Toxicity Prediction of Cosmetics Product through Bioinformatics Tool: T.E.S.T

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Abstract: **Cosmetics are care substances used to enhance the appearance or odor of the human body. Many dangerous substances are used in cosmetics products which are harmful for our skin and cause skin allergies and skin irritation. Everybody should know that they have biological effects and must be used with special care in minimum doses. This reasoning is not applicable to cosmetics. Personal care products are directly applied to the surface of the human body frequently and relatively to the large amounts that affects the skin directly because of the presence of toxic chemicals in it. Chemical reactivity related toxicity is low while biological receptor activity is higher dimensional in chemistry space. In prediction of toxicity, the use of insilico prediction method such as QSAR (Quantitative Structure Activity Relationship) model is required or encouraged in order to increase efficiency and minimize the reliance on animal testing. A total 69 chemical compounds analyzed through T.E.S.T (Toxicity Prediction Software Tool) have been developed to allow users to easily estimate toxicity using the variety of QSAR methodologies by using .T.E.S.T. software version 4.1 predict the toxicity properties (i.e., Oral rat LD50 and mutagenicity). In this work some cosmetic compound shows positive and negative results and this chemical molecule further testing in wet lab.**

Keyword:Cosmetics, Heavy metals, Biological effects, Minimum doses, Chemical reactivity, QSAR(Quantitative Structure Activity Relationship).

I. INTRODUCTION:

A. ***Cosmetics*** *(colloquially)*

known as makeup or make-up) are care substances used to enhance the appearance or odor of the human body(1).Cosmetic product shall mean any substance or mixture intended to be placed in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance and correcting body odors and protecting them or keeping them in good condition(2).Millions of consumers use personal care products (PCP) and their ingredients on a daily basis. Although human external contact with a substance rarely results in its penetration through the skin and significant systemic exposure. Therefore, human systemic exposure to their ingredients can rarely be completely excluded. In addition, natural and synthetic substances may produce local effects in human skin, such as irritation, sensitization or photoreactions. Given significant and relatively uncontrolled human exposure to PCP, these products must be thoroughly evaluated for their safety prior to their marketing (3). Does the composition of the product confirm with the Cosmetic Directive and the Cosmetic Products (Safety) Regulations. Ingredients which are prohibited in cosmetic products ingredients which are restricted in cosmetic products preservatives, UV filters and colorants which are permitted in cosmetic products (preservatives, UV filters and colorants not listed in the Schedules to the Regulations are not permitted in cosmetic products).If the composition of the product is not in accord with these Regulations it cannot be marketed as a cosmetic, regardless of claims made or the absence of such claims i.e., Tooth whitening products are cosmetics. However, there is a limit of 0.1% of Hydrogen Peroxide present in the product or released in use. A tooth whitener with hydrogen peroxide in excess of the limit is an illegal cosmetic. If a product is not a cosmetic, it may fall under another regulatory regime such as that for foods, biocides or general product safety. However, care must be taken to ensure that what is, at first sight, a cosmetic does not become a medicine by virtue of its presentation, its claims or its composition(2).The main ingredients in mineral make-ups are usually coverage pigments, such as zinc oxide and titanium dioxide, both of which are also physical sunscreens. Other main ingredients include mica (Sericite) and pigmenting minerals, such as iron oxide, tin oxide and magnesium myristate. Mineral makeup usually does not contain synthetic fragrances, preservatives, parabens, mineral oil, and chemical dyes. For this reason, many dermatologists consider mineral makeup

to be purer and kinder to the skin than makeup that contains those ingredients. However, some mineral makeups contain Bismuth oxy-chloride, which can be irritating to the skin of sensitive individuals. Others also contain talc, over which there is some controversy because of its comedogenic tendencies (tendency to clog pores and therefore cause acne) and because some people are sensitive to talc. Mineral makeup is non-comedogenic (as long as it does not contain talc) and offers a mild amount of sun protection (because of the titanium dioxide and zinc oxide).Because they do not contain liquid ingredients, mineral make-ups can last in their containers indefinitely as long as the user does not contaminate them with other liquid or fingertips (3).

B. Tools and techinques

A) DATABASE :-

ZINC DATABASES – (http://zinc.docking.org/)
Zinc is a free database of commercially available compounds for virtual screening, it contains about 21 million purchasable compounds in ready to dock, 3D formats.

Pubchem – (http://www.ncbi.nlm.nih.gov/pccompound)
Pubchem compound database contains validated chemical depiction information provided to describe substances in Pubchem substances, Structure stored within Pubchem compounds are pre-clustered and cross-referenced by indentify and similarity groups.

