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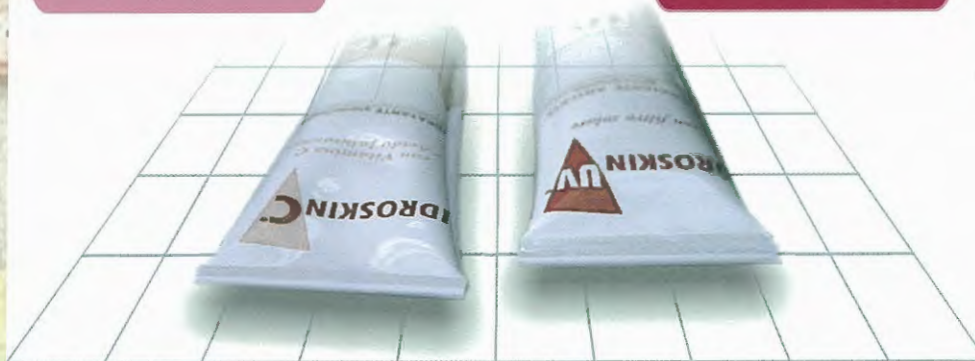
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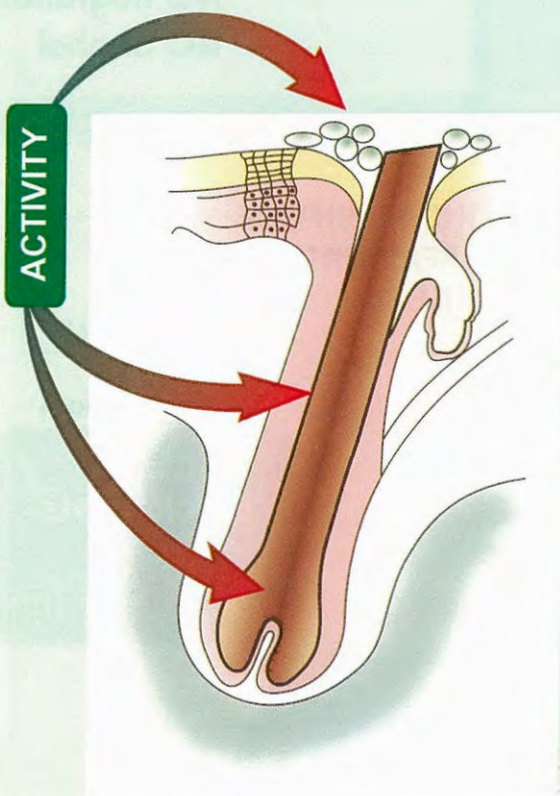
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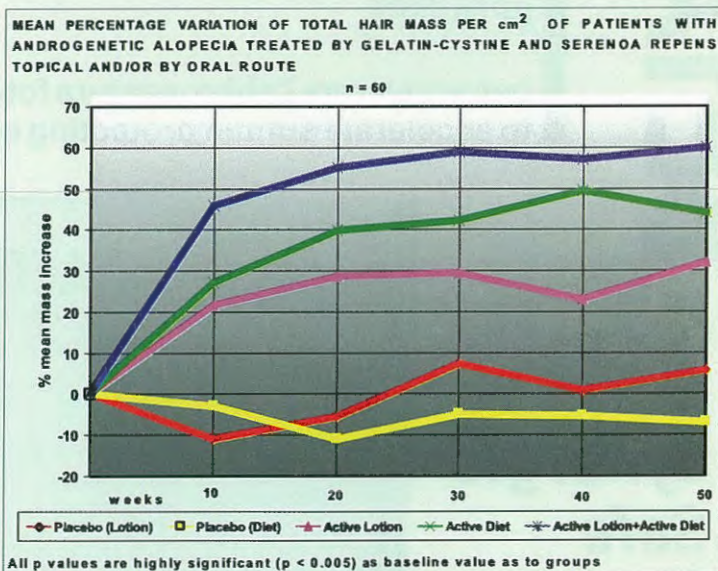


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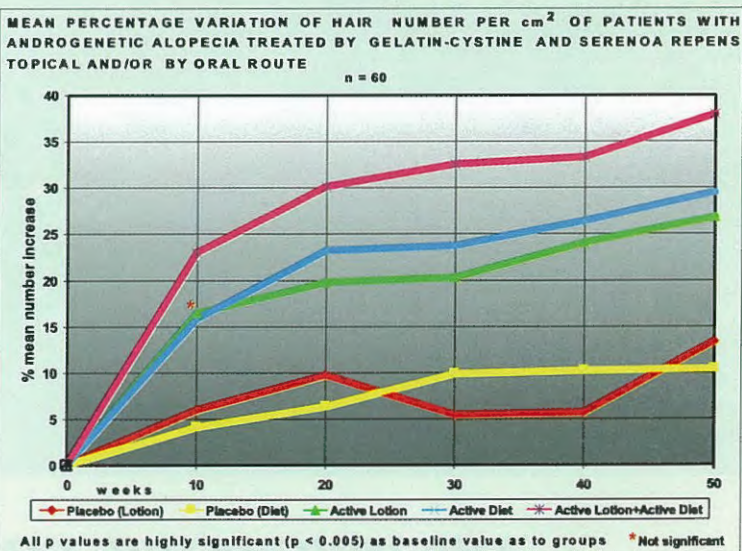
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COFFEE AND HEALTH

Publio Viola

Doctorate in Social Medicine, University "La Sapienza", Roma - Italy

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Key words: Coffee; Composition; Caffeine; Health;

Summary

Coffee has become an essential accompaniment to daily life, so much so that the aromatic cup has become a pleasant ritual that helps equilibrate and tones the nervous system.

Coffee is an aqueous solution containing numerous substances that are present in varying degree according to the type of plant (Arabica, Robusta), the toasting process, and method of preparation used to make the coffee.

Besides the aromatic composts present, coffee contains trigonelline (which during toasting is transformed into nicotinic acid or vitamin PP), chlorogenic acid, caffeic acid, potassium, essential oil of coffee and of course caffeine, a trimethyl xanthine which attracts most of the attention of coffee advocates and detractors.

Caffeine produces its main effects on the nervous, cardiovascular, respiratory and renal systems through its inhibitory activity on adenosine receptors, thus enhancing attention and learning capacities, besides increasing coronary perfusion and diuresis. As for the negative effects, they can appear only after a high intake of coffee, usually more than 650 mg. a day. All studies indicate in fact that these effects aren't produced with moderate intakes. In particular no risks have been seen for atherosclerosis, cardiovascular disease, hypertension, pregnancy, and neoplastic disease (in fact, in this last case coffee is considered a protective agent against colon cancer).

It must be however pointed out that the quantity of caffeine present in "espresso coffee" is not high (40-70 mg.), quite inferior to that in a homemade cup of coffee usually drunk by Italians (80-100 mg.) and to the standard cup consumed by Americans (100-150 mg.). this is due both to the toasting process used and to the time of contact between coffee and water extraction preparation.

Of utmost importance is the presence of two phenol composts, chlorogenic acid and caffeic acid that perform an antioxidant action against free radicals preventing those negative effects of aging and chronic-degenerative diseases. In particular chlorogenic acid has been singled out as the anti-neoplastic factor in coffee.

In conclusion, even if there are some contraindications for some patients with neuropsychological disorders, we can state that coffee taken in quantities of 4-5 cups a day, in particular that processed in the Italia toasting method, can produce only positive effects. These being in the morning a better passage from the sleep to the walking state, and during the day, an increased ability to overcome

tiredness with an improved work performance, besides offering a pleasant moment of relaxation between friends and relatives.

Riassunto

Il caffè è divenuto un complemento essenziale della vita quotidiana, tanto che la sua tazzina profumata costituisce oggi un gradevole rituale che consente di esercitare un effetto tonico riequilibrante sul sistema nervoso.

Il caffè è una soluzione acquosa contenente numerose sostanze che possono però essere presenti in quantità variabile a seconda della pianta (Arabica, Robusta), del sistema di torrefazione, e del sistema di preparazione della bevanda. Tra le sostanze presenti ricordiamo, oltre ai composti aromatici, la trigonellina (che durante la torrefazione si trasforma in acido nicotinico, o vitamina PP), l'acido clorogenico, l'acido caffeico, il potassio, l'olio essenziale del caffè e soprattutto la caffeina, una trimetil-xantina sulla quale si appuntano le maggiori attenzioni dei sostenitori e dei detrattori del caffè. La caffeina svolge i suoi effetti principalmente sugli apparati nervoso, cardiovascolare, respiratorio e renale attraverso una attività inibente sui ricettori dell'adenosina favorendo in questo modo le capacità di attenzione e di apprendimento, oltre a migliorare il flusso coronarico e la diuresi. Quanto agli effetti negativi, per ottenerli è necessario assumerne quantità elevate, oltre i 650 mg pro die. Tutti gli studi indicano infatti che tali effetti non si verificano a quantità moderate. In particolare nessun rischio è stato rilevato per l'aterosclerosi, le cardiovasculopatie, l'ipertensione, la gravidanza e le neoplasie (ed anzi, a questo proposito, viene segnalata un'attività protettiva nei confronti dei tumori al colon).

Deve essere comunque rilevato che la quantità di caffeina presente in un "caffè espresso" non è elevata (40-70 mg.), essendo inferiore a quella di una tazzina casalinga consumata abitualmente dagli italiani (80-100 mg.) ed a quella di una tazzina standard consumata dagli americani (100-150 mg.). ciò dipende sia dal sistema di torrefazione che dal tempo di contatto con l'acqua che ne favorisce l'estrazione.

Di notevole importanza è inoltre la presenza di due composti fenolici, gli acidi clorogenico e caffeico, che svolgono azione antiossidante contro i radicali liberi prevenendone gli effetti deleteri nei confronti dell'invecchiamento e delle malattie cronico-degenerative. In particolare all'acido clorogenico sono state attribuite le attività antineoplastiche del caffè.

In conclusione, anche se possono esistere delle controindicazioni per alcuni pazienti con disturbi neuropsicologici, possiamo affermare che il caffè assunto nella quantità di 4-5 tazzine al giorno, in particolare quello realizzato con il sistema di torrefazione italiano, determina solo effetti positivi, tali da consentire al matti no un migliore passaggio dallo stato di sonnolenza alla fase di veglia e, durante il giorno, un recupero della stanchezza con miglior rendimento lavorativo, oltre a costituire un momento di piacevole rilassamento tra parenti ed amici.

INTRODUCTION

Coffee, which man has instinctively used as a physical and psychic tone, has always been the subject of contrasting judgements, praised for the benefits it gives and criticized as a health hazard.

