

Risk analysis tools for toxicological profile of cosmetics

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Abstract

Cosmetic products made up of mixtures of ingredients used by all age group of person to keep their skin healthier and fresh. Occasionally, undesirable sides effect both local and systemic may occur with the use of cosmetics. Claimed effects and safety of cosmetic products depends upon the ingredients incorporated. Study of risk assessment associated with ingredients is the best way to avoid future problems. By adopting proper methodologies and techniques risk factors of ingredients incorporated in cosmetics can be determined and managed at safety level. This paper enlightened the toxic effects associated with some of the cosmetic ingredients, with the tool used for risk analysis and management procedure. This review encourage the industrialist, cosmeticians, pharmacist and researchers to carry and publish more cosmetic toxicity studies, which would help to explore the myth of cosmetics in front of consumers that will beneficial in terms of human health.

INTRODUCTION

Skin is the effective barrier to the environmental.

Disturbances to this barrier lead to the development of various skin problems. Cosmetic products are widely used by every socio class of human being to cleanse, perfume, protect and change the appearance of skin. Most cosmetic products contain a combination of ingredients such as emulsifiers, preservatives, thickener, colour, fragrance, UV filters (sunscreens), humectants, occlusive agents and pH stabilizers. Sometimes the ingredients in cosmetics can have unintended side effects. Most serious side effects have been noticed from various studies for certain cosmetic ingredients. Thus, it is necessary to have the best knowledge possible about each ingredient used, both in relation to its characteristics as well as to its toxicological data, taking into account the many potential risks related to its cosmetic use. The safety of a cosmetic product is based on the safety of its ingredients, the latter being evaluated by toxicological testing (Pauwels and Rogiers, 2004). Toxicity testing has been concentrated on ingredients, and particularly on those that are intended to react with biological matrices and therefore are of most concern for human health. The Threshold of Toxicological Concern (TTC) is a concept that refers to the establishment of a level of exposure for all chemicals, whether or not there are chemical specific toxicity data, below which there would be no appreciable risk to human health (Kroes, 2005).

Some activist groups have targeted cosmetics as possible

human health threats, claiming that cosmetic ingredients are not adequately tested for safety and may pose risks to consumers. The groups allege that industry practices related to safety testing are flawed, that there is little government oversight, and that cosmetics contain cancer-causing chemicals and other toxicants (Ross, 2006).

When a formulation is being considered for safety a risk assessment must consider the general toxicological profile of the ingredients and their level of exposure. More recently the toxicity and efficacy of cosmetics and their ingredients has been under the spotlight. So cosmetic which are used mainly for beautification purpose is not free from side effects that myth should be cleared in front of consumers. There are some ingredients that found to be toxic and banned by all legislations but highly used by cosmetic industry, about which common consumers even academicians, pharmacist, cosmetician and chemist are also not aware. Various regulatory bodies like Food and drug administration (FDA), European union (EU) e.t.c. has identified the cosmetic ingredients that are either approved or prohibited on the basis of the toxic effects produced by them (Table 1, 2 and 3). Results of toxicology and safety testing are not always publicly disclosed, cosmetic manufacturers have internal processes, programs, and testing protocols that are designed to ensure the safety of the products they produce.

The present paper describe about the key principle of risk assessment used for evaluation of toxicological profile of cosmetics with special reference to the methodologies and

techniques used for managing risk at optimum level. Objective of this review to motivate all academicians, chemists, beauticians, pharmacist, industrialist and researchers to perform risk assessment study of cosmetics by adopting proper legislation and publish. This would be helpful to upgrade the knowledge, increased the trust and disclosed the myths of common consumers regarding cosmetic products.

