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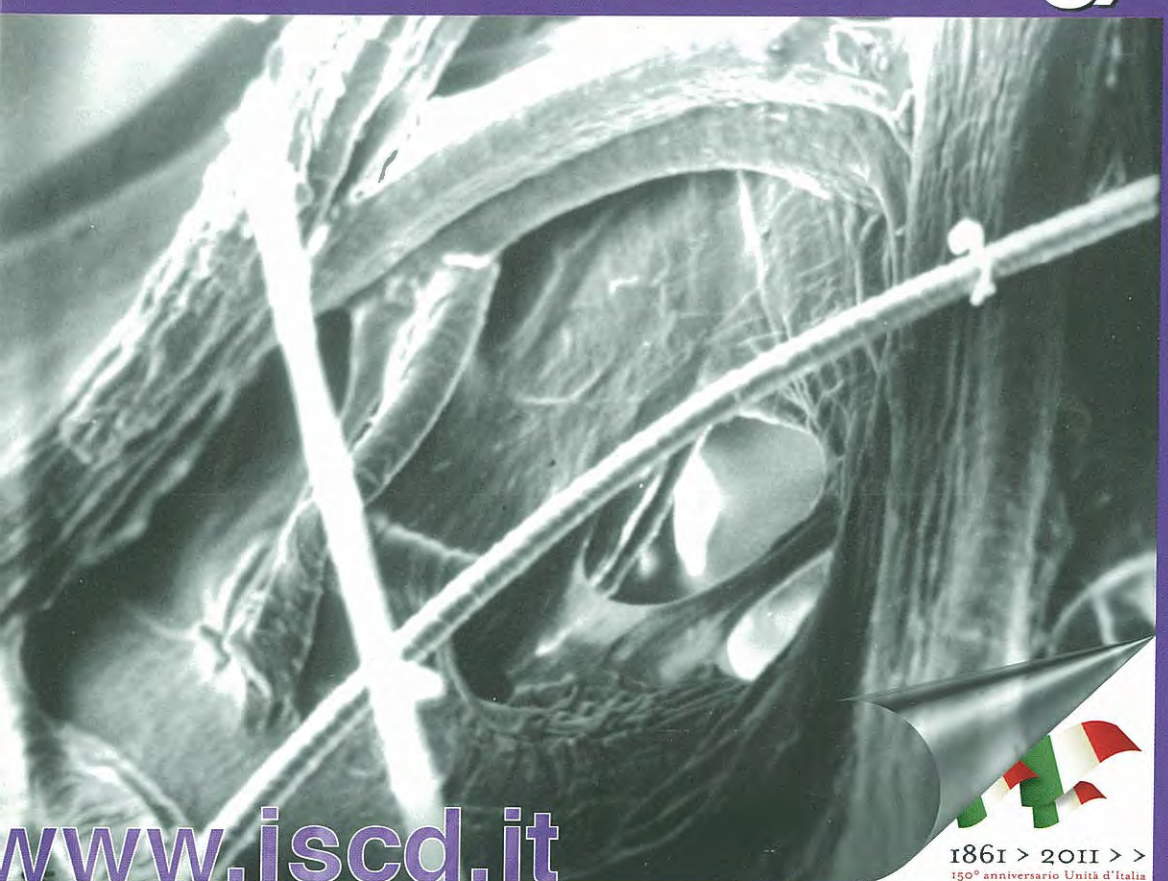

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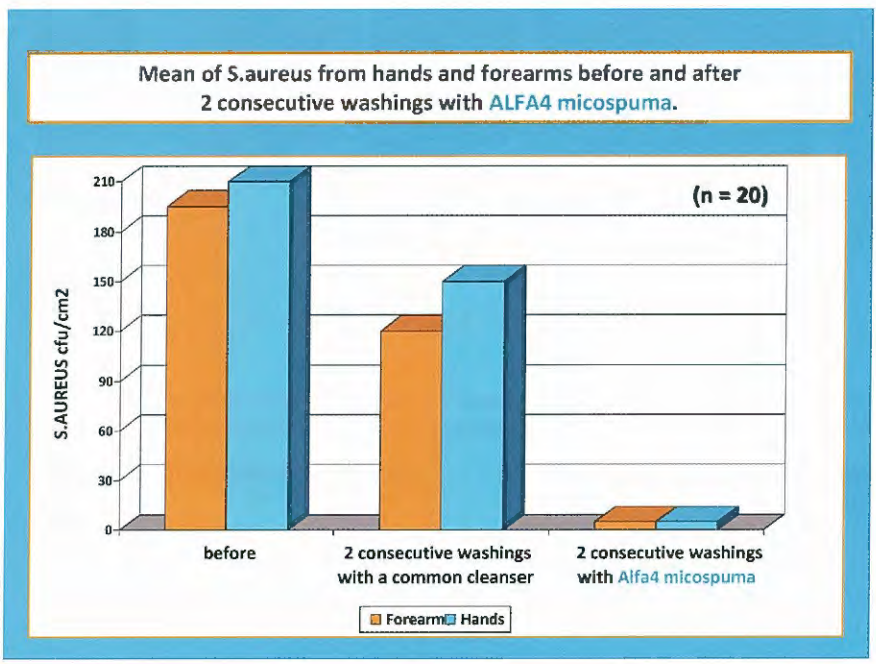

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We wish to dedicate this issue of the Journal of Applied Cosmetology to the memory of Johann Wiechers.

VII International Congress of the I.S.C.D.
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Johann, a well-known member of the International Federation of Societies of Cosmetics Chemists but, first of all, a real friend of mine, passed away on Saturday November the 5th, after contracting a dangerous form of pneumonia.

It is a great loss not only for all the friends and colleagues who worked with him over the years on Cosmetic Dermatology, but also for all the Scientists involved in the study and research of Beauty and Wellness.

I shared with him my ideas about the activity and efficacy of cosmetic products, focusing on their penetration at the different skin layers, because of his great expertise especially on this specific topic.

Huge his knowledge in the cosmetic field proven by the about 450 publications among papers, posters, book chapters, columns and podium presentation, and the interesting book Science and Application of Skin Delivery Systems, launching also the software Formulating for Efficacy.

He loved his work, and those who knew him personally will never forget his passion for Cosmetic Science.

We wish to remember him with a picture taken from the 2004 ISCD Congress.

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Trimestrale di Dermatologia Cosmetologica
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Dermatology: the Stock-In-Trade in Ancient Rome

Gaspare Baggieri[1], Melissa Baggieri[2]

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Summary

Some fundamental instruments are described in this work. They are utilized in a dermatologic and cosmetic ambit and date back to the Classical and Imperial Age. These instruments were employed up until the advent of Arab Medicine (IX century).

Riassunto

Si tratta di alcuni strumenti ad uso medico chirurgico per piccolo interventi in periodo Classico e di età Imperiale, avanti la medicina araba. In particolare l'utilizzo di certi strumenti è specifico per la dermatologia.

INTRODUCTION

The instruments used in modern dermatology have remote origins. They date back to the VI-IV century B.C. Many of these tools had multi-use functions.

Small sticks, spatulas and brushes formed the kits of beauty treatments which were very popular among upper-class women in ancient Egypt, up until the first Dynasties. These devices were employed to spread oils, cosmetics, poultices, colours, and powders. The custom of human beings to decorate their faces and bodies dates back to the Prehistoric Age. They began to adorn their skin in order to distinguish themselves for their authority, membership to a specific group, to remark a conquest, or for an apotropaic or religious purpose, or to recall their attachments to a human being, dead or alive. In the course of time, the ornaments on the skin were used more and more with an aesthetic purpose, achieving sublime moments in the Roman Period (from the III century B.C. to the III century A.D.) when women put cosmetology into practice. In fact, on one hand we have evidence of these kind of utensils in portrait paintings, and on the other hand we can assume that the same kind of tools were used by physicians, as well. For example, pincers, bistouries and cauteries (of the most various sizes and shapes, with plate or ogival extremities) were essentially used to remove small excrescences from the skin.

Ancient medical and surgical instruments represent a subject that is not often discussed. Among these tools there are those that were used to remove the excrescences on the skin.There is a lot of archaeological evidence that proves that our ancestors were interested in and paid a lot of attention to the cure of the skin. There are iron and bronze instruments (2), or ceramic, clay, wood, leather and glass containers for ointments, creams and powders. There are also stones of a particular composition and shape, such as the pumice stone used to abrade calluses, or round basalt stone employed to massage the back by means of a roller.

The physician bag can vary greatly, in fact it can be a classical cylindrical shoulder bag, or just a classical briefcase with small drawers and compartments. And it may contain, in addition to the usual and indispensable instruments, also medication, the sheet of stone to prepare impastos, small flacons and unguentaria in glass, clay or ivory (1).

Strigil

This device was very diffused in ancient Rome. It was known and utilized in Greece during the VII Century. The strigil is similar to a small boomerang, with a grooved and quite sharp side on the margins which served to remove the unguents from the skin, by grazing on the surface of the body. In fact, in a paradoxical way, during the era in which soap was not yet known, they used to clean the skin by spreading ointments over their bodies. According to (4) they used to spread oil mixed with a very fine pumice stone powder and they utilized strigils to eliminate this compound from the surface of the cutis. Afterwards they sluiced abundantly. The strigil was used by gladiators and in a sportive ambit. It was always present in the athletes' equipment. In fact, when we find a strigil or an alabastron near skeletal remains, there is a good possibility that we are dealing with an athlete or a gladiator (3).

Spatula

This tool could be simplex or lanceolated and was used in a similar way already by the ancient Greeks. These bronze *spathulae* had an average length of 10-15 cm. and were utilized also to smear oils, perfumes, make-up, face powders and whitening on the skin of the face and breast

(5). On the other hand, they were also utilized during the preparation of little impastos and medications, such as tablets and ointments, the latter were smeared on the wounds by using the lanceolated spatulas, as well.

Auricular syringe or oricularius clyste

This object has been documented since the IV century. It was utilized for the washing of the auditory canal, both for therapeutic use and for hygienic reasons. The auricular syringe that we employ nowadays is essentially unchanged from the viewpoint of its physical principle (1).

Bistoury

This tool dates back to the Stone Age. In fact, some stone sharp blades with stone handles were found in Italian sites which date back to the Paleolithic Age. The device is generally composed by an iron blade and a bronze handle. It was employed for a culinary, defensive and medical use. For example, it was employed to eliminate the little excrescences on the epidermis by cutting the base of the growth that was previously stretched upwards with the bistoury. If the wound bled, they placed thick impastos mixed with vegetal essences. In addition, the bistoury was utilized with a scarifying function (2).

Pincers

This instrument, *Vulsella*, had different utilizations, as in the case of the bistoury. Its shape did not vary from our modern medical pincers. In fact, we have Roman simplex clockwork pincers, and pincers with a double handle, or more complex pincers which present curved extremities, or internal knurled edge, as well as little pincers for the extraction of spines or little extraneous bodies, or very robust pincers utilized for the extraction of teeth, or of arrows from the cutaneous surface.

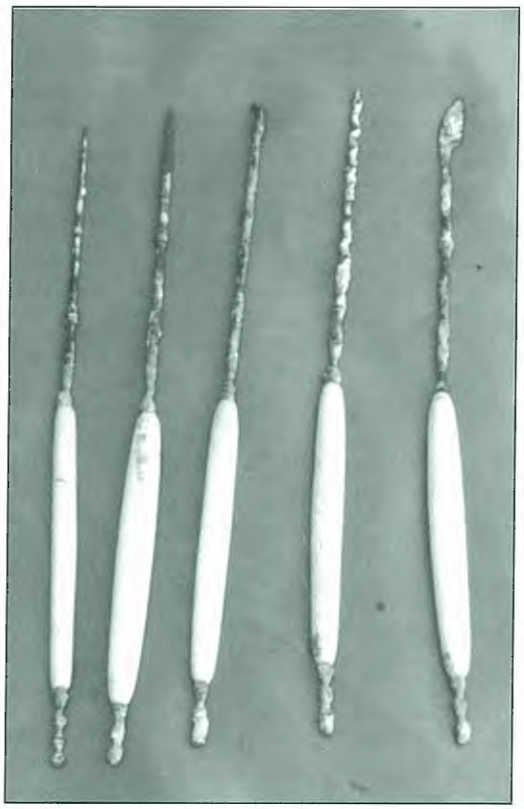

Fig. 1 *Instruments with ivory handles (Middle Ages).*

Cautery, or ferramentum candens

We can find this instrument in bronze and in various sizes. Some of these cauteries had a simple plate on a single axis on their extremities, while others have a well-defined plate on a curved axis on the extremities of the instrument to allow for more pressure. The flat side of this tool was heated, making it incandescent. This part was placed over the side to be treated. In this way excrescences, papillomas, fibromas were burnt, or better cauterized. Cautery was also utilized to make markings similar to tattoos (1).