Classified as a "nervous food", in the last decades it has been studied in a more scientific and systematic manner and many uncertainties stemming from an incorrect approach to its study have been re-examined more thoroughly.

This has led to a clearer idea of how coffee brings about its effects, often misunderstood in the past. This was due to not taking into consideration the different botanical varieties, the different ways of brewing, the often excessive consumption and other dietetic factors associated with coffee drinking as overall uncorrected diet and alcohol consumption and smoking.

Its consumption today is central to a modern life style as an essential addition to the normal diet, and none seems to do without that little aromatic cup. Coffee drinking has also become a ritual not only as an enjoyable pick-me-up at particular moments of the day, but can also accompany moments of leisure and cordial encounters with relatives, associated and friends.

Its great success is not due to its organoleptic properties, but to its both stimulating and reassuring effects.

In fact it is instinctively sought out as a general tonic both for mental and physical needs of the individual.

CONSUMPTION OF COFFEE

Coffee is a watery solution containing numerous substances that however can exist in different concentration according to the particular variety of plant (Arabica, Robusta), the soil where the coffee is grown, the type of roasting process,

and how the beverage is prepared.

Besides the high number of aromatic components, the principal substances present in are trigonelline (which during the roasting process is transformed into nicotinic acid, or vitamin PP), chlorogenic acid, caffeic acid, essential oils and of course caffeine, a trimethylxanthine which attracts the most attention both from coffee's supporters and from its detractors.

The possible different content of the drink can explain the different evaluation by consumers, as well as the differences in effects the beverage can have on the body.

It is to be noted that the caffeine contained in the typical "espresso" consumed by Italians is inferior (40-70 mg) to that contained in a home made cup (80-100 mg) and much less than a standard American cup of coffee (100-150 mg). This is due to the fact that the extraction of caffeine is proportional to the duration of contact with water.

The peculiarity of Italian coffee comes from its highly intense roasting process, in contrast to the lighter used in other countries.

The espresso coffee machine, which was commercialized for the first time in 1901, puts the water under pressure (8-12 bar) with a temperature of 92°-94° C. The efficiency of the caffeine extraction is 80%.

The "moka" coffee, widely used in Italian household, uses forced filtration of vaporized water and produces caffeine extraction of 92-98%. Therefore the caffeine content of homemade coffee is greater than that of caf  s, but the espresso system allows the harnessing of a greater quantity of aromas making it seem stronger. Another particularity in Italy is the various types of mixtures of coffee used. These mixtures are composed of the botanical varieties Arabica and Robusta which have different caffeine content (about double in Robusta respect to Arabica). After, however, to obtain more aromatic varie-

ties, as many 10 different coffee types from various places are used and their concentration are kept secret by their producers.

COMPOSITION OF RAW COFFEE (% dry matter)

Components	Arabica	Robusta
Caffeine	1.2	2.2
Minerals (oxides)	4.2	4.4
of which potassium	1.7	1.8
Trigonelline	1.0	0.7
Lipids	16.0	10.0
Chlorogenic acids	6.5	10.0
Aliphatic acids	1.4	1.4
Carbohydrates	58.0	59.5
Aminoacids	2.0	2.0
Proteins	9.0	11.8

Roasting notably modifies coffee's composition, almost totally destroying the sugars, producing melanoidines and volatile substances which give coffee its aroma. The chlorogenic acids are partly decomposed while trigonelline is not perceptibly diminished but is transformed mainly into nicotinic acid (vitamin PP).

There is no substantial change in mineral and caffeine content.

On the whole, roasting the coffee bean modifies its composition with the formation of volatile substances that made the beverage particularly pleasing, while maintaining its caffeine content. Lastly, it is to be noted that the "filtration" of coffee used in Italian and American preparations remove the fat content to advantage, as we shall see, its cardiovascular effects.

The great success of coffee, which made it the most commercialized product in the world after petroleum, is due essentially to its stimulating and antidepressive effects which increase psychomotor efficiency.

COMPOSITION OF MEDIUM ROASTED COFFEE BEANS

Components	Arabica	Robusta
Caffeine	1.3	2.2
Minerals (oxides)	4.5	4.7
of which potassium	1.8	1.9
Trigonelline, niacin	1.0	0.9
Lipids	17.0	11.0
Chlorogenic acids	2.7	3.1
Proteins, aminoacids	10.0	10.0
Aliphatic acids	2.4	2.4
Volatile substances (aroma)	0.1	0.1
Melanoidines	23.0	23.0

These favourable effects are determined by the totality of substances present in the coffee, but mainly by caffeine. In fact caffeine is the subject of the major part of researches done on the relationship between coffee and health.

Research done in this direction is vast and has examined the effects not only the central nervous system, but also the cardiovascular system, digestive system, renal function, respiratory system, without neglecting effects to gestation and tumours.

CAFFEINE' MECHANISM OF ACTION

Caffeine brings about its pharmacological effects through an inhibitory mechanism on adenosine receptors. This mechanism determines, in normal doses, essentially positive effects on coronary flow, diuresis and antispastic activity, but mostly on cerebral cortex stimulation incrementing attention and learning.

The inhibitory action on phosphodiesterase with increase on cyclic AMP, once believed to be the fundamental mechanism, is no longer considered valid, except at very high doses.

The same holds true for the mobilisation of calcium which plays only a secondary role.

As to its effects on the adenosine receptors, it is necessary to point out that those receptors are present in all tissues since adenosine acts as a modulator of physiologic functions in the body in particular intervening in a series of responses mostly depressive, and those affecting the central nervous system, arterial pressure, intestinal peristalsis, respiratory function and the immune system. Caffeine, binding antagonistically to the same receptors, exercises the opposite effects that adenosine does.

Caffeine is metabolized by the body in the liver's microsomal enzymatic system and does not accumulate in the body.

On the whole, as we shall see, caffeine seems to act in a positive sense, since the negative effects are caused only at very elevated doses.

The toxicity dose is indicated around 10 mg/kg, corresponding to 7 cups of homemade coffee for males and 5-6 cups for females (calculating 100 mg of caffeine per cup).

These quantities are discouraged usually suggesting a maximum of 4-5 cups a day (referring to homemade coffee). At these doses (400-500 mg) all the studies show the absence of negative effects.

NERVOUS SYSTEM

Biologically coffee acts as a stimulant. This effect is due essentially to caffeine through its competitive action on adenosine receptors.

This adenosine's action, as already stated, is primarily inhibitory at the cerebral level since it determines a slowing down of the liberation of certain chemical mediators of neurotransmission.

Caffeine, modulating the action of these neurotransmitters, seems to it that cerebral activity is stimulated leading to a better learning ability, increased ideation and memorization. It allows

not only for a better capability of sensorial perception, but also an increase in cerebral acuity increasing the ability to interpret impressions and to respond more rapidly with appropriate behaviour.

Another favourable neuropsychic effect of coffee is the increase of good temper with improvement of depression. Its use seems to be particularly indicated in those phases of tiredness and boredom that accompany monotonous and repetitive jobs, without any increase in errors performed. Everyone of us has observed how coffee, especially in moments of tiredness, improves thought processes, with improved concept impression and facilitates problem solving.

These favourable effects explain why coffee is instinctively consumed at certain hours of the day. Morning, where it favours the passage from sleep to the awake state, mid-morning, when cerebral activity undergoes a slowing phase, and afternoon, when digestion creates a new slowing down of cerebral activity, bringing about mental well being and renewal of work output.

Bettering depressive status and increasing initiative and psychomotor activity, coffee reduces sleepiness, and can sometimes cause a delay in the start of physiologic sleep, leading to insomnia. This problem is seen only in subjects not used to drinking coffee or in the case of strong doses, especially taken at night. Therefore a certain caution must be used in these instances, and also when dealing with the elderly since they seem more sensitive to caffeine's effects even at low doses. Contrary to what is commonly believed children are not more sensitive than adults to caffeine's effects, even if the consumption of coffee in infancy is generally discouraged.

In anxious subjects coffee can increase the problems so it is wise to reduce or even suspend its use altogether.

It is to be noted, however, that if its suspension is certainly recommended in grave psychosomatic disorders (but even in normal subjects high

doses should be avoided) in situations of moderate anxiety it could have a complementary effect with anxiolytic drugs used as tranquilizers or to bring on physiologic sleep.

In these situations a controlled quantity of coffee can be of use to counterbalance the anxiolytic drug's secondary effects as asthenia due to muscle relaxation properties and the depression which often accompanies anxiety and which is often not resolved by tranquilizers.

CAFFEINISM SYNDROME

This syndrome is repeatedly seen as a part of caffeine dependency, since the body seems to be able to reach to the adenosine receptors block by increasing their number calling for an increased amount of coffee to obtain the same effects as before and also because the suspension of coffee by heavy consumers can cause the so called withdrawal syndrome, consisting of migraine, irritability, reduced concentration and sleepiness.

More than a question of dependency however it would be better regarded as tolerance since these adverse symptoms disappear within a few days and however do not cause a state of anxiety that necessitates therapy or restrictive measures.

CARDIOVASCULAR SYSTEM

Cholesterol

There has been many studies done all over the world to show a possible correlation between coffee and plasma cholesterol levels and therefore between coffee and atherosclerosis.

An overall look at the studies done shows, as already mentioned, that the correlation, when it does exist, is strictly connected to the way the beverage is prepared, when the studies used boiled coffee as is the custom in Scandinavian Countries. In fact no correlation is seen to exist when the same experiment are conducted with

filtered coffee (as Italian espresso or moka or American coffee).

These studies show that cholesterol level increases are associated with certain methods of coffee preparation and not caffeine content, but rather the content of non saponified fractions of lipids. One double-blind study in fact showed no difference in total cholesterol and HDL-cholesterol with the use of normal filtered coffee and with decaffeinated. It has been shown by subsequent research that the use of coffee reduces cholesterol levels experimentally induced in rats. No correlation could be demonstrated between cholesterol and instant coffee.

Myocardium

At normal doses coffee's effects on the heart are slight and only visible on non habitual coffee drinkers. There have been studies done on the effects of coffee and caffeine on the possible connection with myocardial infarction, heart failure and arrhythmias, in particular ventricular arrhythmias and tachycardia.

In regards to arrhythmias, a study conducted with 300 mg of caffeine versus placebo with 24 hours Holter monitoring showed no association between this alkaloid and the appearance of ventricular arrhythmia. In the same way all the epidemiological and experimental studies showed no significant relation between coffee and the pathogenesis of coronary diseases and heart failure.