DRUG BANK – (http://www.drugbank.cal./)
The **Drug Bank** database is a unique bio informatics and chem informatics resources that combines detailed Drug (i.e. chemical, pharmacological and pharmaceutical) data with comprehensive drug target information.

B. SOFTWARE :-

T.E.S.T. SOFTWARE TOOL– (http://www.epa.gov/nrmrl/std/qsar/qsar.html)

T.E.S.T. (Toxicity Estimation Software Tool) has been developed to allow users to easily estimate toxicity using a variety of QSAR methodologies. T.E.S.T. allows a user to estimate toxicity without requiring any internal programme.

Toxicity end points :- T.E.S.T allows you to estimate the value for several toxicity end points :-

- 96 hours fathead minnow LC 50 (concentration of the chemical in water in mg/l that causes 50% of fathead minnow to die after 96 hrs).
- 48 hrs daphnia magna LC50 (concentration of the test chemical in water in mg/l that cause 50% of daphnia magna to dies after 48 hrs).
- 48 hrs tetrehymena pyriformis IGC50 (concentration of the test chemical in water in mg/l that causes 50% growth inhibition to tetrahymena pyriformis after 48 hrs).
- Oral rat LD50 (amount of chemical in mg/kg body weight that causes 50% of rats to die after oral ingestion).
- Bioaccumulation factors (ratios of the chemical concentration in fish as a result of absorption via the respiratory surface to that in water at steady state).
- Development toxicity (whether or not a chemical causes developmental toxicity effects to humans of animals).
- Ames mutagenicity (a compound is positive for mutagenicity if it induces revertant colony growth in any strain of salmonella typhimurium).

C. T.E.S.T also allows you estimate several physical properties :-

- Normal boiling point (the temperature in deg. cel. at which a chemical boils at atmospheric pressure)
- Density (the density in g/cm cube)
- Flash point (the lowest temperature in deg. cel. At which it can vaporize to form an ignitable mixture in air)
- Thermal conductivity (the property of a material in units of mw/mk reflecting its ability to conduct heat)
- Viscosity (a measure of the resistance of a fluid to flow in it defines as proportionality constant between shear rate and shear stress)
- Surface tension (a property of the surface in dym/cm of a liquid that allows it to resist an external face)
- Water solubility (the amount of a chemical in mg/l that will dissolve in liquid water to form a homogenous solution)

