ABSTRACTS
Cosmetics are daily used products. Everybody use cosmetics in one or other forms. Almost all of the cosmetics used by humans caused a lot of adverse effects. These adverse effects are mainly due to the ingredients added in the cosmetics. These ingredients are mainly added as preservative, stabilizer, fragrance and coloring agent. But these ingredients entered into the body by penetrating the skin. However the serious adverse effects occurred on long term use of these ingredients. These adverse effects mainly includes cancer and organ system toxicity. The main classes of cosmetics which have low margin safety include: shampoos, hair dye, lotions, nail polishes, facial makeup etc.

Keywords: Cancer, Food and Drug Administration (FDA), United States National Toxicology Program, Skin care products.

INTRODUCTION
According to the US Food and Drug Administration (FDA), the law defines cosmetics as "articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body for cleansing, beautifying, promoting attractiveness, or altering the appearance." Main example of cosmetics includes nail polishes, eye and facial makeup, shampoos, hair dyes, lipsticks, skin moisturizers, toothpastes, and deodorants, as well as any component of a cosmetic product. [1]

Cosmetics are safe for health?
Does a chemical that caused cancer is present in your cosmetics? This is not very clear whether the cosmetics or the ingredients causes serious health problems or not, because most of the cosmetics products are tested only for minor health problems such as allergies or eye
irritation. These minor health problems are short term and go away after stopping the use of product. Even the data obtained after testing of cosmetics is not fully right because in testing a high concentration is used for testing. Because lack of long term studies we have a little or no knowledge about the long-term effects of the use of cosmetics. So, we cannot claim about the safe use of cosmetics. [2] In the United States, FDA regulated both cosmetics and drugs. For drugs, the FDA rules are different for both drugs and cosmetics. In case of drugs it is to be shown that new products is safe and effective before they are allowed to be marketed. Clinical trials are done on the new drug product before its marketing. But in case of cosmetics, the FDA requires that cosmetics be safe, but FDA does not have the authority to require companies to test their cosmetic products (except some color additives) before they introduced in the market. Products that have not been tested must bear the label, "Warning -- The safety of this product has not been determined." [3] However, the FDA can take action if it has reliable information about the product that it is not safe. It can:
1. Ask a federal court to issue an injunction
2. Request that US marshals seize the products
3. Initiate criminal action
4. Refuse entry of an imported cosmetic
But one more thing FDA cannot recalls of a product from market, it can only request that a company recall a product.

Cosmetic Ingredients which causes adverse effects on human body
Every human use various cosmetics/skin care products in its daily life. Most of the cosmetics contain harmful chemicals which may harm the human body by penetrating into their body. The harmful chemicals responsible for adverse effects are discussed below:

1. Phthalates
Phthalates are mainly the esters of phthalic acid and most commonly used as plasticizers. They are often called plasticizers. Some phthalates are also used as solvents. They are used in hundreds of products, such as vinyl flooring, adhesives, detergents, lubricating oils, plastic clothes (raincoats), and personal-care products (soaps, shampoos, hair sprays, and nail polishes, perfumes, air fresheners). Phthalates are commonly found in human blood and urine samples. A study was done by the U.S. Centers for Disease Control and Prevention and found that 100 percent of people tested had dibutyl phthalate (DBP) in their bodies. The CDC
scientists concluded that these high levels could come from use of personal care products and cosmetics. [4]

**Health problems associated with phthalates**

Research was done and it was suggested that phthalates disrupt hormonal systems, which can cause problems related to development. If pregnant women exposed by phthalates then it causes the shorter distance between anus and genitals in their male [5]. As the level of levels of phthalates increases in the mother during pregnancy, the more likely it causes shortened anogenital distance (AGD). These causes the boys were more likely to have incomplete testicular descent and smaller penises. Breast feeding male babies are also affected by phthalates which causes alteration in their hormones level. [6] Phthalate exposure to girls causes early puberty in girls, which is a risk factor for later-life breast cancer.