The same lack of significant relation was shown for vascular diseases, both peripheral and cerebral vascular disease. However, it should be pointed out that often epidemiological studies, especially with heavy coffee drinkers, seem to be falsified by the fact that frequently these subjects tend to be smokers as well as coffee drinkers.

Arterial Hypertension

All the studies don't confirm that though an

acute intake of caffeine can alter some hemodynamic variable, the chronic intake has no effect on renin activity nor on plasma catecholamine levels.

In normotensive subjects with moderate coffee intake there is no increase in blood pressure or only an increase of negligible proportion (4-5 mm of mercury in systolic as well as diastolic). In non habitual coffee drinkers the increase is greater, but still irrelevant and above all of short duration. However, the recommendation to limit coffee intake in serious form of hypertension is still valid.

To complete our discussion on the cardiovascular effects it is of remarkable importance to mention the two phenolic compounds contained in coffee: chlorogenic acid and caffeic acid.

They exert an antioxidant action that protects against the free radical damage held responsible for ageing and many chronic – degenerative diseases, among which the atheromatose degeneration of arterial wall.

On the whole, all studies examining the effects of coffee, and caffeine in particular, on cardiovascular risk have not shown there is any significant difference between increase of these diseases in coffee and non-coffee drinkers, not even when non-coffee drinkers are compared with heavy coffee drinkers.

Nevertheless all these reassuring studies it seems wise to recommend a certain restriction of coffee intake in highly nervous subject, with frequent extrasystolia, and especially in subjects with acute myocardial infarction, cardiovascular failure, heavy rhythm disorder, serious hypertension.

Digestive System

For long it was believed that caffeine exerted a stimulating action on gastric secretion causing an increase in burning and acid sensation in subjects with gastritis, but presently it is held that is not due to an increase of acidity, but to gastro –

esophageal reflux.

This not being tied to the presence of caffeine, since it takes place even with decaffeinated coffee.

There are also noted an effect of stimulation on intestinal peristalsis which in some cases can cause diarrhoea, but this has not been confirmed by controlled studies and seems to be attributable more to neurovegetative problems, as in the case of “irritable bowel disease”.

A positive effect is often seen in constipated subjects than often resolve after taking their morning coffee.

On the whole therefore coffee appears to be well tolerated by the digestive system, still, even if studies haven't shown a clearly negative effect of coffee, those who suffer from gastritis or peptic ulcer, it be advisable not to drink coffee at least in the acute stage.

Respiratory System

Methylxanthines are habitually used to treat bronchial asthma through their relaxing effects on bronchial musculature. This effect is more evident with theophylline than with caffeine.

These substances also exert at the central level, in fact they are used in neonatal apnoea and in this situation caffeine has a greater effect and is less toxic than theophylline.

Pregnancy

All studies done in this field have not showing relationship between coffee consumption, fetal malformation, abortion or premature births.

Neoplasms

In the past coffee was considered by some to be a risk factor for neoplastic insurgency, in particular in the pancreas and bladder.

Presently, through to numerous clinic and experimental studies conducted worldwide, this risk seems to be excluded.

The studies examined not only the effects of cof-

fee on totum and caffeine alone, but also the possible reinforced effects coffee and caffeine could have on carcinogenetic substances.

These studies showed not only the absence of negative effects, but in some cases it was seen that caffeine had an inhibitory effect on tumour genesis induced by carcinogen and in the case of colon and rectal tumours studies have shown that coffee in totum exert a protective action.

Among the hypothesis tending to explain this positive effect it has been attributed to a reduction of bile acid activity in the intestine, but also to a positive effect from the antioxidant action of chlorogenic acid.

CONCLUSIONS

The majority of research conducted over the world seems to exclude the existence of substantial risk connected to a regular coffee consumption. In fact they seem to reveal that coffee exerts an essential positive effect on our body.

This conclusion brings to mind a rue story that took place in Sweden following a death sentence given two brothers by king Gustave III.

It was decided that the instrument of the death would be the intake of high doses of coffee under the supervision of the medical commission.

Years passed and while some of the doctors of the commission died, as well as king Gustave, but the two brothers survived, one to the age of 83 and the other till 85. It is difficult to know if this outcome can be attributed to the antioxidant action of chlorogenic acid and caffeic acid, or to coffee in its totum.

On this way it is sure its consumption was certainly beneficial.

In the past coffee has certainly encountered authoritative critics, including some religious who saw the signs of the devil in the black beverage. However it also had some famous supporters like Voltaire who claimed to have drunk

50,000 cups. When he was 80 years old he answered to accusation of a friend that coffee was a slow poison by saying "It certainly must be slow if it has allowed me to live to this age in such good condition". It is only right to mention other illustrious supporters as Johan Sebastian Bach who composed a "Cantata of Coffee", Carlo Goldoni who wrote "The Coffee shop", and prince Talleyrand who it's said coined the phrase that coffee must be "black like the devil, hot as hell, pure as an angel, and sweet as love". On the whole therefore, even if there are some contraindications in neurotic subjects, those with severe cardiopathy and in hepatic steatosis, we can state that this beverage taken as 3-4 cups a day, exert essentially positive effects.

Even if in those cases of nervous subjects it would be discouraged or allowed in only as decaffeinated, there are no other real contraindications in most situations where in fact its beneficial effects prevail.

On the morning it promotes the passage from the vagal sleep phase to the sympathetic phase of awaking moment and during the day it promotes improved work performance besides providing an important moment of relaxation between friends or partners over a cup of coffee in a serene atmosphere.

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ZINC AND ITS DERIVATIVES: THEIR APPLICATIONS IN COSMETIC

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Key words: Zinc Coceth Sulfate; Lenitive properties; Stratum corneum deposition; Deodorant power; Dandruff control; Cell Turn over; Dermal innocuity;

Summary

Zinc is one of the most widespread cation present in human body and mainly in skeletal muscles, bones, teeth, hair, and skin (about 6% in stratum granulosum).

Zinc is involved in many metabolism processes and its deficiency results in different pathological conditions.

Zinc plays a major role in epidermis maturation and cutaneous integrity. For all these reasons Zinc salts find several applications in personal care.

Combining skin cleansing with skin care is one of the main goals of cosmetics. A new zinc salt, zinc coceth sulfate, is a surfactant provided with additional functional properties.

The work will illustrate the relationship between Zinc and skin and will quantify the total amount of residual Zinc in stratum corneum at different depths after cleansing with its aqueous solution. Functional properties of Zinc Coceth Sulfate will be demonstrated: underarm deodorant effect (sensorial and microbiological evaluation), dandruff control capacity (corneocytes count and dimension), and skin renewal (dansyl chloride method). Dermatological properties (skin/eye irritation and sensitization) will be also shown.

From all these data we will show that skin cleansing with Zinc Coceth sulfate involves some form of Zinc bond with stratum corneum in its outermost layers, providing so a base for its efficacy and safety.

Riassunto

Lo zinco è uno dei cationi più presenti nell'organismo umano, con le maggiori concentrazioni nei muscoli scheletrici, nelle ossa, nei denti, nei capelli e nella cute (circa il 6% nello strato granuloso). Lo zinco è coinvolto in molti processi metabolici e una sua carenza può originare diverse condizioni patologiche.

Lo zinco gioca un ruolo importante nel ciclo vitale dell'epidermide e nell'integrità cutanea. Per tutte queste ragioni i sali di zinco trovano diverse applicazioni nella cura della persona.

Il riuscire ad abbinare la detergenza della cute con la sua cura è uno dei principali obiettivi della cosmetica. Un nuovo sale di zinco, il cui nome INCI è Zinc Coceth Sulfate, è un tensioattivo con proprietà multifunzionali.

Il lavoro illustra la relazione esistente tra cute e zinco e quantifica lo zinco presente a differenti livelli dello strato corneo dopo l'utilizzo di soluzioni acquose di Zinc Coceth Sulfate. Descrive inoltre con l'ausilio di test le proprietà funzionali di Zinc Coceth Sulfate: effetto deodorante (valutazione sensoriale e microbiologica), controllo forfora (conta e valutazione dimensione dei corneociti), rinnovamento cellulare (metodo del dansil cloruro). Vengono altresì illustrate le proprietà dermatologiche (irritazione cutanea/oculare e sensibilizzazione).

Da tutti questi dati si evince che la detergenza con Zinc Coceth Sulfate implica una sorta di legame del catione zinco con la superficie dello strato corneo che permette di spiegarne l'efficacia e la tollerabilità.

INTRODUCTION

Divalent salts (usually Magnesium salts) of alkyl ether sulfates are known for their skin mildness. Zinc alkyl ether sulfates, obtained by a special synthesis and stabilized as regards hydrolysis, represent a new generation in the field of mild surfactants. They are provided with complex functional properties and a wide potential for special application in skin care. The reason for such functionality resides in the same aspect that originally seemed to hinder most cosmetic applications: the easy precipitation of Zinc salts from anionic surfactant solutions containing Zinc ions. This is also the key of its special activity in functional skin cleansing.

Zinc can influence the activity of 90 enzyme or protein complexes in our body. Following intestinal adsorption, it is rapidly transported to the skin (1). Zinc is important in the morphogenesis of the skin, for collagen synthesis and fibroblast proliferation and in repair processes. Its deficiency leads to specific dermatosis that responds promptly to oral or topical treatment (2). Such improvement does not seem to be related to an easy adsorption, but more probably to the activation of repair enzymes (3). Since when zinc oxide is recognised beneficial in wound healing, zinc became the source of common raw materials also in cosmetics. More recently, zinc oxide in micronized form has found extensive applications in sunscreens, as an effective UV-A filter. The wide use of zinc oxide and zinc carbonate (calamine) has an historical background in diaper rash baby cream, lenitive ointments and lotions astringent, mild antibacterial and soothing agent. Lenitive properties of insoluble Zinc compounds seem to be related to their slow release of Zinc ions and to their slightly alkaline pH. Probably Zinc inhibits the release of TCD4+ cell proliferation and stimulates IL-10 (an immunomodulation cytokine) production by

limphomonocytes (4), a process which is beneficial in the treatment of nickel allergies. Even if this property has been described also for soluble zinc salts, like Zinc Sulfate, toxicological precautions have induced the European legislator to limit the concentration of soluble zinc ions in cosmetics to 1%, while no limits exist for its insoluble derivatives (except zinc sulphophenolate and zinc pyritione). Occlusive patch with 25% zinc oxide are not irritant (5) while neither zinc nor its salts are reported to be significant allergens. In the treatment of oral mucosa, zinc showed a protective effect (6, 7).

Zinc coceth sulfate has the molecular structure reported in figure 1.

