

solvent. When the complexes are added to water, they form a homogeneous microdispersion which at electron-microscopic examination has the appearance of a mixture of microspheres very similar to liposomal suspensions.

The data obtained for the pure substances can be applied to the extracts containing them. The ^{1}H-NMR spectra of the total ginseng saponins and their complex with soybean phospholipids are shown in (Fig.8).

It is evident in this Figure that in the spectrum of the complex there is disappearance of the characteristic signals of the methyl groups of the triterpenic moiety of the saponins along with the methylenic protons of the genine and sugar chains. On the basis of the results obtained with other molecules, including flavonoids and saponins (4,6), and other data very recently reported in the literature (7,8), we have evaluated the potential activities of these novel complexes preliminarly in pharmacology and cosmetics.

In pharmacological experiments we have observed that the complex of ginseng like flavonoids can penetrate more readily across the epidermal barrier and exerts its activity on the tissue structures altered by UV radiation and other irritating agents.

Considering this fact we have tested the complex of ginseng total saponin with soybean phospholipids in man in accordance to the tests herebelow reported.

Tolerability and toxicity in man

Patch-tests were performed in 20 subjects (16 female and 4 male aged between 18 and 41 years) by applying gauzes soaked with 6 ml of an acqueous microdispersion of ginseng PHYTOSOME® (33 mg/ml). The gauzes were applied occlusively on the skin of the back and were kept in place for 48-72 hours. None of the subjects showed allergic or primary irritative responses of any kind. As far as subchronic tolerability is concerned, a preparation of ginseng PHYTOSOME® (33 mg/ml) was applied on the skin of the face of 10 subjects (9 female and 1 male, aged between 50 and 88 years), at a dosage of 3 ml/day for 2 to 4 weeks. None of the subjects showed erythematous, desquamative, vesicular or oedematous reactions or any other sign of primary irritation.

Dermatologic and cosmetic investigation

The criteria used to evaluate the cosmetic effects of ginseng PHYTOSOME® were : a) inspection and palpation data, which were recorded by assessing various dermatologic and cosmetic parameters (hydration, trophysm, sagging, consistency, elasticity, greasiness or dryness of the skin of the face), scored in arbitrary units from 0 to 4 before and after treatment and analysed statistically : b) objective quantiation of 1) the degree of hydration of the corneous layer (moisturizing effect) by corneometry and of deep dermal layers (elasticity and cutaneous tone) by elastometry. 2) possible effects on precapillary vasomotor activity and capillary perfusion, as assessed by thermographic changes in the areas investigated (High Performance Contact Thermography, HPCT).

The corneometric measurmemts were made by using a 420 Corneometer and were taken over the skin of the forehead, temporal-zygomatic region, cheeks and chin under baseline conditions and after application of ginseng PHYTOSOME® both "short-term" and "long-term". In the former case, measurements were made at 0.25, 0.75, 1, 2, 3, 4 and 5 hr after a single application, whereas in subjects who underwent "long-term" treatment measurements were obtained after 10, 20 and 30 days with once daily applications.

Elastometric recordings were made by using a SEC Elasticity Checker and were obtained before and after "long-term" treatment (30 days with once daily applications).

Effects on vasomotor activity and capillary perfusion were evaluated before and 15, 30, 45, and 60 min after a single application.

The above studies were conducted on a total of 60 subjects (54 female and 6 male, aged between 17 and 88 years) who were divided into groups depending on the specific experimental procedure to be used.

A) Subjective scores

In an initial group A of 20 subjects (16 female and 4 male, aged 18 to 41 years, mean age 32 ± 4.4 years), treatment for 30 days with one ampoule/day led to a statistically significant improvement of the global hydration, elasticity and trophysm of the skin of the face (see Figure 9), without affecting skin greasiness, diffuse erythemas