Little drill or terebrum

This instrument has an average length of 17.00 cm., including the handle which measures about 9.00 cm. It is similar to a probe, but it has a spiraliform shape, and it was used to extract filarias from the lakes and sinuses of the varicose veins (2).

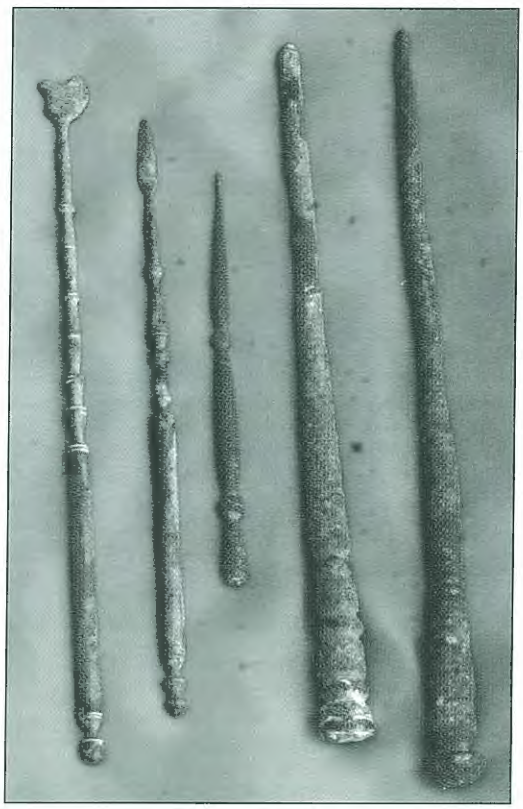

Fig. 2 *Bronze tools, we can recognize probes, sounds, and a small cautery.*

Cucurbit or cupping glass

This bronze device was employed in the treatment of inflammations of several areas of the cutis. The cupping glass was heated up and moistened with oils before been adhered at pressure on the surface of the moistened skin. It was then promptly removed, producing the suction of the subcutaneous inflammatory liquid (1, 5).

Fistula fittili

It is a cautery which passes through a tube in order to directly reach the area to cauterize, avoiding the risk of burning other sides of the body (2).

Specillum or sound

There are different kinds of this tool depending on its use. The *asperatum* was utilized to take away the external granulations of the palpebrae; the *auricularium* to remove cerumen and extraneous bodies from the ear; the *capitulatum, tenue, utriunque tenius, cum nucleo, concavum* were used as an explorative sound in depth. An interesting kind of sound has hooked extremities, useful to quickly extract extraneous bodies from superficial wounds or from the auditory canal. These instruments greatly differ in their dimensions, varying in their diameter (from 1 mm. to some centimeters) and length (from 10 to 30 cm.) (1, 5).

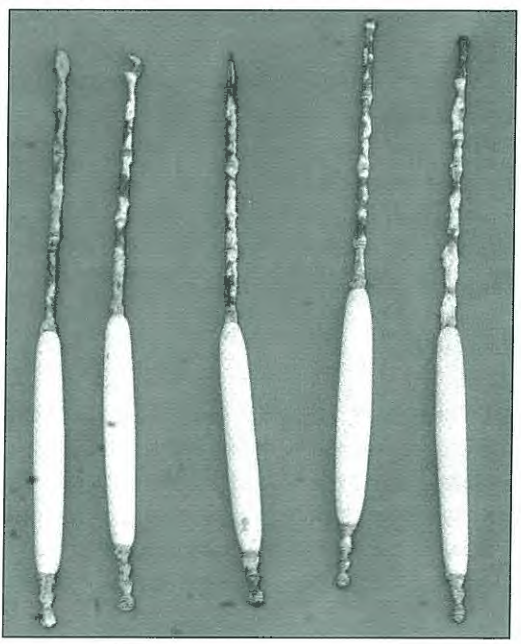

Fig. 3 *Instruments utilized in microsurgery and medical dermatology.*

Fig. 4 Bronze cucurbits employed in the therapy of cutis inflammation (Museum of History of Medical Art, Rome).

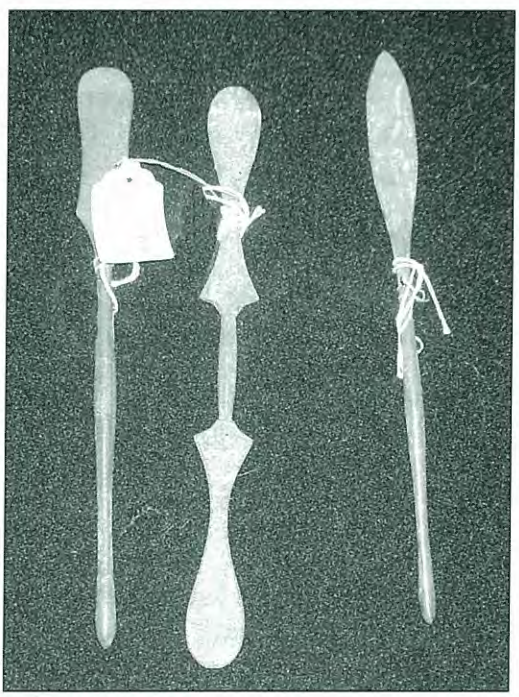

Fig. 5 Three different kinds of spatula employed since the III- IV century B.C. and throughout all the Medieval Age (Museum of History of Medical Art, Rome).

CONCLUSION

This report highlights the use of some important dermatological and cosmetic instruments in ancient period in a few words.

The handles of some of these tools were produced in ivory to emphasize the importance of beauty treatment which aimed toward enhancing the beauty of women.

l'equilibrio fisico, cioè dell'armonia del proprio corpo, presenta infatti riflessi profondi che determinano comportamenti di sicurezza e confidenza in se stessi che saranno tanto maggiori quanto maggiore sarà la certezza di un buon apparire. Siamo pertanto, consapevoli o inconsapevoli, in una continua ricerca della bellezza cercando sempre di migliorare l'aspetto somatico in modo che venga apprezzato da chi ci circonda, e tale apprezzamento si riflette sul nostro comportamento che viene gratificato divenendo più soddisfatto, ma anche più sicuro.

INTRODUCTION

Keeping physically fit can benefit the psyche and contribute to a feeling of internal satisfaction which is fundamental to a state of wellbeing.
But what are the connections related to physical upkeep?
The basic factors are:
- Weight control
- Skin protection
- Anti-ageing
- Non smoking behavior
- Treating hormon imbalance

In confronting the above factors the fundamental aspects are correct hygiene, adequate physical activity, a correct interaction with the environment (mainly sun exposure) and a correct diet.

WEIGHT CONTROL

There is no doubt that being overweight negatively effects one's physical aspect, and even more so if one is obese, but this negative effect can also be associated with excessive weight loss. In both instances we have important problems that are often influenced by complex factors, often genetic, not easily identifiable nor treatable. However, an important role is played by the food we eat, both quantitatively and qualitatively.

Obesity

We won't spend time on discussing a diet against obesity, already so often treated by experts (not always competently) we wish only to state that a weight loss diet should never be drastic nor monotonous but gradual, continued, and mostly varied, containing all the principle nutrients in balanced proportion. The lack of even just one principle nutrient determines in fact negative health effects that also reflect on body esthetics.

It is necessary that a balanced diet should be started from early childhood when the responsibility is mostly in the hands of parents more than the child, and it must be sustained through puberty and adolescents. In this latter period, excessive calories are often counter balanced by intense physical activity, but in adulthood there is a tendency to decrease activity, and if the high caloric diet has become habitual there could be a problem. In fact both women and men tend to gain weight already in early adulthood when life rhythms change.
The important factor in a weight loss diet is to limit (not to eliminate) condiments, both because of their high caloric content, as well as their ability to increase the tastiness of food thereby inducing higher food intake. It is also important to limit the so called "luxury foods", as sweets which are an extra addition to a normal meal. Weight control must never be suspended because once overweight (or worse obese) it becomes very difficult to return to ideal weight.
Dietary restrictions must be accompanied by physical exercise, which however must never be excessive, overexerting and without adequate training. Non controlled excessive physical activity can bring about the formation of oxygen free radicals (ROS) in the body with possible serious repercussions on health. Activity must be moderate and continuous, as walking, climbing stairs instead of using elevators, limited automobile use and sedentary pastimes like watching TV. Non strenuous sports are recommended.
It should be remembered that rapid weight loss has a negative effect on skin (and therefore on esthetics) causing stretch marks, and often the weight returns after finishing a diet at even higher levels than before the diet.

Underweight

Just a few words about underweight. The thin person generally has little appetite and/or dige-

while ω-6 undergoes easy peroxidation, ω-3 seems to be not only resistant, but according to some studies, posses an antioxidant protective effect on the skin as well as on other organs. Saturated fatty acids should however be limited, while monounsaturated fatty acids are highly recommended due to their positive effects on health in general as well as their excellent softening effect on the skin (7, 8).
In conclusion, the intake of fruits and vegetables should be encouraged, along with fish, especially blue fish, and extra virgin olive oil, while seed oils and terrestrial animal fats should be limited along with alcohol.

Solar exposure

Skin exposure to solar rays determines a serious loss of antioxidant factors. It has been observed that after 30 minutes of UV ray exposure the skin's α-tocopherol content is reduced by 50-60%. The topical application of tocopherol drastically reduces the damage and this positive effect is seen, thought to a lesser degree, even when α-tocopherol is taken orally. It should be remembered that ultraviolet rays exert a negative effect on all antioxidants, in particular on carotenoids reducing their amount not only in the skin but also in plasma (9).
An adequate intake of dietary carotenoids and polyphenols is had in vegetables and greens and this intake should begin at least one month prior to sun exposure. Extra virgin olive oil is rich in antioxidants, especially polyphenols, but also α-tocopherol and a certain amount of carotenoids (β-carotene and lutein). Other important qualities of extra virgin olive oil are its high quantity of squalene, that at the skin level acts as a filter for oxygen singlets, and an optimum acidic makeup with its balanced polyunsaturated fatty acid ratio (ω-6/ω-3) and its content of monounsaturated oleic acid. The same cannot be said about seed oils in that their high linoleic acid (ω-6) content exposes them to peroxidative risk (not containing sufficieut antioxidants for protection) and generally poor in α-linolenic acid (polyunsaturated ω-3). It should not be forgotten that olive oil favors intestinal absorption of carotenoids, in particular licopene, highly active against photo-ageing and protective against neoplastic risk of the skin and other tissues, in general and synergistically incremented by lutein (10).
A direct anti-oxidative protection on skin was recently demonstrated also due to olive oil's phenolic component, oleoeuropein, which seems to act at the skin level as a free radical scavenger. Special attention should however be paid to squalene, present in high quantity in the unsaponified part of olive oil which is specifically protective for skin. Squalene represents about 12% of the sebum's composition and acts as a powerful oxygen singlet scavenger inhibiting lipoperoxidation from UVA, and it has been seen that its oral intake increases its presence in the skin thereby increasing photo-protection (11).
To avoid aging and skin damage it seems necessary to guarantee an adequate intake of polyunsaturates, without exceeded their physiologic requirement (taking care to respect the ratio between ω-6 and ω-3) so as not to increase the peroxidative substrate, and to favor the intake of monounsaturates (oleic acid) with its scarce susceptibility to free radical peroxidation, and more importantly to insure an intake of antioxidant agents. These suggestions can be enacted by regular intakes of fish, fruit, vegetables and extra virgin olive oil. The fruit and vegetables must be fresh, mature and pigmented, in fact folic acid (vitamin B_9) is present in green leaves and the red color of tomatoes is due to licopene (a powerful antioxidant even in skin) which is absent in green tomatoes.
A skin protecting effect is exerted by dihomo-γ-linolenic acid, or GLA (20:3 ω-6) towards its barrier function, as well as improving hydration