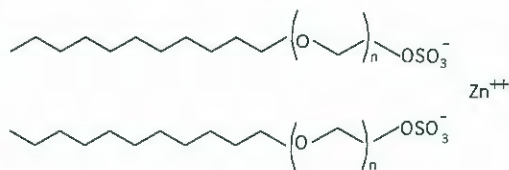


Fig. 1 ($n=3$, alkyl chain coconut based)

MATERIALS AND METHODS

Zinc coceth sulfate solution was provided by Zschimmer & Schwarz Italia, Tricerro.

Other surfactants solutions were provided by the same company. Reagents were analytical grade from Sigma Aldrich.

Solution for evaluation of zinc deposition were prepared at 12.5% a.m. (active matter) Zinc Coceth Sulfate (ZnCS) and respectively 12.5% a.m. SLES. 6 subjects were included in a first study while 4 subjects were included in the second one.

Stripped tapes were extracted by adding 3 ml of 37 % (w/w) HCl, left 5 hours then brought to 50 ml with water and analysed with ICP (Inductively Coupled Plasma Emission Spectroscopy): sample was atomised and exci-

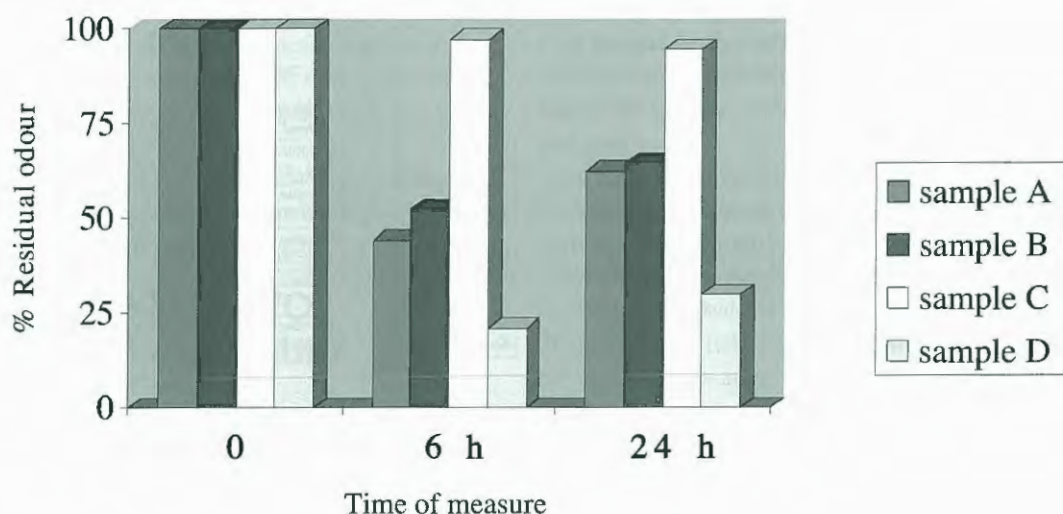


Fig. 4

Dandruff Control Capability

Dandruff is one of the most common and annoying scalp disease induced by disequilibrium of cutaneous homeostasis and worsened by hyperproliferation of saprophyte micro-organisms. Zinc Coceth Sulfate was proved to be able to control dandruff.

16 panellists, in 2 groups, used for two weeks 12% a.m. solutions of, respectively, Zinc Coceth sulfate alone and Sodium laureth sulfate with 0.75% Piroctone Olamine, a well known anti-dandruff agent. Before and after the treatment, the dandruff weight detached after hair brushing was measured. The two solutions gave non significant different results (9).

Table III

SAMPLE	Times	Odour Score			Percentage Decreasing Odour	
		Initial	6 h after last use	24 h after last use	at 6 h	at 24 h
A	Average score	5.4	2.5	3.1	55.7%	37.4%
B	Average score	4.8	1.9	2.8	47.4%	35.3%
C	Average score	3.8	3.7	3.6	2.6%	5.3%
D	Average score	5.0	1.2	1.7	79%	70%

MIC of Zinc Coceth Sulfate for *Pytyrosporum* Ovale and *Malassezia Furfur* was determined in a serial dilution test at pH 5.0. Table IV shows the obtained results.

Table IV

MIC in %	Microorganism
20	<i>Pytyrosporum ovale</i>
12.5	<i>Malassezia Furfur</i>

Cell Turn Over

Experimentally, alpha hydroxy acids effects on cutaneous renewal are measured by the speed of disappearance of a spot (visible under UV lamp) obtained by treating the skin with a solution of dansyl chloride. The comparison between the fluorescence intensity of the skin in the normally washed site (control area) and in skin treated

with 48% Zinc Coceth Sulfate (25% sol.) in presence of 2% alpha-hydroxy acids shows a 28% increase of cell turn-over ($p=0,001$) (10). When the same trial is carried out with the simple aqueous 48% solution of Zinc Coceth Sulfate, a 23% increase over the standard takes place ($p=0,001$) (10).

No significant differences are shown between the two solutions.

Dermal Innocuity

Zinc Coceth Sulfate was tested with the following methods in order to prove it is safe for skin.

Zein Test: Zein, a practically water insoluble cereal protein, when blended with surfactants undergoes a solvation process. A relationship between the irritation potential of a surfactant and the amount of Zein dissolved in water is frequently demonstrated (11).

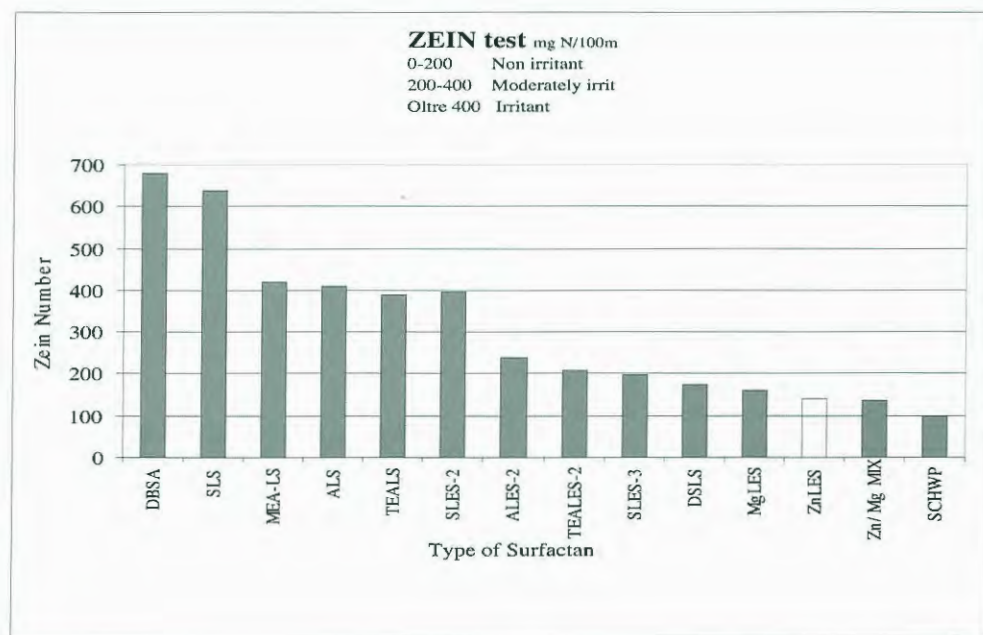


Fig. 5

Table V

DBSA	Dodecylbenzen Sulphonic Ac.	TEALES-2	TEA Laureth-2 Sulfate
SLS	Sodium Lauryl Sulfate	SLES-3	Sodium Laureth-3 Sulfate
MEA-LS	MEA Lauryl Sulfate	DSLS	Disodium Lauryl Sulphosuccinate
ALS	Ammonium Lauryl Sulfate	MgLES	Magnesium Laureth-2 Sulfate
TEALS	TEA Lauryl Sulfate	ZnLES	Zinc Coceth Sulfate
SLES-2	Sodium Laureth-2 Sulfate	Zn/Mg MIX	1/1 Zn Coceth Sulfate/Magnesium Laureth-2 Sulfate
ALES-2	Ammonium Laureth-2 Sulfate	SCHWP	Sodium Cocoyl Hydrol. Wheat Protein

Shelanski and Shelanski Test: Zinc Coceth Sulfate is void of any irritant and sensitising potential. Severe in-vivo trials have demonstrated this quality: as an example, the Shelanski-Shelanski test, carried out on 25 volunteers aged 18 to 70; with 5% a.m. solutions applied in 7 mm Finn Chambers. Treatment was repeated for four weeks, by applying a patch a week. Finally, a revealing patch evidences the possible outcome of sensitisation. Preliminary patches are maintained on the skin for 48 hours. Treated skin site is examined after 15', 1 h and 24 h from patch removal. The revealing patch is identically examined. Evaluation scores are given to the evidenced oedema and erythema, on the basis of their intensity (12).

CONCLUSIONS

The age of functional skin cleansing is still amazing: after various structures of mild surfactants, the use of "colloidal deposition" cations, opened by this new Zinc surfactant, offers elegant and complex formulation potential, allowing interesting blends and tailor-made cutaneous effects for sensitive skin and for restitution cleansing at low pH.

ACKNOWLEDGEMENTS

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EFFECT OF LICORICE (*Glycyhrriza glabra* Linn.), A SKIN-WHITENING AGENT ON BLACK MOLLY (*Poecilia latipinna*)

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Key words: Tyrosinase inhibition; Skin-whitening agent; Licorice extract; Black Molly;

Summary

Glycyhrriza glabra Linn. commonly known as Licorice, is a traditionally herbal remedy with an ancient history for its world wide usage in herbal preparations as a tonic, expectorant, demulcent, mild laxative and for allaying cough. It is also used as a depigmentation agent in cosmetics. Peoples in East Asia particularly females desire to keep skin white. To satisfy this desire many cosmetic companies have been developing melanogenesis inhibitors and discovering skin-whitening cosmetic preparations. Therefore, in this investigation *Glycyhrriza glabra* was evaluated for the inhibitory activity on tyrosinase and chronic fish toxicity test using Black molly fish model. The 50% Tyrosinase inhibitory concentration of Licorice extract was 34.48 µg/ml.

No Observed Effect Concentration (NOEC) for Black molly exposed to Licorice in portable water was obtained by 1mg/L, first observed effect concentration (FOEC) was obtained by 4 mg/l. In the present study the toxicity of Licorice extract was clearly observed in the liver sections and the bioaccumulation of the extract were increased with an increase in the concentration of Licorice extract.

Riassunto

come liquirizia, la *Glycyhrriza glabra* Linn è un rimedio naturale tradizionale usato in tutto il mondo come tonico espettorante nelle forme influenzali, e svolge anche una leggera azione lassativa. Talvolta è utilizzata in cosmesi come depigmentante, soprattutto nel Sud-East Asiatico dove le donne desiderano mantenere la loro pelle particolarmente bianca.