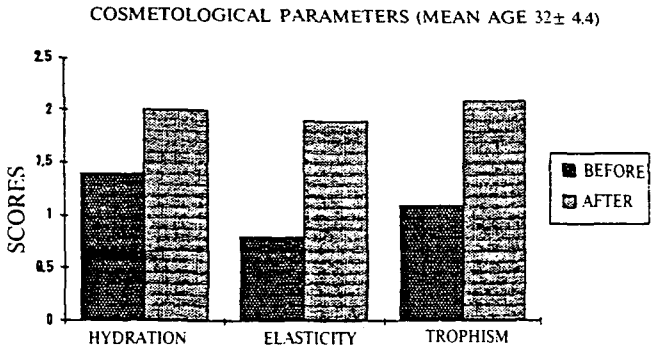

Fig 9. Modifications of some cosmetological parameters induced by Ginseng total saponins PHYTOSOME® after 30 days treatment in aged subjects (32± 4.4 years) Group A.

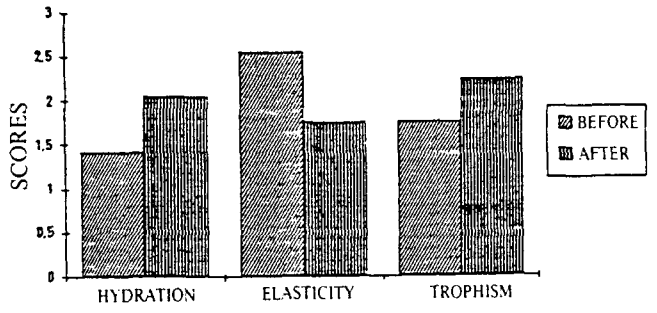

Fig 10. Modifications of some cosmetological parameters induced by Ginseng total saponins PHYTOSOME® after 30 days treament in aged subjects (46± 6.1 years).

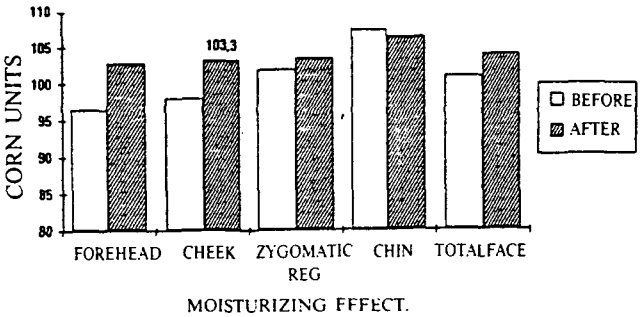

Fig 11. Moisturizing effect of Ginseng total saponins PHYTOSOME® induced in young subjects after short-term treatment (mean age 27 years) within 60 min. in different zones of the face.

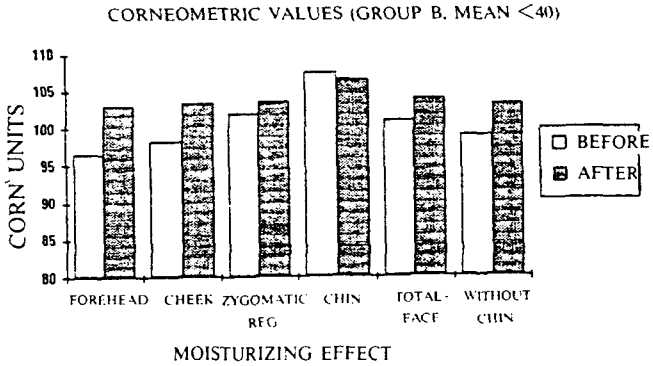

Fig 12. Moisturizing effect of Ginseng total saponins in PHYTOSOME® induced in subjects aged<40 years after long-term treatment

or comedones.

In a second group B of 20 female subjects aged 36 to 56 years (mean age 46 ± 6.1 years), treatment was associated again with a statistically significant improvement in global hydration and cutaneous trophysm. In addition, these subjects showed a change which could not be evaluated in the younger subjects included in the first group, namely a marked reduction of cutaneous dryness (see Fig.10).

In spite of the fact that these studies were conducted by different investigation in groups of subjects whose mean age differed by about 15 years, the results of the subjective scores were in good agreement. The findings at inspection and palpation suggest that ginseng PHYTOSOME® can enhance cutaneous hydration, improve the semeiological parameters of cutaneous trophysm and decrease the abnormal dryness of the skin.

