A conversation with Dr. Ratan Chaudhuri,

President & CEO of Sytheon Ltd. about novel approaches to sun protection

EURO COSMETICS: *What's new in sun protection science?*
Dr. Ratan Chaudhuri: It is well known that UV light acts directly on DNA to form immediate cyclobutane pyrimidine dimers (iCPDs) within picoseconds, which, if not repaired, subsequently result in a mutation—a cytosine-to-thymine change. Most melanomas stem from these fast-forming CPDs that linger and lead to mutations.
Yale Researchers, Professor Douglas Brash and his team, uncoverd a previously unknown way UV light can act on melanin, spurring cancer-causing mutations hours after sun exposure. The fact that this delayed CPDs (dCPDs) appears to be derived from the important photo-protective molecule melanin is an intriguing photochemical irony. This new cellular pathway is an exciting discovery for two reasons – (1) it is enzyme induced and (2) an alternate way by which DNA can be damaged. This may be an important pathway for causing melanoma and skin needs to be protected from this damage. It also provides a reason why UVA exposure is carcinogenic. This is indeed a breakthrough research.

EURO COSMETICS: *What are your thoughts about including antioxidants in sun protection products and what value does this approach add?*
Dr. Ratan Chaudhuri: Skin ages due to the constant exposure to sunlight as UV radiation from the sun penetrates cells and increases the number of damaging free radicals, especially the reactive oxygen species. Too many reactive oxygen species can be harmful because they can damage the DNA within cells, degrade protein, lipids and other biomolecules. Over time, this can lead to the accumulation of mutations which speed up aging and destroy the skin's supportive fibers, collagen and elastin, causing wrinkles. Needless to say, effective antioxidant(s) has to be part of a sunscreen regimen.

Dr. Ratan Chaudhuri,
President & CEO of Sytheon Ltd.
(photo taken by Maya Ganguli)

EURO COSMETICS: *What role do chelating agents play in protecting sun-induced oxidative stress?*
Dr. Ratan Chaudhuri: UVA exposure leads to an immediate measurable increase in free iron in human skin. Free iron is a catalyst of biological oxidations due to its reaction with hydrogen peroxide. This chemistry is very well-known Fenton reaction. Conventional chelating agents, such as EDTA, EDDS, and Desferal failed to stop this oxidative reaction due to inefficient chlelation whereas a new antioxidant-chelant developed by Sytheon was able to completely reduce iron-induced oxidative stress due to efficient chelation. Selection of right chelating agent, which is capable of occupying all six coordination sites in iron, is critical to stop oxidative stress induced by free iron.

EURO COSMETICS: *In an ideal world, how would you select ingredients for reducing sun-induced oxidative stress on skin?*
Dr. Ratan Chaudhuri: Multi-targeted approach is needed to reduce sun-induced oxidative stress on skin. Photostable broad-spectrum sunscreen is a must. This needs to be supplemented with one or more broad-spectrum antioxidants working by multiple pathways, effective iron chelator which is able to occupy all six co-ordination sites in iron, able to inhibit NADPH oxidase activity, one of the key enzymes, responsible for formation of dCPDs. Needless to say, a smart skin hydrator and barrier builder is also needed for maintaining optimum skin hydration of about 70%.

EURO COSMETICS: *Why are delayed Cyclobutane Pyrimidine Dimers (dCPDs) so important vs immediate CPDs (iCPDs) in skin protection?*
Dr. Ratan Chaudhuri: Inhibition of both CPDs are critical for skin protection. Formation of dCPDs and its mechanistic details were unknown before 2015. This means that existing measurements of DNA damage from sunlight – which record only the immediate effect – probably underestimate the true skin damage. Understanding the enemy is the first step to neutralising it. This findings may be the missing link and is particularly important as the most aggressive type of skin cancer, melanoma, is on the rise globally.