A tal proposito, molte aziende cosmetiche hanno studiato e sviluppato preparazioni cosmetiche ad effetto depigmentante.

Per questo motivo è stata valutata l'attività della *Glycyhrriza glabra* Linn come inibitore della tirosinasi utilizzando come modello un particolare pesce nero.

La concentrazione che inibisce il 50% dell'attività tirosinasi è stata pari a 34.48 mg/ml.

Con la concentrazione di 1mg/L dell'estratto di liquirizia non sono stati ottenuti risultati positivi che, al contrario, si sono verificati con la concentrazione di 4mg/L.

Per quanto concerne la tossicità dell'estratto di liquirizia, si è notato che tende ad accumularsi nel fegato e che tale accumulo sembra essere direttamente correlato all'incremento della concentrazione utilizzata.

INTRODUCTION

Licorice (*Glycyhrriza glabra* Linn.), a traditional herbal plant and its roots are widely used as flavoring agent in food and candy. It has been also employed in herbal preparations as a tonic, expectorant, demulcent, mild laxative and for allaying cough. Additional effects such as depigmentation, of Licorice was reported by Nodkarni (1991) and Tanyri *et al.* (1965). In India, it is reported to be cultivated in Baramulla, Srinagar Jammu, Dehra Dun, Delhi and South India (Sastri 1956) (Sharma *et al.* 2001).

Melanins are pigmented biopolymers that impart skin typology and tan. They are synthesized by the dendritic melanocytes dispersed at the dermo-epidermal junction. Melanin synthesis takes place in membrane bound organelles termed melanosomes, which contain specific enzymes controlling the production of the pigments. The first and rate-limiting step of melanin formation is mediated by tyrosinase (Hearing 1999; Ortonne & Ballotti 2000). Increased melanin synthesis or uneven distribution cause local pigmentation in the skin. Pigmentation disorders are caused by various factors including UV radiation, due to the destruction of the ozone layer. Excessive exposure to UV radiation may cause post-inflammatory pigmentation or hyper pigmentation (Kubo & Matshida 1995).

East Asia peoples, particularly the females desire to keep the skin white. To satisfy this desire many cosmetic companies have been developing melanogenesis inhibitors and discovering skin-whitening cosmetic preparations. In cosmetic preparations tyrosinase inhibitors such as Kojic acid, Arbutin, Ascorbic acid and Licorice extract have been exploited as whitening ingredients.

Today's cosmetics consumer is a smart shopper. While attractive packaging is still an important

factor in product appeal, the cosmetic user expects skin care formulations that are elegant, safe and live up to the consumer's expectation of effectiveness. It is becoming increasingly apparent in the competitive field of cosmetics, that efficacy and safety claims are powerful product marketing tools. Unfortunately, statistically significant demonstrations of comparative clinical efficacy and safety of these products are not always met.

Safety assurance is one of the most important requirements routinely used by healthy people without medical supervision. In general an application for the approval of a new chemical as a cosmetic ingredient in globally must be accompanied with an extensive safety data such as acute toxicity, primary skin irritation, repeated skin irritation, sensitization, photo toxicity, photo sensitization, eye irritation, mutagenicity and human patch test, in order to obtain the approval of the Ministry of Healthy and Welfare (Itagari *et al.* 1995).

Only very limited level of studies for the environmental impact assessment is recommended for cosmetic ingredients, since environment issues are becoming recognized as a potential concern for consumer products that are eventually washed "down the drain". Acute fish toxicity test is one, which is used to identify very high environmental effect concerns. Therefore, in the present investigation *G. glabra* was evaluated for its inhibitory activity on tyrosinase and chronic fish toxicity using Black molly fish model.

MATERIALS AND METHODS

Extraction

Licorice roots (*Glycyhrriza glabra* Linn) were obtained from the commercial market. The roots were dried well at 37° C and powdered. Root powder (20 g) was soaked with 80 g of Propylene glycol (PG) solvent for 24 hr.

Followed by filtration, the filtrate was evaporated to dryness under vacuum. About 95% yield was collected and used for the evaluation of inhibitory activity of tyrosinase, Dopa autooxidation and toxicity study.

Animals

Total of 30 intact male black molly (*Poecilia latipinna*) weighing 3.01 to 3.03 g were chosen for the present study. Experimental fishes were obtained from Live Stock Research Institute, Kattupakkam, Chennai, Tamil Nadu, and were permitted to acclimate to laboratory conditions for at least one week prior to use. The animals were maintained in five groups of six (as duplicates) in slate bottomed glass aquaria (12 X 12 X 18) inches (Chavin 1963) under constant conditions of temperature (37° C), photoperiod (12 hrs per day) and diet.

Chronic toxicity

The test compounds were fed in 25 Liters of portable water (at a compound concentration of 25, 50 & 100 mg of Licorice extract / 25 Liters). As a control group, the fishes were fed with Green tea powder (100 mg of Green tea powder / 25 Liters).

Histochemical analysis

Liver organs dissected from different groups were preserved in 10% buffered formalin. A 5-7µm thickness sections were stained with haematoxylin & eosin and photographed under 12.5 X magnification (McManus & Moowry 1956).

Tyrosinase inhibition

Tyrosinase activity is generally determined by spectrophotometry. The procedure followed that described by modified Vanni *et al.* (1990). In control tube 235 µl of 3 mM tyrosine and 285µl of 0.1 M phosphate buffer (pH 6.8) were added and incubated for 10 min at 25° C. Followed by incubation, 180 µl of mushroom tyrosinase (90

Units) from Sigma was added then incubated for 20 min at 25° C. For test samples, test solutions were added and buffer volume was adjusted accordingly. The pink color formed (Dopachrome) was measured as absorbance at 475 nm at the end of 20 min for each tube.

Inhibition of Dopa autooxidation

In case of control tube 250 µl of DOPA (4mM) and 200µl of Riboflavin (26 µM) in 550 µl of Phosphate buffer (0.05 M) was incubated under fluorescent lamp for 15 min. In case of test samples, buffer and test solution were adjusted accordingly. Color developed was measured at 475 nm, following the procedure of modified Joshi *et al.* (1987).

RESULTS

Figure 1 illustrated the toxicity of Licorice, and the mortality of test animals studied. It has been observed, Licorice at 4mg/l exhibited 100% mortality on day 7 of experimental period, whereas, the lower concentrations showed about 17% on day 25 for 1.0 mg /l concentration and 34% mortality on day 15 for 2.0 mg/l concentration.

For Group – I (1mg/L), the remaining fishes were alive even after 45 days and for Group – II (2mg/L), the remaining 66% mortality was observed on 21st day. Group – III (4mg/L), fed uptake was observed to be reduced after three days. In the case of negative (Group – IV) and positive (Group – V) control experiments, no mortality and no reduction in fed uptake was observed through out the experimental period. Figure 2 emphasizes the morphological changes observed in terms of body weight analysis carried out during the experimental period. The percentage reduction in body weight increases as the concentration of the test compound increases. At lower concentration, about 2.645% reduction was observed with group-I animals

and it has been increased to 5.94% with group – II animals and 11.96% with group- III animals. Both the control groups were exhibited about 29

- 50% gain in body weight as illustrated in the Figure.

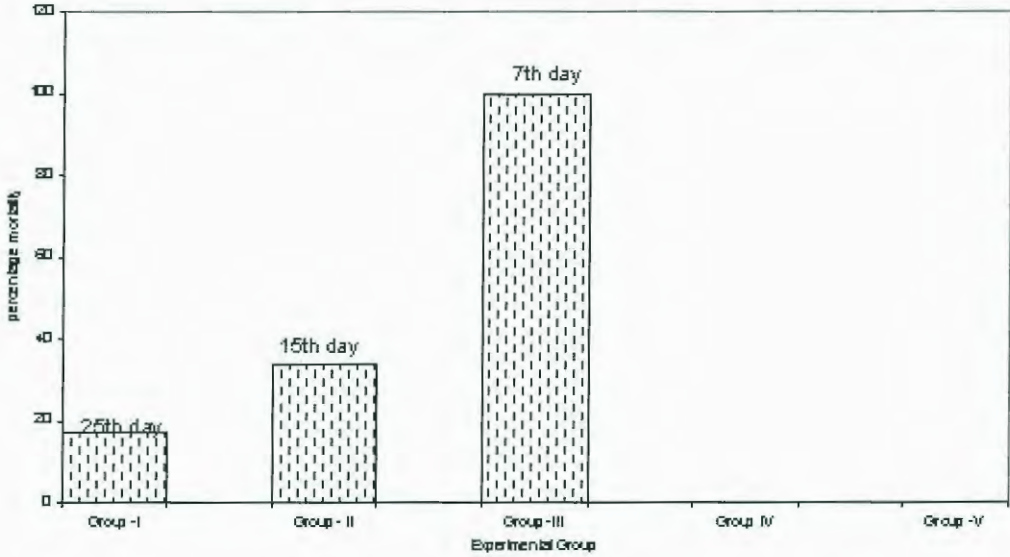


Fig. 1 Percentage mortality of Black Molly (Group – I (1mg/L); Group – II (2mg/L); Group – III (4mg/L); (Group – IV) and V) negative and positive control).

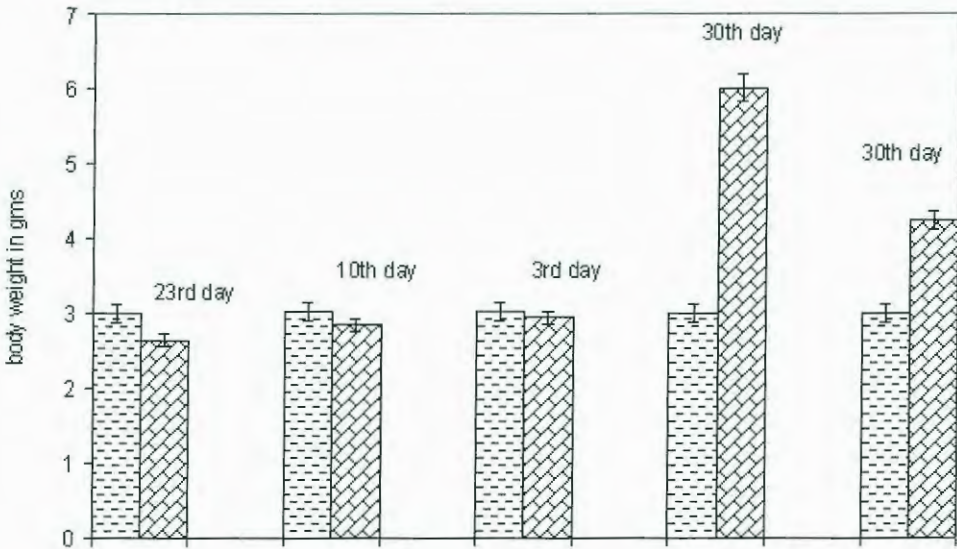


Fig. 2 Change in body weight with respect to concentration of Licorice on Black Molly (Group – I (1mg/L); Group – II (2mg/L); Group – III (4mg/L); (Group – IV) and V) negative and positive control).