and retarding aging. GLA has specific therapeutic activity in the treatment of atopic dermatitis, which is not so for its precursor, linoleic acid. In fact the skin concentrations of linoleic acid of those affected by this illness seem increased presuming a reduced ability of liver conversion of linoleic acid into dihomo-γ-linolenic acid (11).
GLA's therapeutic action seems due to the activity of one of its derivatives (PGE_1 prostaglandin with only one double bond) on inflammatory leucotriens derived from arachidonic acid, but also to a reduction in the formation of immunoglobuline IgE implicated in the genesis of allergies. GLA production in our body is however modest because the body tends to rapidly convert it into its higher derivative, arachidonic acid (20:4 ω-6). To increase its concentration it is necessary to introduce foods that are rich in its preformed state like borage oil, evening primrose oil, and black currant oil.
It should be noted that GLA formation can be inhibited by oxygen free radical peroxidation which limits Δ-6-desaturase activity (an enzyme that forms long chain polyunsaturated fatty acids of 20-22 carbon atoms). Another confirmation that the consumption of antioxidants protects the skin (especially carotenoids as β-carotene and licopene).
Along with consuming foods rich in antioxidants and GLA, it is recommended to consume long chain ω-3 (EPA and DHA) chiefly present in blue fish, which play an important role in anti-inflammatory activity and in maintaining hydration.
It' worthy to remember that fatty fish are healthier that lean fish because EPA and DHA, being fatty acids, are prevalently present in fatty tissue. As we have seen, polyunsaturated fatty acids are exposed to peroxidative risk and this risk increases with the number of double bonds. It seems logical to suppose that even unsaturated fatty acids of the ω-3 series, in particular those with 5 and 6 double bonds (eicosapentaenoic, or EPA, and docosaesaenoic, or DHA) are particularly vulnerable, even more than arachidonic (AA) of the ω-6 series which has 4 double bonds. Recent studies however seem to indicate that ω-3 polyunsaturates not only don't undergo peroxidation, but can actually protect the organism from oxidative stress, even if there are contrasting studies that evidence an increase of peroxidative risk from all polyunsaturates, including the ω-3.
On the whole, the majority of studies done seem to demonstrate a positive correlation between polyunsaturated fatty acid ω-3 intake and total antioxidant capacity of plasma showing even an increase in plasma a-tocopherol concentration. In particular, a recent study done on 99 Icelandic women has demonstrated a positive correlation between ω-3 and plasma antioxidants, of vitamin origin and non. This correlation was slightly negative only with the plasma concentration of licopene. At present it is held that the ω-3 are resistant to peroxidative induction and this resistance can be correlated to the protective activity of some of its metabolites, in particular to prostacyclin with three double bonds, PGI_3.
These observations confirm the protective action of the ω-3 even on skin, however it is always recommended to use caution at high doses, and include antioxidants in the diet which are useful to protect the body in general and the skin in particular.

Tobacco smoking

The negative effects of tobacco smoking on skin is usually incorrectly acknowledged or under estimated, even though it has been calculated that while photo exposure multiplies by three the probability of developing wrinkly skin, smoking one pack a week multiplies it by 5 and one pack a day brings it to 12 times, and naturally the combination of the two factors elevates the risk even more. Females seem to be more damaged

since smoking reduces circulating estrogen levels even annulling the positive effects of substitute hormone therapy in menopause, an important moment to try to maintain and protect the skin and one's physical appearance (13, 14). Even in this instance the pathogenesis of the damage is tied to free radical activity. In fact just one cigarette carries with it hundreds of millions of free radicals, reducing the skin levels of antioxidants (in particular carotenoids). Fifteen minutes of cigarette smoke exposure causes the skin in 24 hours to double lipo-peroxides in the sebum, while reducing cutaneous squalene content, which we have seen is an important ultraviolet ray filter. Even cutaneous blood flow is reduced by nicotine, and this effect is more pronounced and lasts longer in heavy smokers. It is important to also note that smoking dangerously inverts the beneficial haematic effects of β-carotene which is transformed into a factor for increased lung tumor risk (15, 16).

The negative effect on skin is particularly evident facially, causing what is referred to as a "smoker's face", heavily wrinkled and damaging to an harmonious body image, which today has become so important to improve and maintain.

Unfortunately, women who spend much energy to keep their faces attractive and youthful, too often do not listen to the recommendations to limit sun exposure and many continue to smoke. Even when they undergo esthetic treatments.

AGING

Today the theory most accepted to explain aging is oxygen free radical peroxidation (17). In particular, besides altering DNA replication, ROS determine progressive damage to the biologic membrane and to subcellular organelles reducing their functionality.

Over the years, the biologic membrane's sensitivity to peroxidative phenomena increases with a progressive reduction of their biologic activity and functionality. There is an increase in the activity of phospholipase-A_2 enzyme which in the membrane hydrolyzes phospholipids releasing arachidonic acid (20:4 ω-6) . This in turn, besides being easily peroxidable, leads (by action of cycloxygenase enzyme) to an increase of thromboxane synthesis with consequent vasoconstriction, platelet hyper-aggregability and eventual reduction of nutrients to tissues and (by lipoxygenase enzyme action) leads to an increase of leucotriens, with reduction of immune potential in all tissues including the skin.

The skin, as we have stated, represents the mirror of the physiologic aging process (by thining, and reduction of collagen and of elasticity) which involves the entire organism, but the skin also undergoes photo aging caused by solar rays through the formation of ROS which effect mainly ω-6 polyunsaturates. A consequence of lipidic peroxidation is the cutaneous formation of lipofuscine, the spots considered an index of skin aging, while at the same time there is an increased risk for cancer. It should not be forgotten that the ROS inhibit Δ-6-desaturase which limits the formation of long chains (in particular of dihomo-γ-linolenic acid, important for skin). It seems evident that a diet balanced in fatty acids (limiting terrestrial animal fats and seed oils) and rich in antioxidant composts that act beneficially to combat the degenerative phenomena of aging is fundamental. And also that it should be followed throughout one's lifespan.

Hormone modification

Hormones can influence body esthetics, especially in women. Estrogens determine adipose tissue deposits in the glutei and thigh regions, while limiting these deposits in the abdominal area, thereby giving women the very appealing hour glass shape. After menopause, when estrogens are reduced, this effect tends to disappear leading to the unappealing increase around the

abdomen as well as a gradual thinning of the skin which becomes dry and less elastic. (18)
Hair is also influenced by hormonal changes whereby thinning and depigmented hair are phenomena usually associated with age, especially with menopause. The factors responsible for these phenomena, can be genetic as well as due to unhealthy habits, but are mostly due to the fall of estrogen that determines a reduction in sebum secretion and in sweating (dryness), with consequent thinning and fragile hair.
It could be useful therefore to take phytoestrogen supplements (isoflavons and lignans) present in soy protein and in minor measure in other legumes. It should be noted however that dietary phyto-estrogen absorption can be inhibited by phytic acid and oxalic acid present in vegetable fiber (in particular in bran) which are often used in weight loss diets. Finally, regular shampooing though certainly hygienic, it shouldn't be exaggerated since washing tends to dry out hair as it deprives it of its physiologic protective fat.

NOCTURNAL REST

Sleep is a physiologic necessity important for recuperating from the day's stress, but often it is neglected for reasons stemming from social or entertainment activities. Sleep is indispensable for regenerating energy necessary for the psyche as well as the rest of the organism, including the skin. In fact, if sleep is lacking the facial signs of tiredness and aging are more visible, because during sleep the facial muscles relax, eliminating facial tension accumulated during the day. It seems to be accepted that during the night (between 1 and 6 AM) the body works at recuperating damaged cells, including skin cells.

NEOPLASTIC RISK

As we know well age is associated with an increased neoplastic risk, even in the skin, where it is mostly connected to sun exposure. Studies that researched the relationship between skin tumor risk and the lipid makeup of the diet have shown that the level of ω-6 taken in the diet correlates with the degree of increased carcinogenesis. The level of photo-induced cutaneous lipid peroxidation travels linearly with the quantity of ω-6 taken in the diet, while on the contrary ω-3 inhibits the carcinogenetic response induced by UV solar rays.
The fact that ω-3 can, on the contrary cause beneficial physiologic responses has led to speaking of a "*ω-3 peroxidative paradox*", both linoleic as well as α-linolenic are in fact precursors of malonildyaldehide (MDA), one of the many molecules formed from decomposition of the intermediaries of lipid peroxidation. Since dietary supplementation of either ω-6 or ω-3 determines an increase in MDA, but with opposite effects on UV induced carcinogenesis, it has been hypothesized that an intermediary metabolite of the ω-3 fatty acids (for example prostaglandin PGI_3) could intervene favorably towards carcinogenesis and peroxidative damage in general. In fact supplementation with ω-3 drastically reduces the levels of some inflammatory prostaglandins while increasing the immunologic response which is lowered by ω-6 (19).

FOODS RICH IN ANTI-OXIDANTS

As we have seen, peroxidative risk represents an important event that contributes to aging and skin damage. In particular in the skin ROS determines modifications in proteins and enzyme activity, polyunsaturated lipid peroxidation with cell membrane structure damage, DNA modification with possible mutation consequences, and immune-suppressive effects that alter protective mechanisms. Its seems essential to prevent and combat these events by controlling polyunsatu-

rated fatty acid intake (their quantity and ω-6/ω-3 ratio) as well as favoring a high consumption of antioxidant agents through vegetables, fruits, and greens but also using extra virgin olive oil, green tea, dark chocolate and red wine.

Chocolate has been shown to contain a high level of carotenoids and polyphenols, but it should be remembered that with chocolate there is also an intake of sugar which puts it in the luxury food category since it contributes to weight gain. On the contrary, it seems proven that there is no connection between chocolate and acne since this is an expression of hormonal disturbances of a transitory nature and not tied to dietary errors.

With the consumption of wine there is an intake of alcohol which at doses higher than those recommended exerts a damaging effect not only on the liver but also on skin by initiating ROS activity. Therefore wine should not exceed the half liter a day recommendation for males and a third liter daily for females. At these doses no other alcohol can be added as cocktails or after dinner drinks.

Among the antioxidant agents active at the skin level we have mainly the carotenoids and the tocopherols, and also polyphenols, coenzyme Q (ubichinone) and selenium. Vitamin E (α-tocopherol) acts by slowing oxidative damage in the skin aging process by protecting collagen. The carotenoids (α-carotene, β-carotene, licopene. zeaxantine), also active against aging are particularly active in defending the skin from solar rays, and contrary to general opinion, α-carotene and especially lycopene are more active than β-carotene (pro-vitamin A). These carotenoids are present mostly in fruit and vegetables (which contain also numerous polyphenols). Lastly, as already stated, squalene is very important as a tritherpenic hydrocarbon present mainly in olive oil, and a powerful filter against oxygen singlets. From the above we can see the necessity of ensuring a daily intake of these antioxidant agents by the use of extra virgin olive oil, greens, fruits, vegetables and maybe even adding dietary supplements. However it is important to underline that *it is necessary to take in a pool of antioxidants,* since they act synergistically reinforcing each other, and not to take just one of them, which at high doses could even invert the beneficial effects. The regular consumption of different vegetables guarantees that pool, but as stated before, they must be fresh, mature and pigmented. It however is not necessary that they be raw, since it has been seen that licopene is more readily absorbed if the tomato undergoes processing or cooking. In reference to this, some have referred that even β-carotene absorption is improved by cooking carrots, but then there are other studies the say the opposite. It however seems certain that, as already said, the consumption of β-carotene (and of other carotenoids) should be started at least one month before sun exposure not only by eating carrots but also apricots peaches and watermelon.

However all that has been stated above is not intended to support an exclusively vegetarian diet, because in this case there is the risk of other deficiencies, like essential amino acids, vitamins D and B_{12}, of calcium and iron with evident negative consequences. If a rigorous vegetarian diet is begun at an early age, worse if in infancy, the psychic and intellectual development can be hindered. Terrestrial animal foods, though they should be limited, should not be abolished all together.

It must be remembered that the skin is able, up to a point, to autonomously defend itself against the sun through the production of melanin, a physiologic substance that acts as an antioxidant slowing aging and photo induced carcinogenesis. It is important to proceed gradually in sun exposure and to avoid the hottest hours, so that the needed melanin production has time to develop creating a physiologic tanning. Very important indeed is to avoid burning, especially in

infancy, because this type of insult can cause melanomas in adulthood.
Apart from dietetic suggestions, skin protection can also benefit from topical therapies containing substances nourishing for the skin with addition of antioxidant agents, but one should always seek professional dermatologic advice and *not do it yourself treatments*, since creams and ointments used incorrectly can act negatively with a dangerous increase of oxidative stress that causes skin changes.

CONCLUSIONS

As seen it is not a simple matter to preserve or improve what nature has gifted us with and often the damage undergone by the body is our own doing, partly from involuntary mistakes, but also in part from habits that could have been avoided. The skin's main enemy and that which causes aging is cellular peroxidation by ROS, brought about by pollution, sun rays, tobacco smoking, stress and dietary errors. As a consequence of ROS activity, skin cells progressively lose the ability to regenerate and produce new collagen, making the skin thinner, more wrinkled and un elastic. Antioxidant intake is therefore of utmost importance. It seems necessary to point out that the body will use its supply of dietary antioxidants primarily for internal organ use before using it for skin protection. Therefore alongside a correct diet it would be wise to use topical treatments rich in antioxidants that are easily absorbable, always under a dermatologist recommendation. However the diet should always be foremost especially with regards to the polyunsaturated fatty acid ratios.
The recommendations are to not smoke, avoid prolonged sun exposure, to get enough rest and keep the diet contained but varied, rich in vegetables (but not exclusively so) with the correct lipid content and limit alcohol consumption. It would be wise to have regular visits with dermatologists and internist. These are clear and simple recommendations but they are often misunderstood and sometimes ignored.
In fact each of us thinks they know enough and that recommendations are for others not for ourselves.