At this stage of investigation, it was felt necessary to evaluate whether the improved scores of cutaneous hydration were due merely to a non-specific "moisturizing effect", restricted to the corneous layer of the epidermis and presumably casued by inhibition of "perspiratio insensibilis", or whether the hydration was enhanced also in the deeper layers and, especially, in the dermal tissue. In fact, it is know that an improved cutaneous trophysm is associated with an increased "bound water" fraction and with a parallel increment in blood perfusion at microcirculatory level.

B) Objective evaluation of the degree of hydration of the corneous layer.

1) Corneometric measurements after "short-term" application (Group A) and "long-term" treatment (Group B and C).

As shown in Fig.11, the application of ginseng PHYTOSOME® causes within 60 min, even in young subjects, statistically significant changes of the corneometric parameters over the skin of the forehead, cheeks, chin and perilabial region. Similar changes are observed also after "long-term" (30 days) treatment in subjects with a mean age below and above 40 years (Group C, Figs. 12, 13).

These data indicate that ginseng PHYTOSOME® exert a hydrating effect on the most superficial layer of the epidermis, with a moisturizing effect related to imbition of the cells of the corneous layer. Since the PHYTOSOME® complex has a relatively low molecular weight and its physical properties are markedly different from those of collagen, elastin and other natural mucopolysaccharides which inhibit "perspiratio insensibilis" by covering the surface of the corneous layer, a different mechanism of action must be hypothesized. Such a mechanism is probably related to the liposomal-like properties of the aqueous microdispersions of the complex between the phospholipid and the saponins of ginseng. In previous studies (13), it has been possible to demonstrate that simple phosphatidylcholine liposomes, which

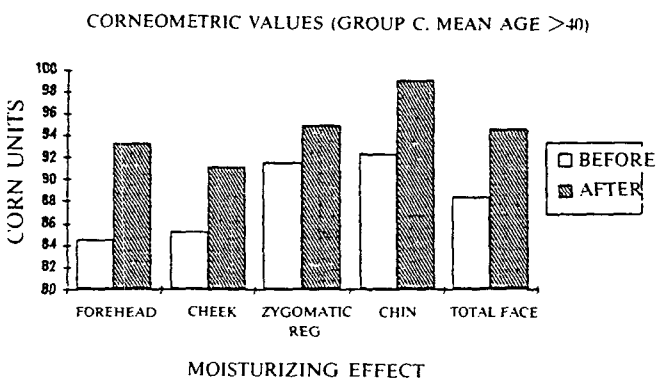

Fig 13. Moisturizing effect of Ginseng total saponins in PHYTOSOME® induced in subjects aged>40 years after *long-term treatment.*

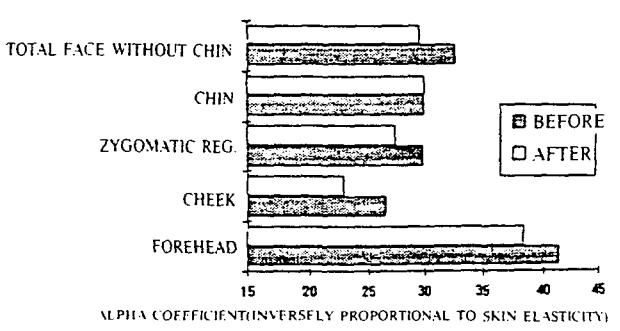

Fig 14. Modifications of the α-skin elasticity coefficient which is inversely proportional to the effective skin elasticity and tone induced by Ginseng total saponins PHYTOSOME® in subjects aged 46 ± 1 years : the response is different in the various zones of the face.

contain water molecules within the central core and the interlamellar spaces, exert a "moisturizing effect" on the cells of the corneous layer which is due to a direct transfer of exogenous water to the cytoplasm of the corneous cells by virtue of the "carrier-like" properties of phospholipids. Similar observations have been made by using liposomes containing oligomineral water: the corneometric data obtained with these preparations are similar to those obtained with ginseng PHYTOSOME®. Therefore, the hydration of the superficial corneous layer is a non-specific phenomenon related not to the chemical structure of ginseng saponins, but to the "liposomal-like" properties of the phospholipids of the complex microdispersed in water.