Histochemical analysis

Examination of haematoxylin and eosin stained sections of liver tissues, for the experimental animals at the time of exposure to the test compound exhibited that the degree of damage increases with an increase in the concentration of the test compound. Similar to the mortality and the reduction in body weight, higher the concentration applied higher the tissue damage was observed. Figure 3a & 3b illustrates the H&E staining of liver tissue obtained from control groups. (Group -IV & V). It has been observed that there was a high level of viable cell architecture pattern with regenerative changes with mild hepatocellular swelling, cholestasis and moderate micro and macrovesicular steatosis with no inclusion of foreign body.

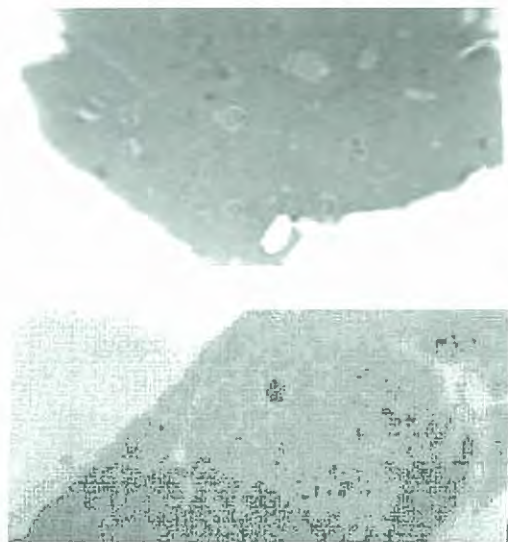


Fig. 3a & 3b H & E sections of liver tissue of both negative and positive controls of Black Molly.

Whereas the test compound treated tissues showed that histopathologic changes in the centrilobular areas. There is a mild lymphocytic infiltrate with focal central vein endothelialitis and hemorrhage with hemosiderin laden macrophages.

Moreover, chronic mural inflammation with non regenerative pattern suggests that the injury to the hepatic cell was only due to the test compound supplied. In addition, inclusion of foreign body was evidently exhibited in Figures 4a, 4b and 4c.

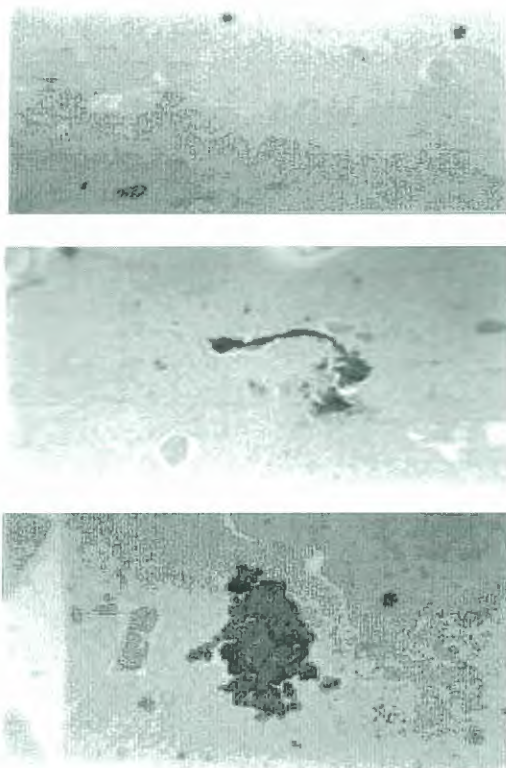


Fig. 4a, b and c H & E sections of liver tissue of Licorice treated Black Molly. (Group -I (1mg/L); Group - II (2mg/L); Group - III (4mg/L).

Tyrosinase inhibition assay

In vitro analysis carried out to assess the 50% enzyme inhibitory concentration of the test compound. Figure 5 illustrated that, about 50% inhibition of tyrosinase activity was exhibited by the Licorice extract was 34.48 µg/ml, compared to the positive test control carried out with kojic acid at 2.0 µg/ml.

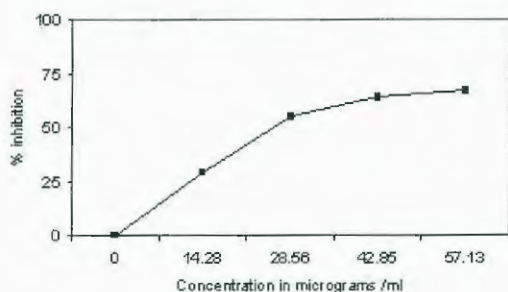


Fig. 5a Dose response curve for concentration dependent inhibition of Tyrosinase (Licorice extract).

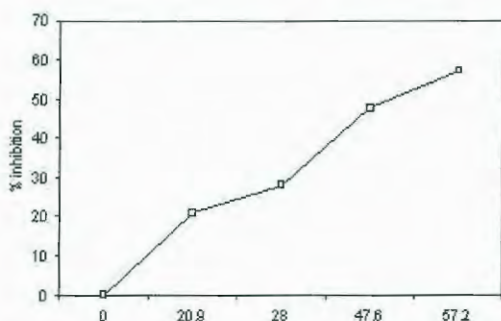


Fig. 5b Dose response curve for concentration dependent inhibition of Tyrosinase (Kojic acid).

Dopa auto-oxidation inhibition assay

Since the test compound exhibited the inhibition of tyrosinase activity, the evaluation of possibility of Dopa auto-oxidation was assessed. It has been observed that, the test compound did not have any action on inhibition of Dopa auto-oxidation.

DISCUSSION

Cosmetic industries are one of the fast-growing industries. Advent of new cosmetics with new formulations is a great challenge to the cosmetic industries.

Most of the new cosmetic products are the different combinations of old ingredients. Salminen

(2002) states that, there has been a significant trend in using new ingredients to give cosmetics unique properties not available from the standard battery of old ingredients.

Interest in discovery of new skin - lightening agents is currently on demand by the cosmetic, consumer product and pharmaceutical industries (Petit & Pierard 2003).

This situation corresponds to a perceived need in the market place for novel agents with increased efficacy and improved safety profiles. Thus, new compounds are frequently appearing in cosmetic industry trade journals. But, the product owners have not statistically proved the clinical efficacy and the safety in usage of the products. Lack of clinical trials betray the products usage.

Chronic effects have been the focus of most recent toxicity studies. The No Observed Effect Concentration (NOEC) for Black molly (Test animal in the present study) exposed to Licorice in portable water was 1mg/L, first observed effect concentration (FOEC) was 4 mg/l. In the present study the toxicity of Licorice extract was clearly observed in the liver sections and the bioaccumulation of the extract were increased with the increase in the concentration of Licorice extract.

Various functions of crude licorice extracts have been shown over many years (Takagi & Ishii 1967). Glycyrrhizin and glychrrhetic acid are the main constituents of the hydrophilic fraction of licorice extracts and are known to be anti-inflammatory agents (Inoue *et al.* 1986). The hydrophobic fraction of licorice extracts, which contains various flavanoids, has been know to have the inhibitory effects on melanogenesis due to its inhibition of tyrosinase activity (Kameyamma *et al.* 1994) and in the similar way Glabridin (oil soluble fraction of licorice) also has been known to have the inhibitory effects on melanogenesis. In addition, contact allergic dermatitis can also be developed by the

application of these compounds (Nishioka *et al.* 1999). Moreover, consumption of licorice of 10-45 g/day causes raised blood pressure together with a block of aldosterone, rennin and electrocardiogram changes (Newall *et al.* 1996). The 50% Tyrosinase inhibitory concentration of Licorice extract was 34.48 µg/ml, earlier similar type of result was reported by Khanom *et al.* (2000). The chosen extract does not have any action on reducing or inhibiting the Dopa auto-oxidation reaction even at 500 mg/ml, earlier similar type of result was reported by Lee *et al.* (1997).

CONCLUSION

Skin care products based on natural materials needs high clinical efficacy and safety. Effect of Licorice extract on inhibition of tyrosinase activity on Black molly showed *in vitro* 50% inhibition on comparison with standard inhibitor kojic acid, but the accumulation of extract in the liver tissue showed damaging effects and toxicity.

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The Epidermis in wound healing

by Rovee D.T. and Maibach H.I.

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Regenerative Medicine is an innovative concept representing a unique approach to the regeneration of functional tissues and organs.

Thus the basic cellular and molecular abnormalities underlying the failure to heal are receiving greater attention.

The focus of investigation is shifting from the normal wound healing process to understanding the micro-environment of chronic wounds. At this purpose we have now more information about signaling pathways that is critical to the understanding of how peptides, for example, work in a specific way and how their actions are regulated at the molecular level.

But a major stumbling block is the poor understanding of how chronic wounds fail to heal and what is their intrinsic pathogenesis that needs to be connected.

There are of course surgical ways to address chronic wounds in a more definitive way and now we have better wound dressings also. Together with dressings, we have accepted the concept of slow-release antiseptic agents which can deliver antimicrobial agents in a way that does not prove detrimental to the healing process. And we have begun to appreciate that much of what we have learned based upon acute wound healing does not always apply to the chronic wound.

The purpose of this book, divided in 5 parts and 19 chapters, is to update the information available on the epidermis and the newest findings, to improve our knowledge on these topics, and finally to stimulate original research and development in wound therapy.

Cellular and Biochemical Issues is the topic of **part I** reported in **chapters 1, 2 and 3**.

Current research tasks involve determining precisely which molecular cues regulate which cell activity, and how these may be modulated in order to stimulate wounds to heal faster and with more perfect tissue regeneration.

Re-epithelization is, in fact, the reconstitution of the cells of the epidermis into an organized, keratinized, stratified squamous epithelium which covers the wound and restores the barrier properties of the skin. And forward migration of keratinocytes across a wound surface is clearly one of the chief components of the tissue repair process.

This process occurs rapidly in acute wounding, beginning with the migration of intact keratinocytes from the free edge of the cut epidermis across the defect. But in order to re-epithelialize a wound, keratinocytes at the wound edges need to be able to detach themselves from the basal lamina.