References

1) **Kielbassa C, Roza L, Epe B. (1997)** Wavelength dependence of oxidative DNA damage induced by UV and visible light, *Carcinogenesis,* **18:** 811-16.
2) **Harman D. (1988)** Free Radical Theory of Aging, In: The Molecular Mechanisms of Aging. Role of Dietary Lipids, Lucca (Italy), **27-28:** 15-27.
3) **Sevanian A. (1988)** The impact of lipid unsaturation ad autoxidation on membrane structure. In The Molecular Mechanism of Aging. The Role of Dietary Lipids, Medical Scientific Meeting, Lucca (Italy), **27-28:** 45-54.
4) **Christiansen EN, Lund JS, Rotveit T, Rustan AC. (1991)** Effect of dietary n-3 and n-6 fatty acids in fatty acids desaturation in rat liver – *Biochim. Biophys. Acta* **1082:** 57-62.
5) **Homer S, Black J. (2006)** Carcinogenesis and antioxidant actions of some nutritional lipids, *J. Plastic Dermatol.,* **2:** 2-6.
6) **Calder PC, Zurier RB. (2000)** Polynnsaturated fatty acids and rheumatoid arthritis, *Cur. Opin, Clin. Nutr. Metab. Care,* **4:** I15-21.
7) **Visioli F, Galli C. (1998)** Natural antioxidants and prevention of coronary heart disease: the potential role of olive oil and its minor constitnents, *Nutr. Metab. Cardiovasc. Dis.,* **5:** 306-14.
8) **Arief B, Nazim UA, An W, Tashiori B. et al.(2000)** Protective effect of topically applied olive oil against photo-carcinogenesis following UVB exposure of mice, *Carcinogenesis,* **21(11):** 2085-90.
9) **Mathews Roth M. (1987)** Photoprotection of carotenoids, *Feder. Proc.,* **46 (5):** 1980-87.
10) **Lasskshimirayana R, Raju M, Keshava Prakash MN, Bakatan V. (2009)** Phospholipid, oleic acid micelles and dietary olive oil influence the lutein absorption and activity of antioxidant enzymes, *Lipids,* **44:** 799-806.
11) **Cornelli U. (2002)** The antioxidant defence system in skin, International Congress on Nutricosmeceutical: a Challenge for the Future, Rome, 6-8 febr. 2002.
12) **Kawashima H, Tateishi N, Shisishi A. et al. (2008)** Oral Administration of Dihomo-γ-linolenic Acid Prevents Development of Atopic Dermatitis in NC/Nga Mice, *Lipids,* **43:** 37-43.
13) **Vessey MP, Painter R, Powell J. (2000)** Skin disorders in relation to oral contraception,and other factors, including age, social class, smoling and body mass index. Findings in a large cohort study, *Br. J. Acad. Dermatol.,* **41:** 27-30.
14) **Bartolomucci GJJ. (2010)** Acne che odora di tabacco, *La Pelle,* **15:** 3-4.
15) **Frances C. (1998)** Smoker's wrinkle: epidemiological and pathogenic considerations, *Clin. Dermatol.,* **16:** 565-70.
16) **Monroe JD, Frei B, Longmire AW. et al. (1995)** Increase in circulating products of lipid peroxidation (F2-isoprostanes) in smokers. Smoking as a cause of oxidative damage, *N. Engl. J. Med.,* **332:** 98-1203.
17) **Harman D. (1986)** Swiss male mice: Effect of dietary fats on skin damage by ultraviolet light, Olive Oil in Medicine, C.O.I. Publisher, Madrid.
18) **De Pergola G, Giorgino F, Garruti G. et al. (1996)** Rapporto tra variabili antropometriche, ormoni sessuali e complicanze dell'obesità, *Metabolismo Oggi,* **13:** 138-4.

19) **Black HS, Thornby JL, Lenger W. (1992)** Influence of dietary omega-6, omega-3 fatty acids sources and promotion stages of photocarcinogenesis, *Photochem. Photobiol.*, **56:** 195-201.

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Use of a Cosmetic Caffeine Lotion in the Treatment of Male Androgenetic Alopecia

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Summary

Androgenetic alopecia (AA) is the most common form of hair loss in men, affecting more than 50% of the male population over 50 years, and it often causes psychological and social distress to those affected, in addition to being one of the most common reasons why a patient consults a dermatologist. There are several cosmetic substances that can complement the medical treatment of this widespread disease, in order to obtain better results.

In the past few years caffeine has been used; this molecule, applied topically in the form of shampoos and lotions, has shown good efficacy in the treatment of AA.

We report the results of a study to test efficacy, safety and cosmetic qualities of a caffeine containing lotion used daily for four months by 40 men with AA.

Riassunto

L'alopecia androgenetica (AA) è la forma più frequente di alopecia nel sesso maschile, colpisce più del 50% della popolazione maschile oltre i 50 anni, ed è spesso causa di disagio psicologico e sociale per i soggetti affetti, oltre a rappresentare uno dei motivi più frequenti per cui un paziente si rivolge al dermatologo.

Esistono diverse sostanze cosmetiche che possono affiancare la terapia medica di questa diffusa patologia, per ottenere dei risultati complessivamente migliori.

In particolare negli ultimi anni è stata utilizzata la caffeina che, applicata localmente sottoforma di shampoo o lozioni, ha dimostrato una buona efficacia nel trattamento dell'AA.

Riportiamo i risultati di uno studio per testare l'efficacia, la sicurezza e le qualità cosmetiche di una lozione contenente caffeina utilizzata quotidianamente per quattro mesi da 40 uomini affetti da AA.

INTRODUCTION

Androgenetic alopecia (AA) is the most common form of hair loss in men, affecting more than 50% of men over 50 years. (1) The hair starts thinning in the temporal area, then continues on the frontal region and to the vertex, to finally involve the entire scalp; the disease progression has been described and classified for the first time in 1975 by Hamilton, whose scale is still used to define the severity of this condition (2).

Behind this widespread disease, there is definitely a genetic predisposition, transmitted with a polygenic inheritance, which explains the widespread familiarity observed in cases of AA.

In this setup we must add the role of testosterone; in fact it has been demonstrated that in patients with AA there is an increase in 5-alpha-reductase, the enzyme that catalyzes, in the hair follicle, the transformation of testosterone to its active metabolite, 5-alpha-dehydro-testosterone (DHT).

DHT binds to the androgen receptor, and this specific binding triggers a series of cellnlar processes that lead to the reduction of the anagen phase of hair cycle. The increased activity of the enzyme 5-alpha reductase is genetic, and depends on a polymorphism of the androgen receptor (3).

There are now only two FDA-approved drugs for the treatment of AA: finasteride (inhibitor of the synthesis of DHT) and minoxidil (a drug that acts nonspecifically on the opening of potassium channels) (4).

But 20-30% of patients with AA does not respond to these drugs; as well as non-responders, we must also consider the contraindications and side effects associated with use of finasteride (oligospermia, teratogenicity, ...) and minoxidil (hirsutism, hypertrichosis, hypotension, tachycardia ...), which limit their use in some patients.

Caffeine is a methylxanthine belonging to the alkaloids family, a group of compounds widely present in many plants.

This substance is mainly extracted from coffee (Coffea arabica, Rubiaceae family ...), belongs to the group of purine alkaloids such as theophylline (extracted from tea, Camellia sinensis, fam. Theaceae), and theobromine (extracted from cocoa, Theobroma, family Sterculiaceae). While the effects on the CNS, cardiovascular system and general metabolism resulting from its oral intake are well known, the effect of its topical use on hair growth cycle is not yet well defined.

The effect of caffeine is biologically mediated by cyclic AMP increase in cells with a combined action on two levels: increased synthesis of cAMP (caffeine blocks the inhibitor of adenylate cyclase enzyme, which converts ATP into cAMP) and slowing of the cAMP degradation (caffeine inhibits the phosphodiesterase enzyme, which converts cAMP to AMP); in this way caffeine promotes proliferation by stimulating the cellular metabolism, a mechanism that could connteract the miniaturization of the hair follicle induced by testosterone and DHT(5).

In a model of male skin in culture, caffeine has been shown to counteract the inhibitory effect of testosterone on the proliferation of keratinocytes (6).

Similar results were obtained by testing the caffeine in an organic model of hair in culture (7), and in human hair follicles extracted ex vivo from male patients with AA (8).

With regard to the ability of topically applied caffeine to penetrate into the follicle, it has already been studied for a shampoo formulation, and good results were obtained (9); Otberg and collaborators have shown that caffeine penetrates the hair follicle and the stratum corneum after 2 minutes. In addition, it was observed that the penetration through the hair follicle is faster and higher than the interfollicular route and that hair

follicles are the only pathway for fast caffeine absorption during the first 20 minutes following application (10).

AIM OF THE STUDY

This clinical study was designed to test skin compatibility, efficacy and cosmetic quality of a cosmetic lotion for the treatment of male androgenetic alopecia after application under normal conditions of use for 4 consecutive months.

MATERIALS AND METHODS

This monocentric study was performed in open. 40 volunteers were included in the study, with age between 19 and 55 years (mean age 37 years), with following inclusion criteria:

- men suffering from androgenetic alopecia in the stages of Hamilton-Norwood II-IV
- age: 18 to 55 years old
- men suffering from an increased hair loss topically
- men showing a hair count of the "Hair Pull Test" of at minimum 15 (last shampoo 2 days before)
- men, who did not use any hair restorer (tablet, capsule, tonic nor shampoo) since the last 4 months
- with a phototype (Fitzpatrick) I, II, III or IV
- exhibiting no cardiovascular, pulmonary, digestive, neurological, genital, urinary, osteoarticular, psychiatric, haematological, immunological or endocrinal pathology which could interfere directly or indirectly with the study
- exhibiting no skin affection which could interfere with the study, for example: dermographism, seborrheic dermatitis, recurrent herpes, pityriasis versicolor, psoriasis, important pigmentary disorders (vitiligo, chloasma, chronic lupus erythematous .....).

The specific non inclusion criteria were the following ones:

- men suffering from a different cause of alopecia:
  - alopecia areata
  - psychosomatic alopecia ie Trichotillomania
  - hair loss due to medication (immunologics, chemo-therapy, etc.)
- men with an unhealthy condition of the scalp:
  - widely spread, highly expressed eczema (sparely stages can be included)
  - high grade of dandruff
  - allergy against an ingredient of the test product
- atopy
- long-term anti-inflammatory treatment stopped less than 4 months before the beginning of the study
- regular use of hair dye, bleaching products or products for permanent wave
- surgical correction of the alopecia performed before the study
- having received excessive or intensive exposure to sunlight (natural or artificial) within the month prior to the study or foreseeing UV exposures for the duration of the study
- under general or local medication such as anti-inflammatory, anti-histaminic or anti-allergic treatment or who have stopped one of this treatment less than 10 days before the beginning of the study.

All volunteers have expressed their consent to the study through a written informed consent.

The experimental conditions were as follows: once a day for four consecutive months, the volunteers had to apply the product on the scalp and massage it with fingers for about 2 minutes, allow to dry hair and do not rinse them, (in case of washing, the application had to be carried out immediately after washing).

During the study, volunteers were unable to use products similar to the one tested, would make the last shampoo at least 2 days prior to dermatological control, should not use products for colouring, hair bleaching, permanent wave,

alpha level of 0.05).
For the primary efficacy variable (hair pulled back to pull-test) mean, standard deviation, 25% - 50% - [average] and 75%-percentiles were calculated at baseline, after 2 months and 4 months after application of the Caffeine Lotion. For the secondary efficacy variables (evaluated using questionnaires, ordinal scales) frequencies and percentages were calculated.
The statistical analysis was performed using 'SPSS for Windows' (version 18.0).