C) Objective evaluation of the hydration of the deep layers (reticular layer of dermis).

The findings obtained at inspection and palpation demonstrated, after "long-term" application, a statistically significant improvement in global hydration, elasticity, tone and trophysm of the skin of the face (Figs. 9, 10). These data suggested that ginseng PHYTOSOME® exert an effect on dermis which certainly can not be ascribed to the phospholipidic component but, rather, is likely to be due to a specific hydrating action of the saponins of ginseng. In addition, these observations suggested that the active principle could penetrate the epidermal barrier thanks to a "transdermal effect" of PHYTOSOME®.

The study of the elasticity coefficient of the skin was carried out in subjects of Group C (mean age 46 + 6.1 years).

Measurements were taken on the skin of the forehead, temporal-zygomatic region, cheeks and chin. As shown in Figure 14, the data demonstrate a statistically significant decrease of the "alpha" coefficient, which is inversely related to the actual elasticity of the skin (13). The improvement in cutaneous elasticity and tone documented by objective measurement is in agreement with the subjective scores and indicates that the PHYTOSOME® possess a transepidermic action which can be ascribed to the ginseng saponins of the phospholipidic complex.

The mechanism underlying the improved cutaneous elasticity and trophysm may be secondary to "cutaneous bioactivation" as reported by Rovesti (2) or to increased blood perfusion "with dilatation of capillaries and arterioles, leading to improved deliveries of nutrients to the skin" as proposed by Chang (3). These mechanisms have not yet been objectively documented. The enhanced hydration of the deep layers and the increased exchanges between microcirculation and tissues are an inter-independent phenomena, which do not occur separately. Since an increased velocity and volume of blood flow in the cutaneous microcirculation is know to be associated with increased skin temperature, thermographic maps over the temporal-zygomatic region and cheeks were determined in a group of subjects before and after application of ginseng PHYTOSOME®.

D) *Objective evaluation of the cutaneous microcirculation* (HPCT).

In subjects older than 40 years, epicutaneous application of a pseudo-liposomal microdispersion of ginseng PHYTOSOME® (10 mg of complex in 3 ml of distilled water) induces important changes in the thermographic map of the hemiface.

In previous investigations (13), it had been shown that the blood perfusion in the microcirculation of the face is not uniform and that the differences in velocity and volume of blood flow becomes more prominent with increasing age. This regional variation in the distribution of blood flow in capillary networks affect the temperature of different areas of the face, resulting in thermographic maps which are characterised by co-existence of hypothermic (less perfused) and normothermic (uniformly perfused) areas. Our investigations demonstrated that epicutaneous application of ginseng PHYTOSOME® increases the temperature of the hypothermic areas which are normally present in female subjects older than 40 years, especially in the skin of the cheeks. This increment is associated with a reduction in the size of the hypothermic areas or with an increase in the thermal gradient of the normothermic areas.

Generally, the initial changes of the thermographic maps can be detected already at 15 min after application and becomes more marked at 30 and 45 min : the maximal effect is observed at 60 min. The overall duration of the effect was not evaluated in this investigation. The increased regional blood perfusion demonstrated in these studies provides an explanation for the subjective an objective findings documenting an improved hydration

and trophysm of the deep layers of the skin after "long-term" application. It should be noted that the regional increase in cutaneous temperature, ranging between 0.3 and 0.8°C in different areas, is not accompanied by reddening of the skin or other manifestations (engorgement, oedema, localized increase in ginseng PHYTOSOME® act as vasodilators by inducting a reactive hyperemia). On the contrary, these substances enhance the vasomotor activity of small arteries and precapillary arterioles and cause the opening of previously closed capillaries : the latter effect is due to an increased volume and velocity of blood flow to the terminal microcirculation as a result of a more efficient arterial-arteriolar sphygmicity ("pump effect").