Figure 1

Table 1: List of ingredients with approved limits in sunscreens

S.no	Ingredients	Limits
1	p-Aminobenzoic acid	15 %
2	Avobenzone	3%
3	Canoxate	3%
4	Dioxybenzone	3%
5	Homosalate	15%
6	Menthyl anthranilate	5%
7	Octocrylene	10%
8	Octyl methoxycinnamate(Octinoxate)	7.5%
9	Octyl salicylate(Octisalate)	5%
10	Oxybenzone	6%
11	Padimate O	8%
12	Phenylbenzimidazole sulfonic acid (Ensulizole)	4%
13	Sulisobenzone	10%
14	Titanium dioxide	25%
15	Trolamine salicylate	12 %
16	Zinc oxide	25%

Figure 2

Table 2: List of Prohibited and Restricted Ingredients

S.no	Ingredient	Side effects	Used in	Jurisdiction
1	Bithionol	Photo-contact sensitization	Detergent bars, shampoos, creams, lotions	March 15, 1968
2	Mercury	Potent allergen, skin irritation	Creams and lotions, hair straighteners, bubble bath, antiperspirants	May 13, 1939
3	Halogenated salicylanilides	Photosensitization	Antimicrobial agents in cosmetics	40 FR 50531, Oct. 30, 1975
4	Vinyl chloride	Dizziness, headache, disorientation, and unconsciousness	Hair sprays, cosmetic aerosol products	39 FR 30830, Aug. 26, 1974
5	Zirconium complexes	Skin granulomas	Antiperspirants	42 FR 41376, Aug. 16, 1977
6	Chloroform	Hepatocellular carcinomas	Cosmetic products	41 FR 26845, June 29, 1976
7	Methylene chloride	Benign and malignant tumors of the lung	Hair sprays, aerosol cosmetic products	54 FR 27342, June 29, 1989
8	Chlorofluorocarbon propellants	Skin irritation	Cosmetic aerosol products	43 FR 11317, Mar. 17, 1978]
9	Hexachlorophene	Toxic effect	Alternative preservative	(37 FR 6775 April 4, 1972

Note: Mercury NMT 0.0065 % in eye cosmetics and NMT 0.0001% in other Cosmetics, Hexachlorophene NMT 0.1%.

Figure 3

Table 3: List of banned Ingredients

S.no	Ingredients	Side effects	Used as/in
1	Paraben	Allergic reactions and skin rashes	Antimicrobial agent
2	Diethanolamine (DEA), Triethanolamine (TEA)	Allergic reactions, eye irritation, dryness of hair and skin	Emulsifiers, foaming agents
3	Diazolidinyl Urea, Imidazolidinyl Urea	Contact dermatitis	Preservatives
4	Sodium Lauryl/Laureth Sulfate	Eye irritation, skin rashes, allergic reactions	Detergent in shampoos
5	Petrolatum	Dryness and chapping	Emollient
6	Propylene Glycol	Allergic reactions, hives and eczema	Humectant
7	PVP Copolymer	Toxic can damage the lungs	Hair sprays
8	Stearylalkonium Chloride	Allergic reactions	Hair conditioners and creams
9	Synthetic Colors	Carcinogenic	Hair dyes
10	Synthetic Fragrances	Headaches, dizziness, rash, hyperpigmentation, violent coughing	Creams and deodorants

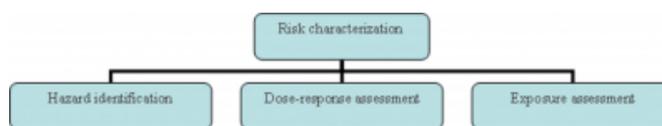
Note: Don't buy a cosmetic that has the word "fragrance" on the ingredients label.

RISK ASSESSMENT AND RISK MANAGEMENT

Each cosmetic finished product is an individual and unique combination of ingredients. No ingredients, whether naturally occurring or manufactured, is absolutely free from potential toxic effects. To allow a better safety evaluation risk associated with cosmetic ingredients should be assessed and properly managed [WHO, 2001; EC, 2000]. General principles and practice adopted for risk assessment process, is represented in Fig 1.