RESULTS

About the skin compatibility,investigators described no clinical signs, nor any sense of discomfort related to the use of the lotion has been reported by volunteers.
Regarding the assessment of cosmetic effectiveness of the product, the results obtained showed that the investigational product has resulted in a reduction of the number of hairs extracted with the pull-test of 8.14% after 2 months and 15.33% after 4 months of treatment, indicating an increase in tensile strength of hair and a decrease in hair loss.
After 2 months of treatment, the percentage of ' positive' volunteers (for which the number of hair in pull test is decreased with treatment) was 75%, and after 4 months of treatment, of' 83%.
These data are represented in the graphs below:

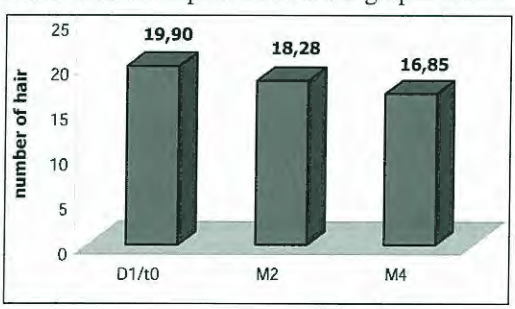

Fig. 1 number of hairs pulled in the pull-test at baseline, after 2 and 4 months of Caffeine Lotion application (means with 95% confidence intervals).

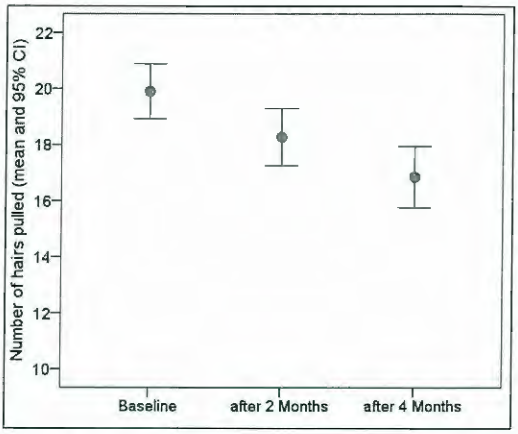

Fig. 2 Means with 95% confidence intervals of the number of hairs taken from the pull-test at baseline and after 2 and 4 months of treatment.

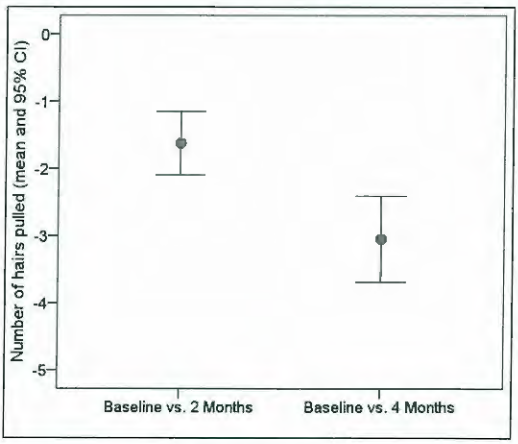

Fig. 3 Decreased hair pulled in the pull-test after 2 and 4 months of Caffeine Lotion application, compared to baseline (before applying the product); here are shown the means and confidence intervals of 95%.

About the assessment of the cosmetic efficacy in the dermatologic questionnaire, the results were as follows:

Items	How do you describe the scalp? Redness														
	At the beginning					After 2 months of treatment					After 4 months of treatment				
Score	absent	very slight	slight	mode-rate	strong	absent	very slight	slight	mode-rate	strong	absent	very slight	slight	mode-rate	strong
Number of vol.	30	4	4	2	0	30	5	5	0	0	32	5	3	0	0
Number and % of volunteers with a decrease in redness referred only to volunteers with redness at the inclusion						3/30%					7/70%				

Items	How do you describe the scalp? Scaling/dandruff														
	At the beginning					After 2 months of treatment					After 4 months of treatment				
Score	absent	very slight	slight	mode-rate	strong	absent	very slight	slight	mode-rate	strong	absent	very slight	slight	mode-rate	strong
Number of vol.	26	5	3	6	0	26	5	9	0	0	31	5	4	0	0
Number and % of volunteers with a decrease in scaling / dandruff referred only to volunteers with dandruff at the inclusion						6/43%					13/93%				

Items	How do you rate the strength of the hair?										
	At the beginning				After 2 months of treatment				After 4 months of treatment		
Score	strong	medium	thin	very thin	strong	medium	thin	very thin	strong	medium	
Number of vol.	0	4	25	11	0	7	24	9	1	14	
Number and % of volunteers with an increase in the strength of the hair					5/12%				21/53%		

Items	How do you describe the progression of the balding?											
	At the beginning				After 2 months of treatment				After 4 months of treatment			
Score	very slight	slight	mode-rate	severe	very slight	slight	mode-rate	severe	very slight	slight	mode-rate	severe
Number of vol.	1	18	16	5	3	18	14	5	9	18	9	4
Number and % of volunteers with a decrease in the progression of the balding					4/10%				17/43%			

Items	How do you rate the extent of the out falling hairs? (comb the hair several times and make a semiquantitative rating)											
	At the beginning				After 2 months of treatment				After 4 months of treatment			
Score	very slight	slight	mode-rate	severe	very slight	slight	mode-rate	severe	very slight	slight	mode-rate	severe
Number of vol.	0	17	18	5	4	18	16	2	13	20	7	0
Number and % of volunteers with a decrease in the extend of the out falling hairs					12/30%				34/85%			

Items	What is your clinical opinion of the efficacy of the test product?			
	The test product has reduced the premature hair loss	The test product has reduced the balding	The test product has improved the scalp condition	The test product has improved the structure of the hair
Number of vol.	17	17	5	21
% of volunteers	43%	43%	13%	53%

Items	Do you recommend the test product as a daily treatment of hereditary hair loss to reduce the number of out falling hairs?	
Score	yes	no
Number of volunteers	34	6
% of volunteers	85%	15%

Items	Please evaluate personally the intensity of your hair loss											
	At the beginning				After 2 months of treatment				After 4 months of treatment			
Score	very slight	slight	mode-rate	severe	very slight	slight	mode-rate	severe	very slight	slight	mode-rate	severe
Number of vol.	0	9	20	11	2	18	12	8	7	20	12	1
Number and % of volunteers which referred a decrease in the intensity of the hair loss					16/40%				32/80%			

Items	Does your hair-loss decrease or normalize with the treatment?							
	After 2 months of treatment				After 4 months of treatment			
Score	quite agree	agree	fairly disagree	disagree	quite agree	agree	fairly disagree	
Number of volunteers	0	16	11	13	10	22	8	
Number and % of satisfied volunteers quite agree / agree	16/40%				32/80%			

Items	During daily combing, do you count a high number of hairs in the basin?										
	At the beginning				After 2 months of treatment				After 4 montbs of treatment		
Score	very few	few	some	many	very few	few	some	many	very few	few	
Number of vol.	0	6	23	11	2	15	15	8	8	18	
Number and % of volunteers which referred a decrease in the number of hair in the basin					16/40%				32/80%		

Items	Please evaluate your scalp condition - Itching														
	At the beginning					After 2 months of treatment					After 4 months of treatment				
Score	absent	very slight	slight	mode-rate	strong	absent	very slight	slight	mode-rate	strong	absent	very slight	slight	mode-rate	strong
Number of vol.	25	2	8	4	1	25	6	8	1	0	28	7	5	0	0
Number and % of volunteers which referred a decrease in itching referred only to volunteers with itching at the inclusion						8/20%					12/30%				

Items	Please evaluate your scalp condition – Tension/dryness														
	At the beginning					After 2 months of treatment					After 4 months of treatment				
Score	absent	very slight	slight	mode-rate	strong	absent	very slight	slight	mode-rate	strong	absent	very slight	slight	mode-rate	strong
Number of vol.	20	6	10	4	0	21	10	9	0	0	25	12	3	0	0
Number and % of volunteers which referred a decrease in tension/dryness referred only to volunteers with tension/dryness at the inclusion						10/25%					17/43%				

Items	Please evaluate the strength and the thickness of your hair											
	At the beginning				After 2 months of treatment				After 4 months of treatment			
Score	bouncy	strong hair	soft, weak	fine hair	bouncy	strong hair	soft, weak	fine hair	bouncy	strong hair	soft, weak	fine hair
Number of vol.	0	1	11	28	4	2	7	27	7	14	5	14
Number and % of volunteers which referred an improve in the strength and/or in the thickness of hair					5/12%				20/50%			

Items	Are you satisfied with the product?							
	After 2 months of treatment				After 4 months of treatment			
Score	very high	high	low	very low	very high	high	low	very low
Number of volunteers	2	14	18	6	11	21	5	3
Number and % of satisfied volunteers Very high / high	16/40%				32/80%			

Items	Do you like to continue with the test product?		Do you like to recommend the test product?	
Score	yes	no	yes	no
Number of volunteers	32	8	32	8
% of volunteers	80%	20%	80%	20%

Items	How do you feel about the use of the bottle, i.e. the dosing?				How do you feel about the viscosity of the test product?		
Score	precisely to dose	simple, comfortable	unprecisely	uncomfortable	exactly right	too thin	too viscous
Number of vol.	10	16	8	6	35	5	0
% of volunteers	25%	40%	20%	15%	88%	12%	0%

Items	Do you like the perfume of the test product?		How do you think about the intensity of the perfume?		
Score	I like it very much	I dislike it	exactly right	too much	too low
Number of vol.	29	11	15	25	0
% of volunteers	73%	28%	38%	63%	0%

Items	How do you feel your dried hair after the hair wash?					Has your hair styling been changed by the test product?		
Score	light	smooth	strong	greasy	uncomfortable	easier than before	unchanged	more difficult than before
Number of vol.	11	19	0	4	7	5	35	0
% of volunteers	28%	48%	0%	10%	18%	12%	88%	0%

Items	How do you think about the bounciness of your hair?			How do you think about the combing of your hair?		
Score	very good	quite normal	bad, very low	very easy	normal	very bad
Number of vol.	7	33	0	5	35	0
% of volunteers	18%	82%	0%	12%	88%	0%

Items	What is the best you like in this test product?					
Score	hair strengthening effect	application	perfume	scalp care, fit for sensitive scalp	feel of hair	freshening
Number of vol.	17	1	11	16	6	2
% of volunteers	43%	3%	28%	40%	15%	5%

Items	What should be improved in this test product?					
Score	hair strengthening effect	application	perfume	scalp care, fit for sensitive scalp	feel of hair	freshening
Number of vol.	8	13	16	0	10	0
% of volunteers	**20%**	**33%**	**40%**	**0%**	**25%**	**0%**

Items	Do you like to continue with the test prodnct?		
Score	yes, it is fit for my daily hair care	yes, but only in case trouble (time-limited)	no, not fit for my scalp and hair care
Number of volunteers	18	14	8
% of volnnteers	**45%**	**35%**	**20%**

DISCUSSION

Male androgenetic alopecia (AA), or more commonly 'baldness', is the most common cause of hair loss or thinning in men; this condition, while having a purely aesthetic and not pathological meaning, significantly affects the social life and the psychology of individuals who are affected, especially if young and of childbearing age. Its development is mainly androgen-dependent and modulated by dihydrotestosterone (DHT) and by the expression of the androgen receptor of the hair follicle. The available medical treatments (topical minoxidil and oral finasteride), prevent the progression of disease in many patients with moderate and severe AA, but there is still a rather high percentage (20-30%) of non-responders.

For this reason, considering the widespread of this imperfection, the cosmetics industry is devoted to finding alternatives that can assist or replace medical treatment, acting on mechanisms unrelated to androgens, or synergistically with the anti-androgen drugs.

Caffeine is one of the substances considered by the cosmetic industry for the treatment of AA; its ability to inhibit the negative effects of testosterone on keratinocyte proliferation has been shown in culture models of male skin as well as in hair follicle models extracted ex vivo from men with AA and cultivated *in vitro*.

In addition, caffeine has shown a high and fast penetration through the hair follicle, and so it was possible to formulate a product containing Caffeine such as shampoo*, which showed a good cosmetic efficacy (9).

In this experimental study, we tested a lotion containing caffeine** for daily use, that accor-

* *Trade name: Alpecin® Caffeine Shampoo*
** *Trade name: Alpecin® Liquid*

ding to the experimental conditions showed a very good skin compatibility after application under normal conditions of use, and a good cosmetic efficacy in the treatment of androgenetic alopecia.

Specifically, the results of the pull-tests showed an increase in tensile strength of hair and a decrease in hair loss in 75% of volunteers after 2 months and in 83% of volunteers after 4 months of treatment.

The dermatological control confirmed the good efficacy of the product; in particular there was an important reduction in premature hair loss hair in 43% of the volunteers, an improvement in hair texture (force, tensile strength) in 53%, an improvement of the conditions of the scalp (erythema, dandruff, dryness) in most of the volunteers who showed abnormalities of the scalp at enrollment.

The subjective evaluation of the cosmetic effectiveness showed that 80% of volunteers were satisfied with the product; in particular they reported, after 4 months of treatment, a decrease in hair loss and an improvement in the hair and scalp conditions.

In addition, the product was also appreciated for its cosmetic qualities (smell, viscosity, ease of dosing, combing hair, etc..).