So far, no data are availble on the behaviour of the microcirculation after "long-term" application : however, it is reasonable to assume that the improvement in cutaneous trophysm (subjective data), degree of hydration of the deep layers of the skin (Figs. 9, 10) and elastometric parameters (Figure 14) is related to an improved perfusion of the regional microcirculation.

Taken altogether, the studies conducted so far with ginseng PHYTOSOME® justify the following conclusions :

- cutaneous tolerability has been found to be excellent.

In addition to the negative responses in the patch-tests after application over the skin of the back for 48-72 h, "long-term" application did not cause side effects such as reddening, burning oedema, wheals or other manifestations of allergic-anaphylactic type (9). Some subjects reported, during the first days of treatment, a transient feeling of stretching of the skin over the temporal-zygomatic or perorbital region : this sensation was more marked in subjects with hypoelastic, very dehydrated skin and with prominent network of wrinkles and initial dystrophic manifestation.

We believe that the stretching sensation, which occurs in these cases 10-15 min after application and persists for about 40-45 min, is due to the rapid increase of the hydration of the deep layers of dermis and to the increment of regional perfusion. It should be noted, in any case, that this sensation is not perceived as unpleasant and is invariably ascribed by the subjects to a "strong activity" of the preparation. Only in one 37-year old subject with normopigmented, dry and dystrophic skin, treatment was discontinued due to an unpleasant itchy feeling at the site of application. In all remaining 55 subjects of both sexes (mostly female) no adverse effects related to the treatment observed.

- The subjective scores after "long-term" application (Figs. 9,10) agree with the objective measurements, particularly with elastometric and thermographic observations, indicating that ginseng PHYTOSOME® favourably affect the hydration of dermis and the global trophysm of the skin of the face.

The preliminary findings indicating improvement of thermal gradients in poorly perfused areas suggest that the effect of the saponins of ginseng applied in phytosomal form is mediated by activation of the exchange between the microcirculation and the tissues, secondary to increased blood flow in the arteriolarcapillary network. This interpretation is supported by recent experimental findings on the microcirculatory effects of flavonoidic and terpenic molecules (5,6,7).

Further studies with blood measurements and assesmen of arterial-arteriolar motility should clarify this interesting and innovative aspect of the action of ginseng PHYTOSOME® at microvasculatory-tissue level.

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F. Soldati : What kind of phospholipids did you use? Are they derivatives of lecithine?

E. Bombardelli : In the preparation of these complexes normally we used soybean phospholipids of about 95% content. That is mixture of soybean phospholipids.

F. Soldati : Do you expect a better resorption of ginseng extract or of pure isolated from ginseng when they are administered orally in form of these phospholipid derivatives?

E. Bombardelli : According to our experience with other molecules I believe that the oral absorption of the ginseng saponins would be increased when they are in complexed form.

Phytosome 형태인 Phospholipids-Panax ginseng Saponin의 미용효과

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인삼 추출물의 피부도말에 의한 미용효과는 거의 연구된 바 없다. 미용에 관한 문헌을 고찰해 보아도, 늘어지거나 주름진 피부를 활성화 시켜주고, 건성이나 유성피부에 바람직한 효과가 있다고 강조한 연구결과는 거의 없다. 인삼의 지용성추출물 제제 몇가지가 피부내성에 탁월한 효과가 있다고 보고된 바 있다. 수분이나 피지조절 효과에 관하여 설명된 것이 없는 반면 노화된 피부에 관한

주제로 피부에 영향을 준다는 효과는 관찰되어 지고 있다. 본 연구는 "Phytosome" 라고 명명한 인삼 사포닌과 인지질의 물리화학적 상호작용에 의하여 얻어진 특정 추출 유도체의 제조방법에 관한 것이다. 이 복합물들은 NMR spectroscopy 와 electron-microscopy로 확인되었다. 더욱이 이들은 새롭고 안정하며 수성 liposome 형태구조안에 수성미세분산형이다. 이 화합물들의 미용효과는 노화피부에 대한 영향과 피부층의 수화능력과 피부탄력성을 연구하기 위하여 corneometry elastometry를 이용하여 실험하였다.