Figure 4

Figure 1: Principles and practice of the risk assessment process



Risk assessment is the process which identifies and quantifies the risk resulting from a specific use or occurrence of chemical or physical agents (ingredients). This risk can be assessed by 4 ways.

Hazard identification: It is based on the results of in vivo tests, in vitro tests, clinical studies, accidents, human epidemiological studies. In this the intrinsic physical, chemical and toxicological properties of the product/ingredient under consideration are studied to identify whether the substance has the potential to damage human health or not.

Dose-response assessment: In this the relationship between the toxic response and the exposure of ingredient is studied. In the case of an effect with a threshold, the dosage at which no adverse effects are observed (NOAEL) is determined. If the NOAEL is not available, the LO(A)EL is used. In the

case of non-threshold carcinogens, a dose-descriptor (e.g. T_{25}) is determined [Dybing et al., 1997].

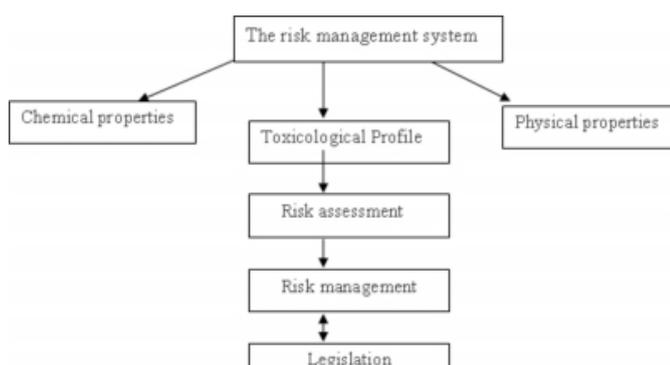
Exposure assessment: Study in which the amount and the frequency of human exposure to the product is determined.

Risk characterization: It is used to examine the probability of the ingredient/molecule to cause the damage to human health and its potency to produce damage.

Risk Management is a decision-making process in which the optimal steps are selected for reducing a risk produced by ingredients to an acceptable level. Risk management (Fig 2) procedure is often controlled by legislation, which lays down allowable limits of exposure and puts specific duties on management and workers [Beck et al., 1994; Dayan, 1999; Loprieno, 1999; Rogiers, 2002a; Masson, 1999; Sanner 2001].

Figure 5

Figure 2: Legislation control over risk management system.



RISK ANALYSIS

Risk analysis of cosmetic ingredients should be carried out by performing physicochemical analysis, toxicological analysis (SCCNFP/0690/03, 2003) and microbial contamination examination.

PHYSICOCHEMICAL ANALYSIS

A small molecular weight hydrophobic compound is more likely to penetrate through the skin than a high molecular weight hydrophilic compound and a highly volatile compound could cause significant inhalation exposure when present in a product applied to the skin. Hence, physical and chemical properties of cosmetic ingredients should be seen as they may be able to predict certain toxicological properties. The basic and minimal specifications such as chemical identity, physical form, molecular weight (M.W), purity of the chemical, characterization of the impurities or accompanying contaminants, solubility, partition coefficient

(Log Po/w) of any ingredient should be considered and the information obtained from study of above points must be included in each toxicological dossier.

TOXICOLOGICAL PROFILE ANALYSIS

The assessment of the toxicological potential is the most important step in the hazard evaluation of a cosmetic ingredient and consists in a series of distinct toxicity studies. This study carried out in terms of evaluations of distinct toxicological parameters which are as follows.

1) ACUTE TOXICITY

It is evaluated to describe the adverse effects on health, which may result from a single exposure to a substance via the oral, dermal or inhalation route [ECB, 2003]. The *in vivo* acute oral toxicity test was originally developed to determine the LD50-value (the dose at which 50% of the animal dies, Table 4) of the compound under investigation. It is now replaced by the alternative methods that are fixed dose method [EC B.1 bis, 1992; OECD 1992], acute toxic class method [EC B.1 tris, 1996; OECD, 1996], up-and-down procedure [OECD, 1998].