Ultimately, we can say that this daily use lotion is an effective and well tolerated cosmetic complement, and that caffeine contained in the lotion is an interesting and promising substance for cosmetic treatment of androgenetic alopecia.

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References

1) **Bienova M, Kucerova R, Fiuraskova M, Haijduch M. and Kolar Z. (2005)** Androgenetic alopecia and current methods of treatment, *Acta Dermato Ven APA*, **(14) 1:** pagg?
2) **Norwood OT. (1975)** Male-pattern baldness. Classification and incidence, *South Med. J.*, **68:** 1359-1370.
3) **Jamin C. (1999)** Androgenetic alopecia, *Ann. Dermatol. Venereol.*, **129 (5 Pt 2):** 801-3.
4) **Price VH. (1999)** Treatment of hair loss, *N. Engl. J. Med.*, **341:** 964-973.
5) **Kren R, Ogushi S, Miyano T. (2004)** Effect of caffeine on meiotic maturation of porcine oocytes. *Zygote*, **12:** 31-38.
6) **Tsianakas A, Husing B, Moll I. et al. (2005)** An ex vivo model of male skin- caffeine conteracts testosteroneeffects, *Arch. Dermatol. Res*, **296:** 450.
7) **Fischer TW, Hipler UC, Elsner P. (2007)** Effect of caffeine and testosterone on the proliferation of human hair follicles in vitro, *Int. J. Dermatol.*, **46:** 26-35.
8) **Fischer TW, Hipler UC, Elsner P. (2006)** Caffeine counteracts the growth inhibitory effect of testosterone in ex vivo human hair follicles from male patients with AGA, *Dermatology*, **213:** 53-80.
9) **Bussoletti C, Mastropietro F, Tolaini MV, Celleno L. (2010)** Use of a Caffeine shampoo for the treatment of male androgenetic alopecia, *J. Appl. Cosmetol.*, **25:** 153-163.
10) **Otberg N, Teichmann A, Rasuljev U, Sinkgraven R, Sterry W, Lademann J. (2007)** Follicular penetration of topically applied caffeine via a shampoo formulation, *Skin Pharmaco. Physiol.*, **20 (4):** 195-8.

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Dermatopathology

by W. Kempf, M. Hantschke, H. Kutzner and W. W.H.C Burgdorf

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Dermatologists, Cosmetic Chemists and consumers are all involved to define and understand the meaning of term cosmeceutical.

On one hand Dermatologists don't yet fully understand if cosmeceuticals might or might not work, while on the other hand Cosmetic Chemists know why many of the modern innovative cosmetic products are really more effective. It seems, in fact, that new active ingredients inserted in new delivery systems give the possibility to the so called cosmeceuticals or neurocosmetics to be really active at the level of skin cells membrane, as well as of the signals they interchange among them and with other different body cells. The use of right ingredients and vehicles can make really a difference between one and another cosmetic product active, for example, for pigment control or collagen stimulation. Thus, the increasing number of links existing between mind and body have shown as excess stress or too little stress can abnormally alter the immune defences, modifying the skin appearance also. For example, it was experimentally demonstrated by the use of magnetic resonance imaging, how the skin has the possibility to stimulate differently the brain following the application of an active cosmetic product on one's hand, and a vehicle on the other. An interesting controlateral activation of the brain emotion was therefore verified, stimulated by the topical cosmetic efficacy. This result suggests that the skin activity seems to be the result of an improvement of the balance of the whole body rather than only a local improvement of skin condition.

Langerhans cells, which play a vital role in the cutaneous immune reaction in the epidermis, frequently contact, in fact, cutaneous nerves that contain calcitonin gene-related peptide as a transmitter to regulate the antigen- presenting function of the Langerhans cells. Thus, these specialized cells, producing factors that affect neuron differentiation, clarify the existence of a bidirectional regulatory mechanism between the nervous and immune system in skin. These connections justify the NICE concept of the so called neurocosmetics in which the human nervous, immune, cutaneous and endocrine systems work all together to activate the skin physiology.

In conclusion, the effect of cosmeceuticals and/or neurocosmetics on mood change and perception of improvement of well-being, should be a common house for both Cosmetology, Dermatology and Neuroscience. Thus the necessity to demonstrate by other studies and scientifically quantifiable linear-logic data these mind-body connections.

For these reasons, we have also defined these products Clinically Correct Cosmetics. The new cosmeceuticals and neurocosmetics in fact, should not only simple improve the appearance of skin aging, but have also the possibility of leading real physiological changes, without being considered drugs or medical devices.

According with the current EU legislation a cosmetic product *"is any substance or preparation*

intended to be place in contact with the various external part of the human body....with a view exclusively or mainly to cleaning, perfuming, changing their appearance, and/or correcting body odours, and/or protecting or keeping in good condition".

At this purpose, as written on a scientific article published some years ago, "the advancements of the science have ripened the possibility that new products, namely functional cosmetics or cosmeceutical, could be used in the treatment of *"minor skin disorders or mild skin abnormalities and recognized (not as drug but) as products that show an activity, and physiological functions different from that of medical device and medicinal products. It is foreseen for functional cosmetics to be a new class of compounds regulated probably under the same cosmetic legislation, with a technical additional requirements of safety and efficacy"* (Clinics in Dermatology I 2008 26: 392-397).

At this purpose this book on *Dermatopathology*, especially written for beginners, represents a precious support not only for young Dermatologists but for Cosmetic Chemists who have to formulate cosmetic products, and marketing experts who have to know the possible related claims to be used for the right consumers understanding.

This interesting book, divided in four parts and 26 chapters, underline in fact as *basic knowledge of dermatopathology is essential for the diagnosis of both inflammatory and neoplastic skin diseases,* and, in our opinion, it is essential to understand the physiology of the skin together with skin disorders or mild skin abnormalities. These knowledge are fundamental especially for Cosmetic Chemists who have to design and formulate innovative and effective cosmetic products lacking in side effects.

It is interesting to underline the simplicity in the book organization, easy to be looked up not only from expert Dermatologists, but also from people working in the Cosmetic Dermatological field, going from Cosmetic Chemists, to Biologists and Marketers.

It is arranged starting with the examination of the epidermis, then moving down through dermis and the subcutaneous fat. The different biopsy techniques are reported and discussed underlining the difficulty of fixation, sectioning, and staining required for the special handling of the skin. Most of normal and fluorescence-labelled antibodies employed in identifying specific skin components or diagnosing tumours, as well as molecular biological procedures used, are described underling their principal advantages, disadvantages, and specific indications.

The most important part of the book concerns all the inflammatory and infection disorders of epidermis, dermis and subcutaneous fat, as well as cysts, hematomas and neoplasms affecting the skin and its appendages. Each chapter of these linear sections consists in two pages: the first reports definition, clinical appearance, histopathology with its related description, complete with differential diagnoses comment, and the front page is related to two coloured histological figures. A Dermatopathologic glossary is also reported especially useful for beginners and students of both the chemical and medical communities.

In conclusion the interesting histological methodologies reported together with the most common and important diseases regarding the human skin, accompanied by the well done 242 representative photomicrographic pointers and related comments, give the readers the basic elements for understanding the skin structure organization, and its cellular changing when affected by different pathological events. The easy readability of this Dermatopathology book enriched with interesting comments and matching histological pictures, make it useful for all people involved in Cosmetic Dermatology.

In my opinion this book should be in the personal library, as scientific and practical to use volume,

for Dermatologists, Cosmetic Chemists, Biologists, and Marketing people, involved in the formulation of innovative cosmetics, as well as for Scientists who want to have a better knowledge on Dermatopathology.

P. Morganti
Editor-in-Chief

Hair care formulation for all hair types

by P. Romanowsky

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Hair performs no vital activity in humans but its psychology function is inestimable. Until today scalp remains, in fact, one of the major social and sexual display feature of the human body.
Hair growth is based on an intermittent and dynamic cycle involving three phases.
The anagen phase of growth, the catagen period of regression, and telogen resting phase. However, also if the identification and the naming of these phases have been one of the most important contributions to modern cutaneous biology, the reason of cycles remains unanswered. We don't really know why and how follicles grow and rest and according to the observation done many years ago from the scientist William Montagna, "*any progress has to be made in understanding the mysterious of these hair growth cycles*".
However, while it appears that the follicles are innately programmed and can be slowly influenced by systemic factors and the environment, it is known that several hormones profoundly affect the passage of the molt cycle, though none alters its sequence. In conclusion, if some of the systemic factors that mediate activity of the hair follicle are known, the question of what controls the intrinsic cycle remains wide open.
The book divided in four parts for a total of 29 chapters, covers the physiological aspects of hair biology and the ingredients used to formulate some hair cosmetic products, reporting some specific formulations (products) and the relative methods to test their efficacy and safeness (testing).
In anyway hair follicle is to be considered a multicellular tissue that retains element of developmental dynamics recapitulated in the hair cycle. Moreover, it is without question that hormones affect hair growth, while it is not clear whether estrogens are important for anagen maintenance and delay in hair shedding. Thus, it is interesting to underline the importance of the enzyme 5-α-reductase in the metabolism of testosterone within the pilosebaceous unit, as well as estrogens activity which seem to have some anabolic actions at the level of the follicle, during the anangen phase. However, according to recent studies, follicle is influenced by its surrounding dermis and, like skin; hair is susceptible to different environmental damages, such as the exposure to the sun.
It is to remember how the skin is now acknowledged as a peripheral neuro-endocrine organ that, without central regulation, provides frontline defense and contribute to general homeostasis. Thus hair growth and hair loss should be influenced in the same way by local and central neuro-endocrine factors at follicle level, expressed by stress factors. This type of research has lead to local and holistic routes to treatment of hair loss both, by inside and outside, in accordance with the NICE and TCM (Traditional Chinese Medicine) approach of formulating innovative products. Examples of hair

loss treatments can be found in more traditional and holistic approaches in Chinese and Indian medicines, as well as in the use of specific biologic ingredients and herbal remedies. In anyways, successful hair growth treatment requires sufficient change for the growth to be perceived. This can be driven, for example, by more hairs per square centimeter and/or hairs of greater diameter, controlled by different clinical methods. What it is important to underline is the accuracy and precision of the adopted methodologies that have to control number size, strength or growth rates of hair, giving reproducible and statistically valid results.

Recently new products are appearing on the market called *cosmeceuticals, nutri-cosmetics* or *neurocosmetics* for their efficacy demonstrated by in vivo and in vitro methods. By new methods of control it seems now possible to find the correlation between the topical and the general activity of these new categories of products, capable to activate the many interchanged signals passing from the skin and the hair follicle throughout specific receptors of nervous, immune and endocrine systems (NICE approach).

In our days more attention has been drawn, in fact, to life style improvement and to the use of drugs and wellness products that aim to provide individuals with better health and more comfortable quality of life. The reasons is an aging population that, non only desires to live longer, but also to remain young.

One of the sign of aging is represented from a thinning of the hair and its more fast loss: the telogen phase becomes longer and the ratio of hair in the telogen stage increases. As a result, a considerable amount of hair falls out without immediate replacements. As this situation continues, the hairs on the scalp become thin, giving rise to noticeable balding results.

These topics are reported and described in the 1st part by the first **5 Chapters** of this book.

Being of fundamental importance the transfollicular delivery of formulation' components, the typology and characteristics of the all active ingredients used are carefully studied and selected. The hair follicle seems in fact, to act as reservoir for topically applied ingredients active on scalp disorders, as well as for effective conditioning polymers used after shampooing. These special compounds, filming on the hair' surface, may increase its shining appearance, repairing both damaged cuticle and hair cortex, thus eliminating split ends. During application, in fact, this typology of cosmetic products interacts with the damaged component of the hair fiber by adhesive ionic interactions; soon after it infiltrates the subassemblies of the broken fiber, and forms cross-linking structures to bind these components together, sealing the hair scales.

Thus, for example hydrolyzed proteins or purified aminoacids provide a base for the development of reparative hair care formulation, as well as block and comb the copolymers used to improve the feel of hair, its hydrophobic effect and its combability, even at high environmental humidity.

It is to remember that a damaged and oxidized hair is always of hydrophilic nature, while virgin hair is hydrophobic, essentially of anionic nature with a low charge density. Moreover, the lipophilic nature of sebum and the ability of formulations to mix with these secretions has been suggested as the reason why lipophilic vehicles, solvents and formulas with additional surfactants (used as wetting agents), appear to be superior to hydrophilic formulations in targeting follicular delivery. Thus, when using a hair cleansing and/or conditioning product such as a shampoo, consumers expect their hair to be perfectly *cleansed, repaired* and *nourished*. But they also expect their hair to be *soft* and *shiny*, with a natural volume and a light feel.