EURO COSMETICS: *Are there any differences between UV-A and UV-B exposure and formation of iCPDs?*
Dr. Ratan Chaudhuri: Yes. UVB readily induces formation of iCPDs and pyrimidine (6-4) pyrimidone photoproducts (6-4PPs) whereas UVA (more specifically, UVA1) clinically shown to induce only iCPDs without 6-4PPs due to DNA damage.

EURO COSMETICS: *Are you aware of any product which can reduce formation of (dCPDs)?*

Dr. Ratan Chaudhuri: Prof. Brash and his team described the mechanistic pathways responsible for delayed CPDs formation. The delayed pathway can be intervened at several points, creating an opportunity for developing a new skin protectant that prevents the enzyme activation or divert the energy from the excited electron into heat before it can damage DNA. Sytheon, being a small company with limited resources, did not stop thinking big and has already made a big jump in developing an "Evening-after Sunscreen". This terminology is coined by Prof. Brash. In fact, the potential of the target compound has been validated by Prof. Brash using his protocol. Give us another six months, this new breakthrough product will hit the market.

EURO COSMETICS: *As you look ahead in the field of suncare research, what path(s) appear most promising for generating further breakthroughs in this field?*

Dr. Ratan Chaudhuri: There is a lot of things to learn about skin damage due to sun exposure. Photon-induced DNA damage is a well-known pathway and much work has been done to prevent skin damage utilizing this pathway. Our understanding about enzyme-induced DNA damage is just over one year old. I would say prevention of skin damage induced by enzymatic pathways would bring many more breakthrough discoveries and novel skin protectants.

EURO COSMETICS: Thank you for the conversation. ■

Broad Spectrum UVA/UVB Sunscreen Lotion with ZnO & Synoxyl® HSS

Formulation #RC-02-13

In-vivo SPF 30 (FDA protocol); Critical Wavelength 370 nm
In-vivo SPF 20 (without Synoxyl® HSS)

INCI name	Trade Name/Supplier	% w/w
Phase A1	**Phase B**	
Water	Water (demineralized)	QS
Disodium EDTA	Versene Na/Dow	0.10
Propanediol	Zemea/DuPont	2.50
Glycerin	Emery 916/BASF	2.00
Propyl Gallate	Sytheon	**0.10**
Phase A2		
Xanthan Gum	Keltrol CG-T/CP Kelko	0.25
Magnesium Aluminum Silicate	Veegum Ultra/Vanderbilt	1.75
Phase B		
Glyceryl Stearate SE	Cerasynt Q/Ashland	1.75
Steareth-21	Brij 721/Croda	1.60
Cetyl Alcohol	Crodacol C-70/Croda	2.00
Steareth-2	Lipocol S-2/Lipo	1.40
Butyrospermum Parkii (Shea) Butter	Shebu Refined/Rita	1.00
Trimethoxybenzylidene Pentanedione	**Synoxyl® HSS/Sytheon**	**1.50**
Phenethyl Benzoate	X-Tend 226/Ashland	7.50
Isosorbide Dicaprylate	**HydraSynol™ DOI/Sytheon**	**2.00**
Dimethicone	Dow Corning 200,100 cst/Dow Corning	1.00
Phase C		
Ethyl Macademiate	Floramac 10/Floratech	8.00
Polysorbate 80	Tween 80/Croda	0.50
Polyglyceryl 3 Diisostearate	Plurol Diisostearique/Gattefosse	0.50
Zinc Oxide, Triethoxycaprylylsilane	Zano 10 Plus/Umicore	10.00
Phase D		
Phenoxyethanol, Ethylhexylglycerine	Euxyl PE 9010/Schülke	1.00
Total		100.00

Procedure

Combine A-1; disperse A2 one by one in A1 while stirring and heat A to 75°C. Combine ingredients of phase B and heat to 75 0C. Premix Phase with high shear and add to phase B before emulsification. Add phase BC to A with good mixing. Homogenize mixture at moderate speed. Cool batch to 450C with propeller agitation. Add phase D while continue mixing.

Notes:

pH - 6-6.50 Viscosity – 40,000- 60,000mPas (Brookfield RVT, Spindle C, 10 rpm) at 25°C