II. METHODOLOGY :-

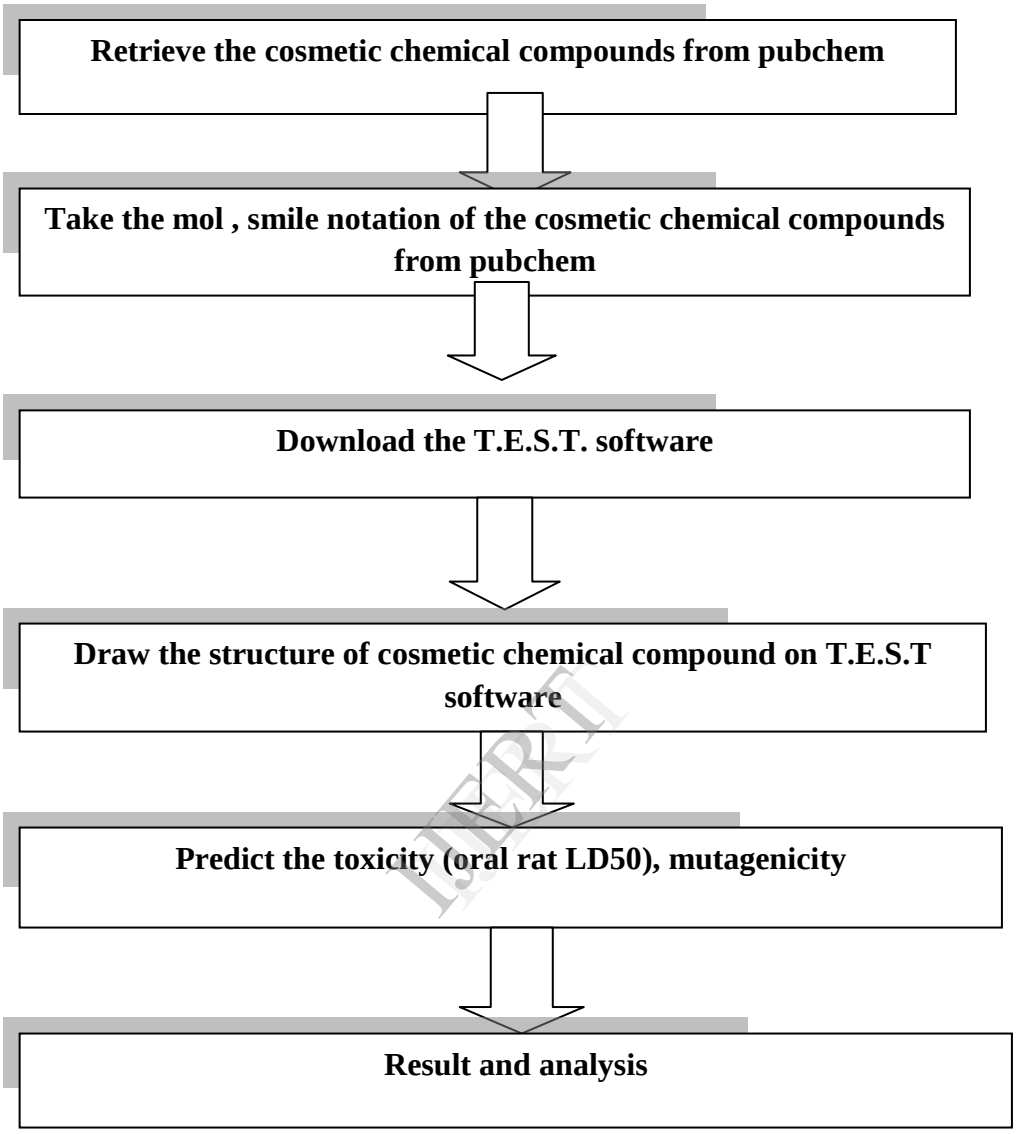

TABLE NO:-1 Information of Cosmetic Chemical Compounds

S.no.	Cosmetic Chemical Names Effects →
1.	2-bromo-2-nitropropane-1,3-diol => immune toxicant
2.	Acrylamide => Possible human carcinogen
3.	Alcohol denatured => Known or suspected teratogen
4.	Ammonium glycolate => Penetration enhancer
5.	Ammonium lactate => Penetration enhancer
6.	Ammonium persulfate => Known human carcinogen
7.	Butoxyethanol => Known human carcinogen
8.	BHT => Immune toxicant
9	Bronopol => Immune toxicant
10.	Butyl methacrylate => Immune toxicant
11.	Benzalkonium chloride => Neuro-toxicant
12.	Carbolic acid => Known human carcinogen
13.	Chlorine dioxide => Reproductive system toxicity
14.	Dibutyl phthala => Potential birth defects
15.	Dimethylamine => Immune toxicants
16.	di-limonene =>Reproductive system toxicity
17.	Di-sodium EDTA => Penetration enhancer
18.	Ethanolamine => Known human carcinogen
19.	Ethelene glycol => Reproductive system toxicity
20.	Eugenol => Immune toxicant
21.	Glutaral => classified toxic
22.	Glycolic acid => Classified toxic
23.	Glacial acetic acid => Classified toxic
24.	Glycerol isostearate => Reproductive system toxicity
25.	Glyceryl hydroxystearate => Penetration enhancer
26.	Glycerine => Occupational hazard
27.	Hexachlorophene => Known human carcinogen
28.	Hydroabietyl alcohol => Possible human carcinogen
29.	Hydrogen peroxide => Known human carcinogen
30.	Hydroquinone => Known human carcinogen
31.	Isopropanol => Reproductive system toxicity
32.	Iodine => Estrogenic chemicals
33.	Isobutane => Immune toxicants
34.	Ketokonazole =>Endocrine disruptors
35.	Kojic acid => Possible human carcinogen
36.	Lactic acid => Immune toxicant
37.	Lauryl lactate => Penetration enhancer
38.	Linoleamide-DEA => Harmful impurities
39.	Metheamine =>