2) IRRITATION AND CORROSIVITY

This is evaluated in terms of skin irritation, skin corrosivity and mucous membrane irritation produced by cosmetic ingredients.

A) SKIN IRRITATION AND SKIN CORROSIVITY

Skin irritation tests have been developed to assess the potential of a certain substance to cause redness and edema after a single topical application and skin corrosion tests assess the potential of a substance to cause irreversible necrosis through the epidermis and into the dermis, following the application of a test substance for the duration period of 3 minutes up to 4 hours. Corrosive reactions are notified by formation of ulcers, bleeding, and scabs. At the end 14 days, discoloration of the skin, alopecia, and scars will be observed to assess the extent of skin corrosion reactions [OECD, 1981]. Validated *in vivo* [Draize, 1965] and *in vitro* [Archer and Liebisch, 1998] method that is used for evaluating skin irritation and skin corrosion is mentioned in table 4 and table 5 respectively.

B) MUCOUS MEMBRANE IRRITATION

Mucus membrane irritation will be accessed by determining ocular irritation produced by cosmetic ingredients after a single application. Ocular irritation tests have been developed to assess the potential of a certain substance to

cause chemosis, discharge, redness to the conjunctiva, swelling of the iris and opacity to the cornea. Classical in vivo ocular irritation test [Kay and Calandra., 1962, Table 5] and the HET-CAM test [Gilleron et al., 1996] is a valid in vitro alternative method for evaluating mucous membrane irritation (Table 5).

3) SKIN SENSITIZATION

A skin sensitizer is an agent that is able to cause an allergic response in susceptible individuals. Three common in vivo laboratory animal test methods (Table 4) widely in being used to evaluate the potential of a substance to cause skin sensitization are Local Lymph Node Assay (LLNA), Guinea Pig Maximisation Test (GPMT) and Buehler test [OECD, 2002; Magnusson and Kligmann, 1969; Buehler, 1965]. Till date there is no validated in vitro test method accepted for skin sensitization.

4) DERMAL / PERCUTANEOUS ABSORPTION

Human exposure to cosmetic ingredients occurs mainly via the skin. In order to reach the circulation cosmetic ingredients must cross a number of cell layers of the skin. The in vivo and in vitro dermal / percutaneous absorption studies have been described by several international bodies [ECETOC, 1993; US EPA, 1996]. Dermal / percutaneous absorption is the amount of dermally applied substance remaining in the residual skin (excluding the stratum corneum) plus the amount of dermally applied substance which has transpassed the skin and is detected in the receptor fluid. The sum is considered to be systemically available [Bronaugh, 2005].

5) REPEATED DOSE TOXICITY

Repeated dose toxicity comprises the adverse general toxicological effects occurring as a result of repeated daily dosing with exposure to, a substance for a specific part of the expected lifespan of the test species [ECB, 2003]. The 28-day and 90-day oral toxicity tests in rodents are the most commonly used repeated dose toxicity tests and often give a clear indication on target organs and type of systemic toxicity. Currently no validated or generally accepted alternative methods are available for replacing animal testing.

6) MUTAGENICITY/GENOTOXICITY

Mutagenicity refers to the induction of permanent transmissible changes in the amount or structure of the genetic material of cells or organisms. Genotoxicity is a broader term and refers to potentially harmful effects on

genetic material that are not necessarily associated with mutagenicity. Several in vitro gene mutation test (Table5) and in vivo tests are available and have been described for evaluating mutagenicity and genotoxicity of cosmetic ingredients [OECD, 1984; ECB.17, 2000], but for most cosmetic ingredients, in vivo tests are not considered imperative. For testing the potential genotoxicity/mutagenicity/carcinogenicity of oxidative hair dye ingredients a new strategy was adopted by the SCCNFP in June 2003 [SCCNFP/0720/03, 2003].