**Sex problem**

Research in adult human males has also found poor sperm quality and infertility problems on exposure of phthalates. [7] Other health problem includes hypospadias (problem causing an abnormal location for the opening of the urethra on the underside of the penis) and smaller testicles than normal – results in low sperm level and infertility. [8] Phthalates also reduces the level of sex hormones causes the improper development of sex organs.

**Breast Cancer**

women are also at higher risk of adverse health effects of phthalates due to increased cosmetic use. Diethyl phthalate and dibutyl phthalate are especially ubiquitous in cosmetics and personal care products. [9] According to in vivo and observational studies by Davis et al. (1994) and Lopez-Carillo et al. (2010), there is an association between phthalate exposure and endocrine disruption which is responsible for occurrence of breast cancer. Furthermore, it was also reported that phthalate is additive which can interact with other chemicals and can cause adverse effects. [10] A 2010 study published in Environmental Health Perspectives for the first time showed that the exposure to diethyl phthalates (DEP), a parent compound of the monoethyl phthalate (MEP) metabolite, may be associated with increased risk of Breast Cancer. Points to be remember about phthalates

1. Phthalates are found in Color cosmetics, fragranced lotions, body washes and hair care products, nail polish etc.

2. Health Problems: Endocrine disruption, hypospadias, Breast Cancer, developmental and reproductive toxicity, organ system toxicity.
3. Susceptibility populations: Pregnant women and breast-feeding mothers are more susceptible to phthalates.

4. Regulations: Phthalates are banned in cosmetics sold in the EU.

2. Hydroquinones

Hydroquinone, also benzene-1,4-diol or quinol, is an aromatic organic compound that is a type of phenol, having the chemical formula \( \text{C}_6\text{H}_4(\text{OH})_2 \). It is very commonly used in skin care products as whitening agent to reduce the skin colour. [11] It is most toxic substance used in cosmetics. It is most commonly used ingredients in facial cleansers, facial moisturizer and hair conditioners. [12]

**Health problems associated with hydroquinones**

**Cancer**

Hydroquinone act by decreasing the melanin production in the skin. Due to reduction of melanin production the UVA and UVB rays enter deep in the skin. This entry of UV rays deep into the skin is responsible for cancer. [13]

**Organ toxicity**

Hydroquinone also causes a skin problem known as ochronosis (skin become dark and thick). This toxicity is mainly due to long term use. [14]

Points to be remember about Hydroquinone:

1. It is used in skin lighteners, facial moisturizer, hair conditioner and other skin care products.
3. Susceptible population: Women of color are more susceptible to hydroquinone.
4. Regulations: Banned in cosmetics sold in European Union and Canadian cosmetics.

2. Parabens

Parabens are widely used in many cosmetics as preservative. These are used to prevent the growth of microbes in various cosmetic products. [15] Parabens are found in biopsies from breast cancer. Generally they are added in the form of methyl, propyl, butyl and ethyl paraben. They are most commonly used in shampoos, conditioner, scrubs and in many more cosmetics as preservative. A 2004 UK study detected traces of five parabens in the breast tumors of 19 out of 20 women studied. This study showed the presence of intact paraben which is not metabolized by breast tissues, thus prove its ability to penetrate into the skin.
After this study one more study was done and a high level of n-propyl paraben was found in axilla quadrant of the breast (the area nearest the underarm) [16-18]. This is the area in which the highest proportion of breast tumors are found.

**Health problems associated with Parabens**

Various study was done in UK which showed that parabens causes breast cancer by penetrating into the skin and by increasing genes expression which are responsible for the growth of human breast cancer cells. Parabens also hinder with the normal functioning of the hormones which causes the reproductive toxicity. Other adverse effects associated with parabens are irritation, immunotoxicity, neurotoxicity, reproductive toxicity.