Therefore, conditioning polymers are usually of cationic nature (positively charged) because of the

anionic nature (negatively charged) of the hair surface. These active ingredients, pre-eminently derived from chemical modification of polysaccharides (chitosan, chitin nanofibrils, cellulose derivatives, etc), can deposit on the hair surface thanks to a mechanism called *flocculation* or *coacervation* that occurs while the shampoo is applied on a wet head. Naturally surfactant base, pH, ionic strength of the formulation, as well as nature of the polymer backbone and its hydrophobicity, has a significant effect on the polymer ability to flocculate. Hydrophobic flocs deposit on the surface, but during the rinsing step these flocs are more easily washed out from the hydrophilic, amphoteric surface, than from the hydrophobic one.

Therefore, there is a direct correlation between the ability of conditioning polymers to form hydrophobic flocs during the shampoo process, and their effective deposition on the hair surface. Efficient conditioning polymers are, in fact, those that flocculate during hair shampooing, i.e., before dilution in rinsing. Polymer that does not flocculate is not effective. Moreover, it has been shown that hydrophobic flocs has to be about a few tens of microns in size, to be regarded as effective potential vehicles to deliver, for example, particulate antidandruff agents, such as zinc pyrithione. For all these reasons, the right formulation design is regarded as a fundamental step to efficiently restore the natural look of the hair, and maximize positive signals to consumers such as hair shine, smooth, feel, volume and manageability.

Coming back to the use of aminoacids in hair care, it is to underline two fundamental factors involved in their interaction with hair surface and structure: *diffusion* and *electrical charge* of these molecules. Given the small molecular size of aminoacids and their hydrophilicity, *diffusion* is considered to play a major role in their uptake, while the hydrophobic nature of human hair represent, apparently the barrier. The problem is totally different considering the damaged hair characterized by a lower hydrophobicity. Aminoacids which contribute to the maintenance of water balance in the skin' stratum corneum, results, in fact, highly beneficial also to prevent the decrease of hair tensile strength, as well as its surface hydrophobicity. These specific characteristics of the hair are modified by the oxidizing activity of the environmental aggressions, and by the colouring treatment both acting on the layer of fatty acids covalently linked to the hair surface. However, a better understanding of the chemistry involving the cosmetic ingredients used, as well as the interaction between aminoacids and the hair structure, will provide new knowledge for the development of innovative hair care formulations.

Further studies on block polymers are also necessary to understand the possibility to protect in a better way, hair fibers from cuticle damage and reduced tensile strength, caused by the use of UV filters. UV and the environmental aggressions affect, in fact, the hair cortex proteins, degrading contemporary its protective scales.

The promise of extending one's youthful appearance is driving the personal care industry today. Hair colour and style is an easy method to quickly change the appearance and the personal image in few hours. Thus women and increasing number of men find themselves hiding their gray, adding highlights or low-lights, and lightening or darkening a few shades, in an attempt to make a visual statement about themselves through their hair.

At this purpose, different polymers with a variety of functional groups and side chains are described and reported to offer diverse features and benefits to the formulator. Thus many data and interesting formulations are reported in the 2nd and 3rd Part of the book by further **22 Chapters**, describing also the concept of *beauty from within*, developed by the contemporary use of cosmetics and diet supplements.

In these chapters interesting considerations about a green lifestyle and innovation in hair styling technology, connected with racial differences also, are briefly discussed.
Total hair density, number of terminal follicles, and number of anagen hairs are, for example, lower in the African-Caucasians, as well as black hair appears to be inherently more dry. This dryness is related to the decreased ability of sebum to coat black hair adequately. For this reason, Africans use more frequently moisturizing and hair styling products to add shine, and assist their hair with a better combing and manageability.
In conclusion hair product has to be sufficiently effective not only to support the adopted claim, but also to be accepted from the final consumer. Therefore, formulators and brand marketers would need to partner more closely to insure that products deliver their claimed benefits in a statistically significant way using industry-recognized methods. Thus, formulators should expected brand managers to take new and heighted interest in test data and in the product development cycle, while marketers should expect the need to settle on a more supportable claims language earlier in the product development cycle. Operating in this way the credibility of claims will hold a clear advantage in the market place with the full satisfaction of the consumers.
These are the final considerations of this interesting book, reporting many data on hair biology, ingredients to be used for the hair product' formulations and the necessary testing indispensable to verify the product effectiveness. This publication written for Cosmetic Chemists could be useful also for Marketers and University Researchers of the Medical and Chemical communities, as well as for all the students in Cosmetic Dermatology, whishing to share their knowledge with the industrial problems involved in designing formulation and production of hair' cosmetics.

P. Morganti
Editor-in-Chief

Pathogenesis and Management of Atopic Dermatitis

By T. Shiohara

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Atopic Dermatitis (AD) is a multifactorial multigenic disease which appearing itchy, recurrent with eczematous eruption arising as a result of the interaction of may genes with environmental factors. It generally begins early in life, follows period of remissions and exacerbation, and usually resolves by the age of 30. The disease characteristics vary with age. Infants have facial and patchy or generalized body eczema. Adolescents and adults have eczema in flexural areas and on the hands.

Fifty percent of patients presenting with AD will develop asthma or hay fever together with eczematous manifestations while, seventy percent have also a family history of one or more of these characteristics. However, defective skin barrier at level of the filaggrin structure, as well as genetic interaction with an hostile environment and abnormal immune response are at the base of this pathological skin disease.

This book tries to address in 11 chapters, all the questions raised by the medical community on the pathogenesis, management and therapies of AD.

One of the most important functions of the skin is to provide protection from infections and pathogens. This is achieved by two complex and complementary powerful strategy (1) by preventing pathogen invasion, and (2) by raising innate and/or adoptive immune responses following infection. Thus, human skin represents a physical/anatomical barrier including the epidermis with the stratum corneum, composed of several layers of cornified keratinocytes embedded in a lipid matrix of water-retaining ceramides, cholesterol and sphingosines with direct antibacterial activities. Keratinocytes are able, in fact, not only to provide the skin physical barrier because of their hydrophobicity and resistance to the environmental aggressions, but participate in bacterial clearance by releasing antimicrobial peptides as well as signalling cytokines and chemokines. Additional barrier mechanisms include sweat and sebum production as well as body temperature and acidic pH. Finally, cutaneous infections are also controlled by a functioning skin innate immune system represented by neutrophils, dendritic cells, macrophages, mast cells and eosinophils. These rapidly mobilized cells can recognize structurally conserved motifs of bacteria, viruses, parasites and fungi by the so-called pattern recognition receptors. These receptors allow the culaneous innate immune system to rapidly detect potential danger and to raise protective responses, alerted also and helped by keratinocytes, peptides cytokines and chemokines responses. For all these reasons most pathogens cannot penetrate healthy skin.

Patients with AD exhibit both impaired skin barrier function and defects in skin innate immunity, frequently developing skin infections with a chronic inflammatory condition. They in fact exhibit several changes in skin barrier functions, being thus predisposed to cutaneous infections. At this purpose, AD patients present: (a) changes in skin pH values toward alkalinity, with a consequent increase of transepidermal water loss (TEWL), bacterial counts and microbial infections; (b) ceramides and sphingosines deficiency, with a reduction of antimicrobial activity and a further increasing of TEWL, contributing to dryness (pruritus, and extensive scratching and cracked skin: (c) loss of filaggrin function, with an impaired aggregation of the keratinocytes' keratin filaments, and a consequential improper formation of the physical barrier; (d) reduction of natural moisturizing factors and skin hydration for the mutations in the filaggrin gene.

Moreover according with the *Hygiene Hypothesis* reported on **chapter 1**, possible environmental and lifestyle-related factors seem to be associated with an increased AD risk. Epidemiological researchers have, in fact, focused as (a) AD is more common in urban then in rural communities; (b) immigrants in western industrialized countries have a higher risk to develop AD, than in developing nations, as well as (c) children growing up in a smaller family of higher socio-economic status. In addition, children with filaggrin mutations who were exposed to a cat during the first year of life had an up to 11 times higher risk of developing AD, compared to world-type children.

In anyway, there is a convincing evidence for an inverse relationship between, for example helminth infections and AD but no other pathogens. However, recent studies have suggested how probiotics given to both pregnant mothers and their infants post-natally, balancing their immune systems, can reduce AD risk by around 40%. Thus, developing preventive and complementary treatments and methods for high-risk children would certainly represent a significant therapeutic step, achieving symptoms control rather than cure AD.

As reported on **chapter 2**, in patients with a high risk of filaggrin abnormalities, early interventions by the use of topical moisturizers or a lipid replacement therapy seems to be another effective option in improving skin barrier function and decreasing antigen sensitization.

Moreover, according to what reported on **chapter 4**, increasing in AD skin the keratinocytes antimicrobial peptides expression by different options as well as repairing the skin barrier defects, could have certainly a further therapeutic effect. Keracinocytes, in fact, express, several pattern recognition receptors, such as Toll-like receptors, which recognize conserved microbial products like lipopolysaccharide, lipoteichoic acid, peptidoglycan, flagellin or nucleic acids.

As previously reported, these keratinized cells represent the major cell population in the epithelial skin barrier and actively participate in innate immune responses by recognizing pathogenic microorganisms, followed by a fine-tuned production of cytokines, chemokines, and antimicrobial peptides. In this respect, keratinocytes sense signals from the environment, initiating a differential immune response to harmless commensals and harmful pathogens.

If the permeability barrier and antimicrobial barrier dysfunction represents the primary event in the development of AD, the evaluation of the relative sweating responses is the place to look for changes that predispose to this disease.

AD patients seems, in fact, to exhibit a defective ability to deliver sweat to the skin surface in response to thermal stress. However, due to some observed marked augmentation in the sweating response with abundantly detected sweat, not only in the sweat glands and ducts, and lumen, but also in the dermal tissues adjacent, a compensatory mechanism of hyperidrosis has been supposed. Thus, chro-

nic inflammation in AD seems to be caused in part by a dysfunction of the sweat delivery system. This is the topic discussed on **chapter 6**. The cellular compartment of the cutaneous innate immune system, in addition to keratinocyte, consists of many rapidly mobilized cells, such as neutrophils, dendridic cells, macrophages, mast cells and eosinophils. These receptors allow the cutaneous innate immune system to rapidly detect potential danger and to raise protective responses. Thus, regulatory T-cells play a pivotal role in immune suppression and are integral to the control of allergic responses and chronic inflammatory skin condition is severest in patients who, affected by this disease, are sensitized to allergens from diverse sources including foods, pollens and animal danders, as well as skin-colonizing organisms.

Allergic diseases are, therefore, driven by the development of Th2 cells which mastermind antibody isotype switching to IgE production and an inflammatory cascade, involving recruitment and activation of diverse cell types including mast cells, basophils, dendritic cells, and fibroblasts. However, while there is no doubt that T cells infiltrate the inflamed skin of patients with AD, there is a considerable debate surrounding the nature of these cells. Identification of new surface markers could facilitate improved methods of detection and isolation of T cells for functional studies.

In anyway the variations, in the functional level and/or impact of all the different immune cells between individuals, may explain differences in the ability of each individual to control viral or microbe infections. Moreover, immune homeostasis in the skin immune system may rely on a delicate balance between the ability to react or not to react with other harmless microbes. If so, the imbalance may result in loss of viral clearance and overwhelming Th2 responses to environmental allergens in AD.

In conclusion, AD is a multifactorial genetic disease arising as a result of the complicated interaction of many genes with environmental factors, all well reported and discussed in this book, by authored and well known scientists.

The systemic review of all the different hypothesis at the origin of this skin diseases, affecting approximately 15-30% of children and 2-10% of adults in industrialized countries, will be of great help for all people involved in Cosmetic Dermatology, such as Dermatologists, Plastic Surgeons, Paediatricians, Practicing Physicians, as Cosmetic Chemists, Basic Immunologists, Biologists and Pharmacologists, and students in Medicine and in Cosmetic Science, willing to know more on the pathogenesis, management and therapies of AD.