This cell-detachment-migration is made possible by the dissolution of *desmosomes*, which are the keratinocyte's primary anchoring contact, that bind keratin cytoskeletal network to laminin (hemidesmosomes) in the basal lamina via α -6 β 4 integrins.

The signals for obtaining the temporary dissolution of intercellular attachments (desmosomes) and

basal membrane attachments (hemi-desmosomes), together with the projection of pseudopodia, enabling cells to move, are today not entirely understood.

These and other interesting *ideas* considering the stratum corneum as a *biosensor* that regulates the various signalling mechanisms mediating these metabolic responses to a variety of exogenous insults, are reported in these introductory chapters.

However, challenges still remain in achieving a comprehensive understanding of the wound healing mechanism and the utility of using human-like tissues in these studies are surely helpful to mimic and better understand this complex process.

Examples of dressing functions that relate to wound needs include absorptive capacity, conformability, adhesive level, hydrating ability, ability to facilitate detriment, and to control odour. But what all categories of dressings have in common is that they create or maintain a moist wound environment for healing.

Thus they are also referred to as occlusive, *advanced* or *moisture-retentive* dressings.

And on **Part II, chapters 4 and 5**, are discussed the limits and purposes of the occlusive dressings. These kind of physical barriers may be defined as *dressings retaining sufficient moisture to maintain healing equivalent to that in a physiologically moist environment*.

Their effects on wound healing are reported and documented by many data and the ability of occlusive dressings to accelerate wound healing has been well described.

However, since the wound healing process is complex, and aspects of the natural wound, such as wound induction, depth, size, site-to-site variability, and environmental factors, may vary, it is difficult to evaluate the effects of therapy upon the repair process.

This important topic is focused on **Part III: Quantifying repair in the Epidermis**.

At this purpose the quantitative wound models are important to objectively evaluate topical wound agents, thus measuring the treatment effects. Therefore highly developed objective and non-invasive techniques for wound assessment have been brought into use.

These techniques are important research tools in investigating the different phases of wound healing and in determining therapeutic effects.

However, to date, none standardized wound model to evaluate topical agents has been established. Each model described in **chapters 6, 7 and 8** (Part III) may offer substantial advantages and limitations.

Therefore, a realistic estimate of human wound healing for topical agents is to be determined by *in vivo* studies in humans.

The up today focus of investigation is clearly shifting from the normal wound healing process to understanding the micro-environment of chronic wounds.

Epidermal wound healing is, in fact, a well-orchestrated cascade of events that lead to repair when the underlying dermis is also compromised, but lead to regeneration when only the epidermis is injured. This process is restoration of skin integrity occurring within a period of days to weeks.

Conversely, when this process is disrupted and healing is prolonged, delayed, or does not occur, the wound is termed "a chronic wound". An exact time when acute wound healing becomes chronic does not exist.

Among the many factors suggested as being causal in retarding healing is an abnormal microbiologic environment of the wound, tissue anoxia for a low oxygen presence, some degree of body protein loss to provide the necessary aminoacids for energy.

Physical and Chemical Factors Affecting Repair is focused on Part IV in **chapters 9 to 12**.

Wound microbiology affects healing in a number of ways and appreciation of the true role of bacteria is critical.

Bacteria present in wounds consume glucose and oxygen and therefore may lead to tissue anoxia. Moreover the majority of wounds are polymicrobial, with both aerobes and anaerobes present.

Pathogens such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and beta-hemolytic streptococci have been the most frequently cited as causes of delayed wound healing and infection. Therefore bacteria may be a detriment to patients by causing infection or prolonging or preventing healing, at this purpose a variety of topical antimicrobial treatments are utilized and reported on **chapter 9**.

Lack of oxygen is another frequent reason why skin wound fails to heal.

Oxygen concentrations i.e., PO_2 , in wounds are low and most of the variations in collagen synthesis, deposition and cross linking, angiogenesis, and epithelization in human wounds are due to variations of local PO_2 .

While the normal oxygen demands of wounds are relatively low, they are heightened by excessive inflammation. The result is a lower PO_2 that prolongs healing and may cause excessive scarring in the long run.

Therefore restoration of oxygen concentration in tissue allows wound cells to deposit collagen, to resist infection, to epithelize, and to develop new vasculature.

This is the fascinating topic discussed in **chapter 10**.

Optimum nutrition is recognized to be also a key factor in maintaining all phases of wound healing. Adequate energy, protein and micronutrients delivered to the wound are necessary, in fact, to maintain an adequate rate of new tissue synthesis, as reported and discussed in **chapter 11**.

As we have previously seen, wound healing is a dynamic process, and the performance requirements of a dressing can change as the wound progresses towards healing. Therefore an effective wound management requires an understanding of the process of tissue repair and a knowledge of the properties of the dressings available.

Only when these two factors are considered together, the process of dressing selection can be undertaken in a logical and informed fashion.

In **chapter 12** are brilliantly reviewed the types of dressings that are available and illustrated how these may be used to facilitate wound healing or otherwise improve patients' quality of life.

New Approaches to Understanding and Treating Wounds are discussed in **Part V, chapters 13 to 19**.

Despite the best efforts of a medical device industry, no single product has been developed that combines all the required features in an effective manner, so problems encountered in wound management are often addressed by the use of a *dressing system*, which consists of a number of individual components, each of which fulfills a specific function.

In this system skin needs to be optimally prepared to maximize the treatment's benefits.

Thus *wound bed preparation* has been defined as the global management of wounds to accelerate endogenous healing or to facilitate the effectiveness of advanced therapeutic products. Among these genetic manipulation of cells and tissues shows, for example, enormous promise for correcting a myriad of metabolic disorders and to be used on wound repair also.

Gene Therapy of Wounds and Wound Bed Preparation are the interesting topics of **chapters 13 and 14**.

An approach to chronic wound treatment through the concept of wound bed preparation will help to guide both the general practitioner and wound care specialist in their approach to care of chronic

wounds.

On the other side, skin is a good candidate for gene therapy not only because of its obvious accessibility but also for its capacity to regenerate and for its abundant vascularity.

Therefore using gene therapy to selectively elevate or down regulate expression of a particular growth factor in the healing wound microenvironment has great premise in promoting tissue repair and regeneration.

Gene transfer of growth Factors for Wound Repair is the topic of **chapter 15**, meanwhile on **chapter 16** (*Autologous Skin Transplantation*) the possibility of transplanting gene-modified cultured skin has discussed.

Restoration of an intact barrier is in fact, of critical importance, following wounding and may be achieved by normal wound healing, by direct wound closure, or by skin transplantation.

Skin transplantation, commonly referred to skin grafting, is the really transposition of skin from one part of the body (donor site) to another location (recipient site).

This transplantation lacks its own blood supply and therefore relies on vascularization from the recipient site. But skin may also be transferred without disruption of its main vascular supply by use of the so called skin flaps.

The most component of successful skin grafting is preparation of recipient site and, first of all, a great anatomical knowledge performed by plastic and reconstructive surgeons.

However the active treatment of acute and chronic wounds has been a subject of considerable effort in these last years, generating new pharmacologic agents and tissue engineered skin products such as retinoids or combined epidermal and dermal layers.

As a matter of fact, there are many advantages to tissue-engineered products as opposed to autologous skin grafting, even if the exact mechanism by which tissue-engineered skin products aid in healing acute and chronic wounds is not completely understood.

Thus these new raw materials and techniques are becoming to be frequently used to minimize the effects of intrinsic and extrinsic aging, photodamage and scar repair changing the goal from a simple wound closure to a functionally regenerative repair.

Clinically outcome requirements for these procedure are substantially different from the prevailing wound healing standards for chronic and acute traumatic wounds.

These procedures use, in fact, unique methods necessary to induce a controlled repair response in the epidermis and/or dermis that delivers a superior cosmetic outcome.

All these topics are focused on the last part of the book from the **17th** to **19th** chapters.

Written by an expert and known team of researchers, this interesting book provides an extensive description of the advances in epidermal biology as related to wound healing, reposting critical evaluations of the new tissue-engineering skin products and the current clinical practices in this fascinating field.

It will be surely of interest not only for the expert plastic surgeons and dermatologists but also for all the scientists and/or the students of the chemical and medical community that wish to know in the best way all the newest findings developed in wound therapy.

P. Morganti
Editor-in-Chief

Mechanism of epithelial defence

By D. Kabelitz and J.M Schröder

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Skin, the largest organ in the body, is a composite of a variety of cell types and organellar bodies, each of which has a particular function.

The major function of the skin is protective, to save the organism from the external hostile environment.

Achieving this goal has resulted in the evolution of a complex structure involving different layers (epidermis, dermis and hypodermis), each with particular properties.

While it has been known for a long time that various physicochemical features including low pH and lipid lamellae contribute to the natural protection of the skin, it is a rather recent discovery that the skin and other epithelia harbor a large array of naturally occurring antimicrobial peptides. Thus the production of antimicrobial peptides (AMPs) is an important aspect of host-defense in multicellular organisms and the emerging scenario indicates that such peptides are instrumental in maintaining the skin's homeostasis.

These antimicrobial peptides, in fact, protecting the organism against infection, are at the center of epithelial defense mechanisms, forming an important part of the innate immune system.

Innate immunity is an ancient metazoan feature, which allows animals to recognize typical chemical structures presented by invading microorganisms, and to activate a sophisticated set of responses to control the infection.

In vertebrates, these responses include the induction of cytokines and co-stimulatory molecules that will trigger adaptive immunity.

Higher insects, as *Drosophila Melanogaster*, control infection by an array of innate immune reactions among which eight classes of AMPs. These peptides can be grouped into three families based on their main biological targets, gram-positive bacteria (defensin), gram-negative bacteria (cecropins, drosocin, attacins, diptezicin, MPAC (Maturated Pro-domain of Attacin C), or fungi (drosomycin, metchnikon).

In humans, the three AMP families are 1) defensins (in genome), 2) cathelicidins (in neutrophils) and 3) histatins from saliva.

And the *Antimicrobial Peptides in Drosophila Structures, Activities and Gene Regulation* are the topic of **chapter 1**.

Thus, it is very clear now that antimicrobial peptides are in the center of epithelial defense mechanisms, forming an important part of the innate immune system.

Therefore the discovery of several skin-derived antimicrobial proteins has brought new insights into the role of antimicrobial proteins for cutaneous host defense.

As a matter of fact, the production of these antimicrobial proteins provides a rapidly acting defense system that is already engaged before adaptive immune interactions take place.

Therefore these compounds seem to represent essential factors to combat and prevent microbes from establishing an infection.

This is the topic responded and discussed on **chapter 2, *Antimicrobial Peptides in Human Skin***.