Points to be remember about Parabens:
1. It is mainly used in shampoos, conditioner, scrubs, lotions etc.
2. It causes breast cancer, irritation, immunotoxicity, neurotoxicity, reproductive toxicity.
3. **Susceptible Population**
   The group of pregnant women and young children are susceptible to parabens.
4. **Regulations**
   Some forms of parabens are banned in Denmark in cosmetics products for children upto the age of 3 years. [19, 20]

**5. Formaldehyde**

Formaldehyde is most commonly used as fixative, disinfectant in water based products. Formaldehyde and formaldehyde releasing preservatives are used in many cosmetic products. Formaldehyde releasing preservatives released small amount of formaldehyde over time. [21] These formaldehyde releasing preservatives are used in place of formaldehyde and examples include: Quaternium-15, dimethyl-dimethyl (DMDM) hydantoin, imidazolidinyl urea, diazolidinyl urea, sodium hydroxymethylglycinate, and 2-bromo-2-nitropropane-1,3-diol (bronopol). In all of above Quaternium-15 is most sensitizing agent. [22]

**Health problems associated with Formaldehyde**

**Cancer**

Peoples are exposed by inhaling the formaldehyde that is off-gassed from the product, by ingesting it or by absorbing it through the skin. Various studies showed that the formaldehyde is a cancer causative agent and it was also considered as human carcinogen by government bodies, including the United States National Toxicology Program [23, 24] and the International Agency for Research on Cancer. After experimental studying on animal it was
Praveen

concluded that formaldehyde can be easily penetrated into skin after application of skin care products containing formaldehyde. [25]

Allergy

Allergic reaction is very common problem associated with the repeated use of formaldehyde. The concentration of formaldehyde is very low in cosmetic products which is not harmful but after repeated use of these cosmetics causes the sensitivity reactions. [26-28]

Points to be remember about Formaldehyde:

1. It is used in Nail polish, nail glue, eyelash glue, hair gel, hair-smoothing products, baby shampoo, body soap, body wash etc.
3. Susceptible population: Infants and salon workers are more susceptible to formaldehyde.
4. Regulations: Banned in cosmetics and toiletries sold in Japan, Sweden and EU.

5. Lead and other metals

Lead and other metals are used in more than 650 cosmetic products. These were found in lipstick, eye liner, and nail color. [29] Other metals include zinc, iron, chromium, arsenic, aluminium, mercury. Some metals are necessary for normal functioning of our body for example iron. But if it accumulated in the body then it causes many adverse effects. Some metals are added intentionally but some are present as impurities. For example iron oxides, chromium, aluminium compounds are used as colorants in eye shadows, blushes, lip gloss, lipsticks and nail polishes.

Health Problems associated with lead and heavy metals

Lead and heavy metals are found in higher concentrations in biopsies from breast cancer. Lead is an impurity in various skin care products. Lead caused the reduction in fertility both in men and women, menstrual problems etc. [30] Pregnant women are very much susceptible to lead because lead can easily cross the placenta and reached the fetal brain and it may also lead to miscarriage. Lead, has already been proven as a neurotoxin and causes brain impairment as well as other birth and developmental effects. [31] Mercury is also a heavy metal which is found in thiomerosal which act as preservative. It is absorbed by skin and health problems associated with mercury includes nervous system toxicity, immune and reproductive system toxicity and respiratory system toxicity. other metals such as aluminium,chromium also causes many adverse effects where as titanium dioxide and zinc oxide can be used in their natural form instead of non-naonized form. [32,33]
Points to be remember about Lead and heavy metals:

1. These are found in lipsticks, nailpolish, foundations, eye shadow and other skin care products.

2. **Health Problems**
   These causes cancer, reproductive toxicity, organ toxicity, immunotoxicity etc.

3. **Susceptible Population**
   Pregnant women and young children are susceptible to lead and heavy metals.

4. **Regulation**
   They are banned for use in cosmetics in Canada, Japan, EU and U.S.