P. Morganti
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Topical Applications and the Mucosa

by C. Surber, P. Elsner and M.A. Farange

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The mucosa is a non-keratinised epithelium covering the surface of buccal-gastro-intestinal, respiratory, urinary, anal and genital tracks, as well as the nose and the eye.
The topic of this book organised in **IV Sections and 16 Chapters,** regards the buccal, nasal, anal and genital mucosa only.
Mucosal tissue is generally more permeable and more susceptible to topical irritations than the well-keratinised skin, elsewhere, on the body. The absence of a keratinised surface, as the skin's *stratum corneum*, removes a principal barrier to entry by external agents, as well as the presence of a well structured lipid barrier facilitates the molecular diffusion throughout the mucosal membranes. In addition, thin, larger and more loosely packed cell layers, create a structure with less resistance to para-cellular movement, the principal mechanism whereby most penetrants traverse tissues. Moreover, penetration of different ingredients thoroughly mucosal membrane can be facilitated by irritant materials. Finally its non-keratinised structure may also be more vulnerable to breaches in tissue integrity, which can further augment tissue penetration.
For all this reasons the difference in the structure and physiology of mucous membranes, compared to the skin may make the mucosa more susceptible to the effects of topical agents.
Section I, by Chapters 1 and 2, is dedicated to morphology and physiology of the mucosa.
Anal and vulvar mucosa, differently from the skin, are forms of a specialised tissue with unique morphological and functional properties; thus, anal canal mucosa does not contain skin appendages. The female external genital organs have size and shape, and distribution of hair showing considerable variance depending on their hormonal state, pelvic architecture, race and age. Age-dependent changes are significant ever though the mucous membranes are not subject to photoageing. However, vulvar dermis shows elastotic degeneration similar to actinic damage in elderly woman, and its surface pH is more than 1 pH unit higher than forearm pH. The higher skin surface is, therefore, an important cause for the high density of microbial colonization. Moreover, due to its lower Trans Epidermal Water Loss (TEWL), the barrier function of vulvar skin seems to be imperfect, compared to other body sites as the forearm.
Hence, the vulva tends to be more permeable than other sites and to have specific proclivity to irritant activity. Regarding unwanted effects of topical applied to vulvar skin, both the spectrum of irritants and allergens, and clinical presentation of contact urticaria, as well as irritant and allergic contact dermatitis may be different from other sites of human body.
In addition, with the high relatively stable density of bacteria on vulvar skin, the microbial genera-

tion of fishy odours is a physiological, though cosmetically important feature of this area. It is to underline how the morphology and physiology of the vulva and vagina change over lifetime. The most salient changes, especially influenced by hormones, are linked to puberty, menstrual cycle, pregnancy, and menopause.

At birth, in fact, the vulva and vagina exhibit the effects of residual maternal estrogens. During puberty they mature under the influence of adrenal and gonadal steroid hormones, while during the reproductive years the vagina responds to ovarian steroid hormone cycling. Following menopause, both vulva and vagina athrophy.

At this purpose, a proper hygiene and the correct use of effective products are needed to obtain the best results, avoiding dermatitis and skin deterioration.

On **Section II** dedicated to *Topical Treatment of Impaired Membranes*, different topical treatments are focused and discussed.

The nose is a complex multifunctional organ characterized by the function of cleansing the inhaled air, and enabling the olfactory perception. The nasal mucosa with its hairs and sticky mucus has, in fact, the capacity to filter, heat and humidify the inhaled air, before it reaches the lower parts of airways. In this way filtering more than 500 liters of air hourly, it prevents xenobiotics, like allergens, pathogens or foreign particles from reaching the lungs.

Moreover, the olfactory region with its direct nervous interface to the brain, by thousands of specialized receptors, seems to be important for the skin delivery of cosmetic ingredients by the so called NICE approach (nervous, immune, cutaneous and endocrine systems).

In anyway, the intranasal administration represents a viable option for local and systemic delivery of many therapeutic agents. This practical entrance portal for systemically acting molecules, provides in fact, a true alternative to oral or parenteral routes of administration, avoiding the gastrointestinal degradation of drugs, being also non invasive, painless and easily administered.

Naturally, the specific delivery target of the drugs as well as the intended dosing schedule, is depending on the designed formulation, i.e. the *vehicle form*, the *active ingredients*, and the selected *application device*, which determines the drug deposition within the nose and its efficacy. It is obvious that drug stability represents a basic prerequisite for a marketing product.

Thus, the skilfully chosen vehicle/ingredients are able to temporary modulate the mucociliary clearance, increase drug absorption, as well as the muco-adhesive polymers may increase the drug efficacy, prolonging its contact with the mucosa. Moreover, it is possible to significantly improve the absorption of molecules if they are applied in combination with absorption-enhancing ingredients. Polysaccharide biopolymers, as chitin nanofibrils and chitosan, are, for example, an interesting class of ingredients useful for this purpose, because of their mucoadhesive capacities and their properties to open transiently the tight junction of the nose ciliated cells, increasing paracellular transport of polar drugs.

In order to meet the dual needs of procreation, as well as microbial defence, the immune mechanisms in vaginal mucosa are unique. At this purpose, estrogen plays a significant immune role in women by inducing a mature epithelial barrier and by promoting cytokine production. This hormone, promoting glycogen deposition in the vaginal epithelium, and supporting the innate immune system, defends mucosa against candida infection.

Thus, conditions that compromise cell-mediated immunity, such as smoking, leukemia, severe illness etc, must be considered as predisposing factors for recurrent oral candidiasis. Identification and

elimination of these risk factors for mucosal infection are necessary in order to achieve control of these recurrent diseases. At this purpose vaginally applied antimicrobial and antiyeast agents are widely used together with a therapy, capable to increase the activity of the mucosal immune factors. Many bacterial vaginosis, desquamative inflammatory vaginitis, as well as infections with *Staphylococcus aureus* or *Candida vulvovaginitis* may be treated in this way.

The most often encountered protozoal vaginitis, which is caused by *trichomonas vaginalis*, may be susceptible to topical medications also, although this infection is treated systemically.

On the other hand inflammatory mucosal disorders are treated conventionally with potent or super-potent topical corticosteroids.

Recently, the medical armamentarium has been expanded by the use of topically applied calcineurin inhibitors, having their best indication in the treatment of different immunologically mediated disorders. Finally topical antineoplastic agents constitute another important tool in the armamentarium of dermatologists for the management of diseases affecting the mucous membranes and surrounding skin.

However, further studies are needed to fully elucidate their applications in the treatment of mucocutaneous diseases.

All these topics are amply focused on the five chapters of the section II, reporting and discussing the efficacy and the effects of the many drugs used today in therapy.

A special part has been dedicated by **Section III** to consumers products used today in the area of mucosal membranes. The opening chapter focuses on the evolution in the treatment of baby skin: *Diaper area and disposable diapers*.

Disposable baby diapers are absorbent products designed to absorb and contain urine and faeces and lock the wetness away from the baby's skin. Compared with the first generation diapers made of cellulose which comes into direct contact with the baby's skin and support plastic wrapping to prevent leaks, disposable diapers have now become *breathable*. The today's super-adsorbent diapers offer clear benefits of less skin wetness, decreased diaper dermatitis commonly referred to a diaper rash, less transmission of faecal contamination and improved hygiene versus cloth diapers.

Maintenance of healthy skin and hygiene has been the key focus behind these innovations. The risk factors identified for the occurrence of this baby-dermatitis are (1) a combination of skin wetness, (2) urine and (3) faecal protease, from which the increase in enzyme activity is a result of increased pH levels in the skin, caused by the conversion of urea to ammonia.

The effect of *skin wetness* and *friction* in combination with increased *chemical irritation* due to excessively high pH levels and contact of faecal waste with the skin, are the aetiological factors at the origin of diaper dermatitis.

Absorbing and catching urine, distributing within the absorbent core made of special polymers, is one of the latest innovation. Once absorbed by the superabsorbent polymer, the urine is unable to re-exit the gel formed, even under the pressure generated by the infant. For this new technology, the number of reported cases of severe dermatitis has fallen from 67 to 9% during the last decade.

The next two chapters are dedicated to the wide variety of products used by women in the genital area, such as cleansing agents, emollients, lubricants, moisturizers or products used for menstrual protection. These products, coming all into contact with genital mucosa, have real or perceived benefits for the women who use them, but may have adverse health effects also.

However, when produced by a reputable manufacturer with careful safety testing programs, most of

these products have minimal or no adverse health effects.
Many are the products reported and the most used worldwide are focused on these chapters, where them use and abuse, benefits and side effects, are amply discussed.
In conclusion, several chemical studies have confirmed the safety and efficacy of these products controlled by clinical studies, when topically applied.
Last chapter of section III on *consumer products* is completely dedicated to dental and oral hygiene for elderly people as well as for young children. Poor dental hygiene can result, in fact, in tooth decay, gingivitis, periodontitis, tooth loss, fungal infection and grim diseases causing often alitosis also. Tooth-cleansing, reducing the micro-organisms activities, helps prevent the formation of plaque at the origin of these disfunctions, avoiding bad breath also. Correct dental and oral hygiene is, therefore, a challenge for all users, who should be instructed by health care professionals for the better device to be used for this purpose.
As bacteria, fungi, plaque and tartar can become deposited on dentures, these must be taken out after every meal and cleaned of food remnants by the use of toothbrushes with soft bristles, operated manually or via an electrical device. Antiseptic mouth washes can additionally be used, as well as the surface of the tongue should be daily cleaned with a specific scraper, all supported by the additional use of interdental cleaning, such as dental floss and fluoridation with fluoride gel.
Finally, for patients undergoing or having undergone radio/chemo-therapy, a mouth wash that concomitantly moisturizers the oral mucosa is advisable.
On **Session IV** the safety of products used for mucosae is reviewed by 5 chapters assessing their irritation and sensitization potential. At this purpose the stepwise approach, employed from manufacturers to ensure the skin safety and compatibility of these consumer products, are focused and described. Likely, exposures are calculated using the manufacturer's unique knowledge of the intended product matrix consumer usage patterns and measurements of particular exposure variable. Moreover, the irritation potential of each ingredient and the finished product are evaluated by clinical testing protocols, involving single and multiple patch tests, and extended use testing, with visual and/or instrumental assessments.
As an example, the knee clinical (BTK) test system, generally employed today from manufacturers, has been focused and amply discussed. The BTK clinical test has been developed as a test model to evaluate a combination of chemical and mechanical irritation of products intended to come into repeated or prolonged contact with the skin and mucous membranes, such as feminine protection pads. It is intended for use as a comparative toxicity test, i.e. a side-by-side comparison with a product of known safety profile, being less intrusive than other known tests and less impacted by the confounding factors that accompany the normal in-use clinical tests, especially regarding the mucous membranes. The mucous membranes are, in fact, generally considered, to be more susceptible to irritant than exposed skin. Therefore, commercial products intended for use in this area must be demonstrated to have minimal inflammatory responses.
At this purpose, the mucousa of the women genital tract represents a complex biological system highly difficult to control by the normal in-use tests.
Thus the BTK clinical test conducted at level of the legs' popliteal fossa, has revealed to meet all the theorical and/or anatomically protected site testing, such as mucous membranes.
Many others studies are reported in these last chapters regarding, for example, the control on the perceived sensitivity of the skin genital area, or the higher risk to develop sensitization to topically

applied products and drugs on patients affected by anal dermatoses.
This book, dedicated to all the problems regarding the human anatomical and physiological properties of mucous membranes, but primarily to the today cosmetic treatments, may be of great help for all the scientists involved in the study of all the pathological and physiological conditions of this delicate area, such as Dermatologists, Gynaecologists and Paediatricians, but also Cosmetic Chemists and Marketing people involved to design these useful products.

P. Morganti
Editor-in-Chief

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FOR IMMEDIATE RELEASE

CATALENT ANNOUNCES EXPANSION OF ITS ADVANCED DOSE FORM FACILITY IN ITALY

Somerset, NJ – September 12, 2011 — Catalent Pharma Solutions' Consumer Health business, a market leading supplier of advanced delivery solutions including vitamins, minerals and supplements, announces the completion of the first phase of a multi-million dollar expansion of its facility in Aprilia, Italy.

Catalent is a specialist in overcoming solubility, stability and bioavailability issues for a wide-range of liquid and semi-solid formulations. Innovative products manufactured at the Aprilia site include Vegicaps® capsules, easy-to-swallow plant-derived capsules that are free from animal derivatives and gluten. "We needed to expand capacity for both traditional gelatin and Vegicaps capsules to ensure reliable supply of strong customer demand" said Gerry Purnell, European Commercial Director for Catalent's Consumer Health business. "Customers are increasingly considering Vegicaps capsules because the technology accommodates a wide range of formulations and provides access to markets that require products free from animal derived gelatin."

Over the last 12 months, Catalent's Aprilia site has been expanded to include a new dedicated gelatin production area. New encapsulation machinery has been added for the production of traditional gelatin and Vegicaps capsules, increasing output by almost one third. Catalent has also added key processing equipment, such as a new turbo emulsifier to replace open roll-milling equipment. Capacity within inspection and drying areas has been increased and workflows and environments have been reviewed and enhanced to maintain high standards of safety and current Good Manufacturing Practice (cGMP).

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Capello danneggiato da alcali.
Foto al microscopio elettronico a scansione (SEM). Archivio privato MAVI SUD S.r.l.
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Hair damaged by alkaline solution.
Scanning Electron Microscopy (SEM) micrographs. MAVI SUD S.r.l. Private Database.
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