The open problem is that, as yet, we do not have data concerning the local concentration of antimicrobial proteins *in vivo*.

Therefore it is of substantial interest to investigate, whether the concentration of antimicrobial proteins reached *in vivo* are sufficient to exhibit microbial properties, keeping in mind that the action of these compounds largely depends on the environmental conditions (pH, ion and protein composition, etc).

However a decrease or lack of mucosal peptide antibiotics seems to play a central role in the etio-pathogenesis of Crohn's disease, as reported on **chapter 3**.

As we know today, AMPs are expressed in the respiratory tract as effector substances of the innate immune system, acting as endogenous antibiotics by direct destruction of microorganisms.

These antimicrobial peptides have broad spectrum activity against gram-positive and gram-negative bacteria, as well as against fungi and enveloped viruses.

Interactions between the peptide and surface membranes of the target organisms are considered to be responsible for activity. Thus AMPs bind to receptors and activate variety endothelial cells, mast cells, macrophages.

All these topics are reported and discussed on **chapter 4: *Antimicrobial Peptides in Lung Inflammation***.

Therefore on one side AMPs seem to represent multi-functional effector molecules acting as endogenous antibiotics. On the other side they seem to have additional functions as mediators of inflammation in the host defense scenario.

However we have to remember that most of human body surface are densely colonized with a variety of microorganisms.

This intimate coexistence between higher host organisms and microbes has generated a myriad of adaptation strategy at both sides to cope with, or even benefit from the given conditions.

Thus, on one side, epithelial cells at many body sites are well-equipped to recognize and respond to microbial challenges and provide a wide spectrum of antimicrobial strategies. On the other side microbial organisms have evolved an equally large number of mechanisms to avoid, circumvent or modulate the host response.

Therefore the initial microbe-host interaction might provide effective targets for therapeutic and prophylactic strategies to enhance resistance against microbial infections. This is the fascinating topic reported on **chapter 5: *Bacterial Evasion of Innate Defense at Epithelial Linings***.

Another important discovery of recent years is the identification of a set of pattern recognition receptors which display specificity for defined microbial molecules including bacterial lipo-polysaccharide, bacterial DNA, viral RNA, and others.

Thus Toll receptors in species as diverse as *Drosophila* and humans, and the identification of their role in distinguishing molecules and structures that are common to microorganisms has led to a renewed appreciation of the innate immune system. And it is now discovered that Toll-like receptors

(TLR) or able to recognize various components of invading pathogens, representing critical molecules to induce not only inflammatory responses but also fine-tuned and selective adaptive immune responses.

Therefore they are the early sensors of microbial material in both, epithelial cells and dendritic cells, initiating innate immune response way before the specific or adaptive immune system is attested.

And this new physiologic role of defense is discussed on **chapters 6 and 7**.

In addition to these basic epithelial defense mechanisms, it has been appreciated that subsets of lymphocytes also contribute to local immune surveillance and defense in epithelia.

And various reported studies support the idea of a crucial role played by γ dT cells.

These special epithelial cells seem to form a bridge between the innate and adaptive immune system, playing also a crucial role in local immune surveillance and in maintaining the epithelial integrity.

As a matter of fact, at the functional level γ dT cells rapidly produce a variety of cytokines and usually exert potent cytotoxic activity.

However despite tremendous progress over the years, the significance of γ dT cells in health and disease is still not completely clear. But all these multiple and independent new recovered mechanisms of defense effectively protect the epithelia from infection and contribute to tissue repair.

Moreover the increasing capacity to identify precisely which molecules are used by such unconventional lymphocytes to exert their effects, should have future applications in the clinical treatment of inflammatory disease, cancer, and other forms of tissue disruption.

These and other considerations are reported in the last chapters of this interesting book.

The role of antimicrobial peptides, Toll-cells receptors and γ dT cells in epithelial defense and infection are brilliantly reported on this book that offers to the readers an up-to-date review on these interesting and new topics.

The book is to be considered a fundamental tool not only for immunologists, dermatologists, microbiologists, plastic surgeons, and infections disease specialists but also for all those scientists and students of chemistry and medicine interested to learn more and have up-to-date insights on all the mechanisms of epithelial defense system.

P. Morganti
Editor-in-Chief

Silicones for personal care

By Anthony J. O' Lenick Jr.

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The book, divided in 27 chapters, highlights the various steps on construction, functionalization, derivitization and, of course, synthesis of the relatively new and great family of silicone compounds. Silicon atomic number 14, is the second most abundant element known, composing about 25% of the earth's crust, although it does not occur naturally in its free state.

Thus it is often found in nature in the form of silicon (sand) or silicates, minerals comprising not only silicon but also oxygen and metals such as aluminium, magnesium, iron, calcium, or mica.

Silicones, as organic materials, are polymers of silicon, carbon, hydrogen and oxygen, sometimes including nitrogen or sulphur.

Although it might be assumed that silicon, lying directly beneath carbon in the periodic table, would react in a similar manner to carbon, there are numerous differences between silicone and carbon chemistry. The silicon atom is larger than carbon and less electronegative, thus the resulting bonds to oxygen and chlorine are more polar.

In combination with organic moieties, silicon provides unique properties that function in a wide temperature range, making the silicone-based products less temperature sensitive than most organic polymers.

Therefore silicones are generally resistant to the types of substances that attack organic materials (i.e. UV rays heat, oxidation, etc.) while they are susceptible to attack from strong acids or bases to which hydrocarbon polymers are generally resistant.

Thus the low surface energy characteristic of silicone polymers renders them excellent water-repellent lubricants and good antifoam agents.

As a consequence of these combined properties, polydimethyl-siloxane, for example readily separates from the other ingredients in a cosmetic formulation, when they are spread over the surface of skin or hair.

However a great variety of silicone derivatives which differ both in structure and functional properties, are now available to the formulator.

These derivatives with their characteristic properties are responsible for the unique attributes of silicone polymers, rendering them useful in a large variety of applications in such diverse industries as aerospace, electronics, automotive, construction, textile, and cosmetics.

The increased use of silicones in personal care compositions becomes obvious when looking at ingredient listings for new products being introduced into the market place, over half containing some type of silicones.

Over the years in fact, these silicone polymers have become more and more important in advanced

cosmetic formulations providing benefits not attainable with other traditional raw materials. But it is critically important to properly select the right silicone compound and it's crucial the understanding of its structure and characteristics.

As a matter of fact, *dimethicones* act as skin protectant, functioning as a breathable barrier. Additionally they may act as emollients, providing a velvety soft, lubricious film while reducing the whitening effects during rub-in of various skin care products.

Polyether-modified silicones, including terpolymers containing an alkyl or polyglucoside moiety, are very efficacious emulsifiers for water-in-silicone, silicone-in-water, or three-phase water/oil/silicone systems.

They are also utilized to reduce irritation to skin and mucous membranes caused by primary surfactants in personal cleansing and shampoo compositions.

Silicone Quats analogues of traditional quats are likewise important compounds in personal vis-à-vis conditioning and softening of skin and hair.

Volatile silicones improve sub-in characteristics and are frequently utilized as diluents in hair and skin care applications. They provide transient conditioning benefits in hair care applications and act as transient emollients as well as detachfying agents in skincare formulations.

Alkyl modified silicones import an occlusive barrier to the skin, reducing transepidermal water loss values to levels helping to improve formulation stability and acting as rheology modifiers.

These materials have also demonstrated applications as hair volumizing agents.

Finally, numerous specialty silicones are available incorporating standard sunscreens, fragrances, proteins, aminoacids, quaternary groups, phospholipids, natural waxes, and the like.

An area of great interest is also fluoro silicones, which have additional groups present.

The development of synergistic blends of dimethicone copolyol compounds with traditional fatty compounds to provide new products that achieve a benefit that was not possible with either compound alone is yet another area of commercial interest.

However, the amount silicones incorporated into personal care formulations is quite small in comparison to all other applications for silicones. And the marketing of such materials will be less a selling of a product line and more and more a development of highly functional materials for the specific high-demand application.

At this purpose this interesting book is of a great help for all the cosmetic chemists and dermatologists involved in the formulation of innovative *cosmeceuticals*.

It will be also useful for all the chemists, medical doctors or marketing-oriented people that need to understand the science of these unusual and highly functional raw material: the silicones.

What it is interesting to remember is that late studies have shown that silicones degrade and don't contribute to the formation of ozone or greenhouse gases.

P. Morganti
Editor-in-Chief

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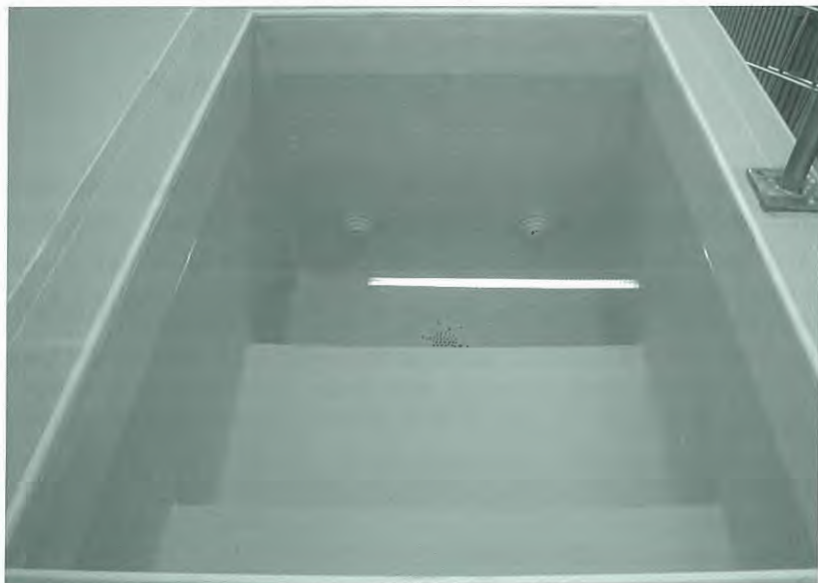
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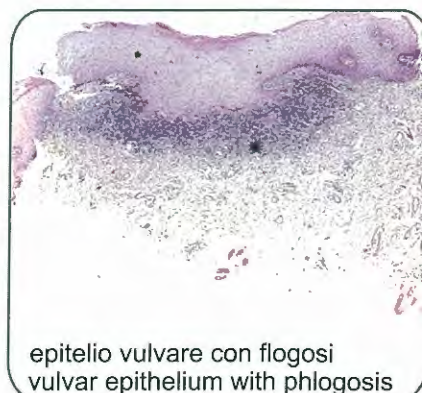
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