	Possible human carcinogen
40.	MEA => Known or suspected teratogen
41.	Methyl salicilate => Reproductive system toxicity
42.	N-phenyl-P-Phenylenediamine => Known human carcinogen
44.	Nephazoline hydrochloride => Known human carcinogen
45.	Niacin => Classified toxic
46.	O-amino phenol => Known human carcinogen
47.	Octozynol-9 => Immune toxicant
48.	p-phenylenediamine => Known human carcinogen
49.	p-amino phenol => Known human carcinogen
50.	Parabens => Reproductive system toxicity
51.	Propyleneglycol => Immune toxicant
52.	Quartz => Known human carcinogen
53.	Quaternium-15 =>Immune toxicant
54.	Quaternium-22 => Harmful impurities
55.	Resorcinol => Possible human carcinogen
56.	Rosin => Immune toxicant
57.	Toluene => Known human carcinogen
58.	Triethanol amine => Possible human carcinogen
59.	Triethylene glycol => Reproductive system toxicity
60.	Tocopheryl acetate => Immune toxicant
61.	Uracil => Possible human carcinogen
62.	Urea => Skin/sense organ toxicant
63.	Yohimbine => Classified toxic
64.	Butylacetate => Skin irritation
65.	Citric acid => Reproductive irritation
66.	Decene (petroleum) => Chronic toxic effects
67.	Dioxane => Skin allergen
68.	Malic acid => Skin rashes
69.	Polysorbates => Skin irritancy

III. RESULT AND DISCUSSION

The primary goal of the project was to unearth chemical compounds like propylene glycol, Sodium chloride, Mineral oil, Alcohol, BHT and Ammonium lactate etc, these can be used in the cosmetic products like Lipstick, Lotions, Make-up removers, Liquid foundations and Shampoos etc. A total 69 chemical compounds analyzed through T.E.S.T (Toxicity Prediction Software Tool) have been developed to allow users to easily estimate toxicity using the variety of QSAR methodologies by using .T.E.S.T. software version 4.1 predict the toxicity properties (i.e., Oral rat LD50 and mutagenicity). Physical properties (normal boiling points, vapour pressure, flash points melting point, water solubility etc) in chemical compounds.

Oral rat LD50 in which LD is lethal concentrations of 50% of the test animals during the observation periods.

The values ranging 10 or less than in this no compounds form.

The value ranging 10-100 is highly toxic the compound such as Acrylamide etc.

The value ranging 100-1000 is moderately toxic the compound such as ammonium glycolate, bronopol etc.

The values ranging 1000-10,000 are slighty toxic the compounds such as amine, uracil, , malic acid, p-amino phenol, urea etc.

Practically nontoxic 10,000-1,000,00 the compounds such as salicylic acid, zinc oxide, retinol, glycolic acid lactic acid etc.

Toxicant Compound such as :- Propylene glycol, Mineral oil(petroleum), Sodium lauryl sulfate, Uracil, Parabens, Sodium chloride, Titanium dioxide, Rosin, Alcohol, Ammonium glycolate, Ammonium lactate, Bronopol, Carbolic acid, Dioxane, Ethanol amine, Glutaral, Glacial acetic acid and BHT etc.

Non-Toxicant Compounds such as :- Salicylic acid, Zinc oxide, Retinol, Glycolic acid, Alpha hydroxyl acid, Lactic acid, Citric acid, Malic acid and Mandelic acid etc.

The cosmetic chemical compounds which are shows positive value in mutagenicity such as Butyl methacrylate, Acrylamide, Alcohol denatured, Ammonium glycolate, Dioxane, Citric acid, Carbolic acid and BHT etc. The cosmetic chemical compounds which are shows negative values that are leave and which are shows positive valves are taken further project work.

Normal boiling point, Flash point, Thermal conductivity, Vapour pressure, Melting point, Water solubility the physical value is predicted.

IV. CONCLUSION

The identification and development of chemical compounds and their derivatives have greatly used in Cosmetic Products. This study investigated the level of toxic chemicals in Cosmetic Products are very high. It provided a new data on toxic chemicals concentration in cosmetic products. There are very high level of lead concentration and also a high level of Fe in cosmetic products. Cosmetic like Lipstick, Talc powder, Kajal, Cream and Shampoo. Dermal exposure is suspected to be the most significant exposure root. Since they are direct contact with the skin. The data obtained clearly showed that further studies are also needed of these toxic chemicals in cosmetic products of daily use. It has been shown in the above result analysis table that there are some side effects shown in chemical compounds which are used in cosmetics. If the value of chemical compounds are positive it will show less lethal toxicity. In 69 chemical compounds by use of T.E.S.T (Toxicity Estimation Software Tool) predict the mutagenicity value (shown in above table) and that prediction it has been shown that there is some chemical compounds showed positive.

In conclusion, the application of cosmetic chemical compounds is the cause of many skin diseases. The very common plague of modern times has resulted in increased skin allergies. Research result bottle testified to the evolution of knowledge coming from the dermatology and its historical roots, as well as to the great possibilities of future progress to the removal of toxic chemicals from personal care products and improve the quality of cosmetic products and save the beauty of the environment.

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