7) CARCINOGENICITY

Substances are defined as carcinogenic if they induce tumours, increase their incidence, malignancy when they are inhaled, ingested, dermally applied or injected [ECB, 2003]. In vivo carcinogenicity tests [Amdur et al., 1991, Table 4] and in vitro Syrian Hamster Embryo (SHE, Table 5) Transformation Test [OECD, 1996b] is the most commonly performed methodologies to evaluate carcinogenic action of cosmetic ingredients.

8) REPRODUCTIVE TOXICITY

Reproductive toxicity is used to describe the adverse effects induced by a substance on any aspect of mammalian reproduction. The most commonly performed in vivo reproduction toxicity studies are done by teratogenicity test [Amdur et al., 1991, Table 4]. Three alternative in vitro methods (Table 5), Whole Embryo Culture test (WEC) Micro Mass test (MM) and Embryotoxic Stem cell Test (EST) are used to evaluate reproductive toxicity of cosmetic ingredients [ESAC, 2001].

9) TOXICOKINETIC STUDIES

Toxicokinetic studies explain the time-dependent fate of a substance within the body. This includes absorption, distribution, biotransformation and its excretion [ECB, 2003]. In specific cases, in vivo or in vitro biotransformation studies are required to prove and to exclude certain adverse effects associated with cosmetic ingredients. Several in vitro models (hepatocytes in suspension or culture) are suitable for biotransformation studies (Table5), however, none of these models has been validated [Blauboer et al., 1994; Coecke et al., 1999] since so far for evaluation purpose. Finally, toxicokinetic studies are of importance in extrapolating both in vitro and in vivo animal data to man.

10) PHOTO-INDUCED TOXICITY

It is measured in terms of photoirritation and photomutagenicity of cosmetic ingredients.

a) Photoirritation /photosensitization – in vitro method for the determination of the phototoxicological profile of all UV light absorbing chemicals and especially for those cosmetic ingredients to be used as UV filters [SCCNFP/0069/98]. The reliability and relevance of the in vitro 3T3 NRU phototoxicity test (Table 4) is already being evaluated for a number of substances with a chemically different structure [Spielmann et al, 1998] and various in vivo methods used for assessment (Table 4).

b) Photomutagenicity/ photogenotoxicity – photomutagenicity / photogenotoxicity test is desirable for UV radiation absorbing cosmetic ingredients is adopted by SCC, guidelines in 1990 [Dean et al., 1992].

11) HUMAN DATA VS / DATA

Tests in animals and alternative methods carried out for toxicity evaluation of ingredients are of limited predictive value with respect to human exposure. Therefore, a skin compatibility test with human volunteers is needed scientifically and ethically, to confirm that there are no harmful effects when applying a cosmetic product for the first time to human skin or mucous membranes.

In general, acute toxicity, irritation and corrosivity, skin sensitization, dermal / percutaneous absorption, repeated dose toxicity, mutagenicity/genotoxicity studies are considered the minimal base set requirements for toxicological evaluation of all cosmetics ingredients. However, when considerable oral intake is expected or when the data on dermal / percutaneous absorption indicate a considerable penetration of the ingredients through the skin then only carcinogenicity, reproductive toxicity and toxicokinetics studies may become necessary. Photo-induced toxicity data are specifically required when the cosmetic product is expected or intended to being used on sunlight-exposed skin. Human data are extremely useful and should be included whenever available.