6. **1,4-Dioxane**
   The Environmental Working Group in its study found that 97% of hair relaxers, 82% of hair dyes, 57% of baby soaps, 43% of body-firming lotions and 36% of facial moisturizers contain 1,4-dioxane—a chemical by-product produced in cosmetics manufacturing. The International Agency for Research on Cancer (IARC) has declared it as a possible carcinogen, and the National Toxicology Program (NTP) has identified it as a reasonably anticipated carcinogen. 1,4-Dioxane is not mentioned in ingredient list of label because it is produced during manufacturing. It is found in shampoo, liquid soap, bubble bath hair relaxers etc. Main problems associated with this include Cancer, organ-system toxicity, irritation and Pregnant women, infants, teenagers are susceptible to 1,4-Dioxane. Due to its carcinogenic property it is in Banned/unsafe for use in cosmetics in Canada. [34,35]

7. **Ethanolamine**
   These are comprised of amino acid and alcohols. Diethanolamine (DEA) and Triethanolamine (TEA) are comes under the class of Ethanolamines. These ethanolamines react with the nitrites to form nitrosamine which is a known carcinogen. A study was done by the National Toxicology Program, on mice to see the affect of ethanolamines. when ethanolamines are applied on skin of mice then it caused the cancer of liver and kidney. [29] DEA present in cosmetics react with other ingredients to form nitrosodiethanolamine which is a carcinogen.

   **Health Problems associated with Ethanolamines**
   Cancer is a major adverse effect of ethanolamine exposure. Ethanolamine produced nitrosodiethanolamine (NDEA) which is listed as a carcinogen in National Program’s Report on Carcinogens. NDEA causes kidney and liver cancer. It also has a major adverse effects on male reproductive system which hindrance with the normal functioning of the sperm
including change in sperm structure. Other problems includes organ toxicity and alteration in memory and brain functioning. Points to be remember about Ethanolamines:

1. Ethanolamines are found in Soaps, shampoos, hair conditioners and dyes, lotions, shaving creams, paraffin and waxes, pharmaceutical ointments, eyeliners, mascara, eye shadows, blush, make-up bases, foundations, fragrances, sunscreens.

2. Health Problems
   Cancer, bioaccumulation, organ system toxicity

3. Susceptible populations
   Almost all the population group are susceptible to ethanolamines.

4. Regulations
   Banned in EU in all cosmetics product. [36-38]

8. Coal Tar
Coal tar is used as ingredient of shampoos, hair dyes and lotions etc. it is a brown black thick liquid produced during burning of coal. The chief constituents of coal tar includes benzene, toluene, naphthalene, xylene and benzpyrene. These constituents are mainly responsible for carcinogenic activity of coal tar. National Toxicology Program and the International Agency for Research on Cancer also listed coal tar as carcinogenic agent. [39,40]

Coal tar is responsible for organ toxicity and cancer. Cancer is mainly occurred in kidney, lung, bladder and Gastrointestinal tract. Organ toxicity includes neurological damage, emotional and sleeps disturbances. [41] Points to be remember about Coal Tar

1. Coal tar is found in Soaps, shampoos, hair conditioners and dyes, lotions.

2. Health Problems
   Cancer, organ system toxicity.

3. Susceptible populations
   Almost all the population group are susceptible to coal tar.

4. Regulations: According to the FDA regulations, any drug products containing coal tar at levels of 0.5% to 5% must specify on a label the concentration of coal tar. If coal tar is used in hair dye and skin care products then label must bear a warning about the presence of coal tar in product and specific precautions about coal tar. 0.5-5% concentration of coal tar is safe and effective for therapeutic purpose. [41]

CONCLUSION

Cosmetics demands are increasing day by day. Every group of population using the cosmetics in one or other forms. This article emphased on the adverse effects asociated with long term
use of these cosmetics. Actually these cosmetics contained a lot of ingredients which were very harmful for our life. FDA also do not have so much strict regulations on the marketing of cosmetics. So the safety margin of cosmetics is very low. Various studies were done regarding the effects of various ingredients used in cosmetics and it was proved that these ingredients are not safe for human body. These are listed as carcinogen by National Programme report on carcinogen. Everybody must read the label ingredients and instructions so as to avoid the adverse effects associated with these ingredients. This review article listed the various ingredients which are harmful are present in cosmetics.

REFERENCES


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