Figure 6

Table 4: methodologies, test and animal models

S.No	Test	Animal model	References
1	Comedogenicity	Albino rabbits	Fulton et al, 1984; Kligman et al, 1979
2	Primary Dermal Irritability	Rabbits	Draze, 1965; Draze et al, 1944
3	Ocular irritability	Rabbits	Kay et al, 1962 Draze, 1965
4	Accumulated Dermal Irritability	Rabbits	Draze, 1965
5	Dermal Sensitization	Rabbits	Buehler, 1965
6	GPMT	Rabbits	Magnusson, 1969
7	Primary Dermal Photo-Irritation	Albino guinea pigs	Guillot et al., 1985
8	Accumulated Dermal Photo-Irritation	Albino guinea pigs	Guillot et al., 1985
9	Maximized Dermal photosensitization	Albino guinea pigs	Mailbach et al, 1996
10	Non-maximized Dermal Photosensitization	Albino guinea pigs	Waggoner, 1979
11	Phototoxicity	Albino guinea pigs	Mailbach et al, 1996
12	Oral LD-50	Mice or rabbits	OECD, 1992, 1996
13	Genital Mucous Irritability	Albino rabbits	Minsky et al, 1982; Eckstein et al., 1969
14	Oral Mucous Irritability	Hamsters	Draze et al., 1944; Aruta et al., 1991
15	Carcinogenicity	Mice/Rodents	Amdur et al., 1991
16	Teratogenicity	Mice/Rodents	Amdur et al., 1991
17	LLNA	Mice	OECD, 2002a

Figure 7

Table 5: methodologies with evaluation parameters

S.No	Technique	Evaluation parameters	References
1	HET-Cam	Ocular Irritation	Spielmann et al., 1997 Gilleron et al. 1996
2	BCOP	Ocular Irritation	Chamberlain et al., 1997
3	Cytotoxicity (Agarose gel diffusion test)	Ocular Irritation	Wallin et al., 1987, Combrier et al., 1992; Harbell et al., 1997
4	Cytotoxicity (Neutral Red method)	Ocular Irritation	Harbell et al., 1997, Borenfreund et al., 1998
5	Cytotoxicity (MTT Method)	Ocular Irritation	Harbell et al., 1997, Borenfreund et al., 1998
6	Corrosivity Test Rat skin TER	Skin Irritation	Archer et al., 1998 OECD, 2002b
7	Phototoxicity Test	Phototoxicity	Spielmann et al., 1998
8	Ames test	Photoirritation and sensitization	OECD, 1983a; ECB.13/14, 2000
9	Aberration test	Photoirritation and sensitization	OECD, 1983b; ECB.10, 2000
10	Gene mutation test	Photoirritation and sensitization	OECD, 1984; ECB.17, 2000
11	SHE transform test	carcinogenicity	OECD, 1996b
12	WEC test	Reproductive toxicity	ESAC, 2001
13	MM test	Reproductive toxicity	ESAC, 2001
14	ESC test	Reproductive toxicity	ESAC, 2001
15	Hepatotoxicity test	Toxicokinetic study	Andre, 1998

TER-Transcutaneous electrical resistance, HET-CAM- Hen's Egg Test – Chorio Allantoic Membrane

III) MICROBIAL EXAMINATION

Preservatives are added as ingredients in cosmetic products to make the products free from microbial side effect. To evaluate the potency of preservative efficacy challenge test is widely used which determines that preservative are in sufficient quantity to keep the product free from toxic effect [BIS, 2006]. COLIPA has proposed the microbial limit for the purity of cosmetics (Table 6). Membrane filtration and

plate count method is used for qualitative and quantitative specifications of microbes [Behravan et al, 2004].

Figure 8

Table 6: Limit for microbial purity of Cosmetics

S.No	Category	TVC (CFU per gm or per ml)	
		Aerobic Bacteria	Yeast & Moulds
1	Baby/Eye Products	>10 ²	> 10 ²
2	General Products	> 10 ³	> 10 ²
3	Products containing Natural Raw Materials	> 10 ⁴	> 10 ²

METHODOLOGIES AND TECHNIQUES

Some validated in vitro methodologies are already reported in the literature for monitoring specific toxicological parameters, but presently no validated in vitro alternative methods are available for the repeated dose animal toxicity studies nor there relevant proposals are ready for prevalidation/validation [Worth and Balls,2002; Rogiers, 2002b]. The toxicological evaluation of a cosmetic product should be certainly carried out with full knowledge of the pharmacotechnical, toxicological, pharmacokinetic, regulatory, clinical phase's areas and Scientific Committee of Cosmetics and Non-Food Products Intended (SCCNFP), Organization for Economic Cooperation and Development

(OECD), European Cosmetic, Toiletry and Perfumery Association (COLIPA), Cosmetics, Toiletries and Fragrances Association (CTFA), Bureau of Indian standard (BIS) and world health organization (WHO) guidelines. There are various in vitro (Table 1), in vivo (Table 4) and clinical methodologies (Table 7) for evaluating the toxicological potential of chemical substances.

Figure 9

Table 7: Clinical methodologies for evaluation of ingredients toxicity

S.No	Test/ Compatibility Assays	Number of Human Volunteers	References
1	Primary & accumulated cutaneous irritation	50	Mailbach et al,1996, Basketter et al,1997
2	Photourritation	25	Scott et al,1970, Kadbey et al,1997
3	Soap Chamber Test	15	Agrup 1968; Herman et al, 1972; Frosch et al,1979
4	Comedogenicity	5	Zahlove et al,1987
5	Dermal Sensitization	50	Mailbach et al, 1965; Kligman et al, 1967;
6	Photosensitization	25	Stork, 1965; Willis et al., 1968

CALCULATION OF RISK FACTORS

Risk factors for a cosmetic ingredient are calculated in terms of Margin of Safety (MoS), Systemic Exposure Dosage (SED) and Life time cancer risk.

1) MOS

Figure 10

$$MoS = \frac{NO(A)EL}{SED}$$

NO(A)EL : The No Observed (Adverse) Effect Level is the outcome of long-term toxicity studies, such as 28-day, 90-day tests .

SED: The Systemic Exposure Dosage of a cosmetic ingredient is the amount expected to enter the blood stream (and therefore be systemically available) per kg body weight and per day. It is expressed in mg/kg body weight/day.

This MoS value [Renwick, 1998] is used to extrapolate from a group of test animals to an average human being, and subsequently from average humans to sensitive subpopulations (Fig.3). These factors can be further subdivided as indicated in Fig .4 [WHO, 1994]. It is generally accepted that the MoS should at least be 100 to declare a substance safe for use.

Figure 11

Figure 3: Schematic representation of the extrapolation from animal to man

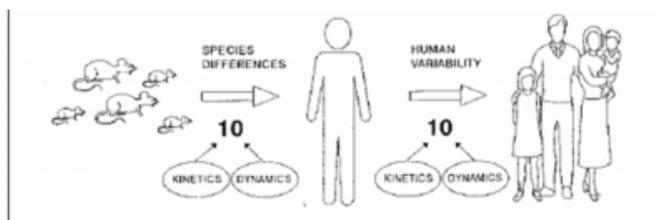
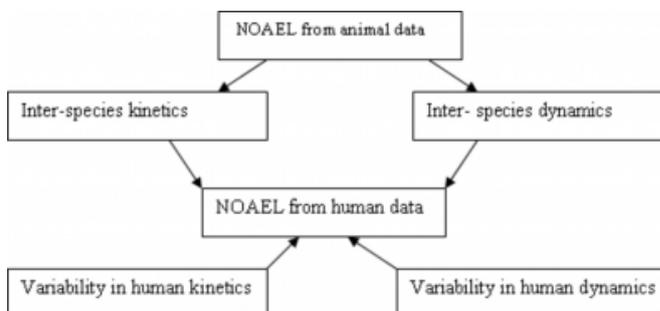


Figure 12

Figure 4: Subdivision of the Margin of Safety



2) SED

For testing skin absorption of product that mimics human

exposure, normally 1-5 mg/cm² for a solid and up to 10 µl/cm² for liquids should be used in vitro tests. Exceptions may exist with oxidative hair dyes, where 20 mg/cm² usually are applied for 30 minutes. There are two ways of calculating the SED

A) DERMAL ABSORPTION IN µG/CM

Calculations of the SED should preferably be based on the absolute amount bioavailable (µg/cm²) after a certain time period, based on the highest anticipated concentration.

Figure 13

$$SED = \frac{DA_a (\mu\text{g}/\text{cm}^2) \times 10^{-3} \text{mg}/\mu\text{g} \times SSA (\text{cm}^2) \times F (\text{day}^{-1})}{60 \text{ kg}}$$

SED (mg/kg bw/day) = Systemic Exposure Dosage

DA_a (µg/cm²) = Dermal Absorption reported as amount/cm²

SSA (cm²) = Skin Surface Area expected to be treated with the finished cosmetic product

F (day⁻¹) = Frequency of application of the finished product

60 kg = Default human body weight

B) DERMAL ABSORPTION IN PERCENTAGE

Calculations of the SED may also be based on the percentage dermally absorbed, lowest concentration anticipated.

Figure 14

$$SED = \frac{A (\text{g}/\text{day}) \times 1000 \text{mg}/\text{g} \times C (\%)/100 \times DA_p (\%)/100}{60 \text{ kg}}$$

SED (mg/kg bw/day) = Systemic Exposure Dosage

A (g/day) = Amount of the cosmetic product applied daily

C (%) = Concentration of the ingredient under study in the finished cosmetic product on the application site

DA_p (%) = Dermal Absorption expressed as a percentage

60 kg = Default human body weight

3) LIFETIME CANCER RISK

Determination of the lifetime cancer risk is carried out in several distinct steps. The dose-descriptor T₂₅ is defined as the chronic dose rate that will give 25% of the animal's tumours at a specific tissue site after correction for spontaneous incidence, within the standard life time of that

species. The determination of T₂₅ is described in details by Dybing et al. [1997]. From the experimental data an animal dose descriptor (T₂₅) is determined and converted to a human dose descriptor (HT₂₅) by using the following formula [Sanner et al. 2001]. Subsequently, the lifetime cancer risk is determined by linear extrapolation to the actual exposure dose. Finally, a commentary statement is generated stating whether an overall evaluation of all data available indicates that the actual risk may be higher or lower than the calculated risk.

Figure 15

$$HT_{25} = \frac{T_{25}}{(\text{body weight human}/\text{body weight animal})^{0.25}}$$

$$\text{Lifetime cancer risk} = \frac{SED}{HT_{25} / 0.25}$$

SED represents the lifetime daily dose expressed in mg/kg bw/day.

CONCLUSION

As time progressed, through invasions and migrations and cultures merged there has been profound effect on the value of cosmetics. Cosmetic products are developed to be applied to human skin and external mucosa and to be used by the general public. Skin and mucous membrane irritation are the most frequently observed reactions. Cosmetic products should be free from side effects as their use is concern to human health. To access the risk and the safety of cosmetic products it is necessary to determine the characteristics and toxicological data of cosmetic ingredients. With a view to checking the chemical nature of the ingredient and its degree of purity, methods should be devised for identification, qualitative and quantitative control. The maximum admitted concentration of ingredients in formula of cosmetic product must be based on toxicological values, as it is a dose that makes the poison. Toxicological data can be obtained by adopting standard methodologies and techniques. Study of risk assessment reveals specific toxicity associated with the particular ingredients that can be useful to avoid its use in cosmetics. Calculations of risk factors determine the margin of safety of ingredients that can be helpful in risk management. Paper upgrades the knowledge of common consumers, academicians, chemist and beautician about cosmetics. At last study conclude that there is a need of integrated research by adopting proper guidelines at scientific level to eliminate the risk at zero level to produce safe cosmetics.

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