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Review

The Beast of Beauty: Environmental and Health Concerns of Toxic Components in Cosmetics

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Abstract: Cosmetic products are used in large quantities across the world. An increasing number of chemical compounds are being added to the formulation of cosmetic products as additives, fragrances, preservatives, stabilizers, surfactants, dye and shine to potentiate their quality, property and shelf life. Owing to their widespread use, active residues of cosmetic products are continuously introduced into the environment in several ways. Many of these chemicals are bioactive and are characterized by potential bioaccumulation ability and environmental persistence, thus exerting a major risk to humans and the health of ecosystems. Hence, the indiscriminate consumption of cosmetics may present a looming issue with significant adverse impacts on public health. This review intends to spotlight a current overview of toxic ingredients used in formulating cosmetics such as parabens, triclosan, benzalkonium chloride, 1,4-dioxane, plastic microbeads, formaldehyde, diazolidinyl urea, imidazolidinyl urea, sunscreen elements (organic and inorganic UV filters) and trace metals. Specific focus is given to illustrate the biological risks of these substances on human health and aquatic system in terms of genotoxicity, cytotoxicity, neurotoxicity mutagenicity, and estrogenicity. In addition to conclusive remarks, future directions are also suggested.

Keywords: cosmetics; toxic ingredients; environmental pollutants; human health; biological risks; parabens; microplastics; Triclosan

1. Introduction

The global cosmetics market is projected to register a CAGR (Compound annual growth rate) of 4.3% during the forecast period (2016–2022) and is anticipated to reach $429.8 billion by 2022 [1]. Reports have documented that the average man and woman practice six and twelve cosmetic products per day, respectively, in the USA [2]. However, among a list of more than 12,000 industrial and synthetic chemical ingredients included in the formulation of cosmetics, less than 20% of these have been considered safe to use [3]. Therefore, over the past few years, substantial concerns have been raised for increasing use of pharmaceuticals, cosmetics, and many personal care products (dietary supplements, insect repellents, disinfectants). The cosmetic products are continually introduced into the aquatic systems and their ecological impacts are related to bioactivity, toxicity, and bioaccumulation potential [4]. Sewage treatment plants do not always effectively remove many of the cosmetic ingredients or chemicals such as micro-plastics [5], UV organic filters, perfluoroalkyl compounds, and synthetic musks [6,7]. Besides, these compounds are accumulated in sewage sludge during wastewater processing and find a way into the environment because of using this sludge as crop fertilizer [8]. In contrast to pharmaceuticals, cosmetic products pose the most tenacious ecological

risks due to their continuous utilization throughout life. Since they are designed for use in external surfaces and are not intended for metabolic transformation, they enter the environment unaltered in large quantities during washing and showering [9]. The present review is aimed at providing a recent overview of toxic ingredients that are commonly used in the manufacture of cosmetics such as parabens, triclosan, benzalkonium chloride, 1,4-dioxane, plastic microbeads, formaldehyde, diazolidinyl urea, imidazolidinyl urea, sunscreen elements (organic and inorganic UV filters) and trace metals. Particularly, the focus is devoted to pinpointing the biological risks of these substances of concern on human health and the aquatic system in terms of genotoxicity, cytotoxicity, neurotoxicity mutagenicity and estrogenicity. In addition to conclusive remarks, future directions are also suggested.

2. Parabens and Their Associated Biological Risks

Parabens are a class of chemicals that have been extensively employed as preservatives in pharmaceuticals, and cosmetic products due to their potential antimicrobial activities. Chemically, parabens are esters of the 4-hydroxybenzoic acid with aryl (phenyl, benzyl) or alkyl (butyl, ethyl, isobutyl, heptyl, methyl, propyl, isopropyl, pentyl) substituents [10]. Although plants or bacteria can naturally produce these compounds, all commercially used parabens are produced by synthetic methods. It is meaningful to mention that the European Union has circumscribed the inclusion of parabens in formulating cosmetics. Particularly, the consumption of benzyl paraben, isobutyl paraben, isopropyl paraben, methylparaben, and phenyl paraben has been prohibited in cosmetic products (Regulation (EU) No 358/2014). Furthermore, the possible highest level of butylparaben and propylparaben was reduced and their incorporation in products was forbidden especially those used by children (Regulation (EU) No 1004/2014). Notwithstanding all these constraints, there is still extensive paraben use in personal care and cosmetic products due to their low price, marginal toxicity, and pronounced inhibitory activity against bacteria, molds, and yeasts [10].

Parabens have been identified in the environmental milieus such as water, dust, and air due to their discharge from manufacturing units and continuous release at elevated concentrations into urban and hospital wastewater effluents given the widespread utilization of paraben-containing household chemicals, and pharmaceutical products. Notably, the level of parabens can reach up to 20,000 and 30,000 ng/L for propylparaben and methylparaben, respectively, in raw wastewaters [11]. Many of the parabens in the aqueous media can be effectively removed by wastewater treatment plants by bio-degradation or adhering to the sewage sludge [12]. They can undergo the rapid bio-degradation process with the production of 4-hydroxybenzoic acid as the main by-product or might efficiently react with free chlorine resulting in the formation of various chlorinated products [13]. In spite of their effective elimination by wastewater treatment plants, these chemicals are still identified in surface waters, particularly rivers [14].

Among the list of parabens, propylparaben and methylparaben are the most frequently identified paraben compounds in surface waters due to their frequent utilization in cosmetics [10]. The occurrence of paraben has been reported in marine mammals and the tissues of fish and marine organisms [15]. The extensive presence of parabens and their degradation compound, p-hydroxybenzoic acid, in animals reveal their ubiquitous occurrence in the environmental media. Parabens were generally not detected or found at very low levels in tap water. Nevertheless, a survey documented the paraben's occurrence with a concentration range of ng/L in bottled water [16]. In addition, parabens have been observed in human serum, urine, milk, amniotic fluid and adipose, placental and human breast cancer tissues [17–19]. In humans, dermal exposure to products containing paraben is the source of its absorption since some parabens can penetrate human skin. Moreover, some reports have also confirmed the systemic absorption of parabens following environmental exposure, though it is less likely to appear a significant source of paraben [20]. Likewise, oral ingestion of parabens is also not a meaningful way because orally ingested parabens are readily transformed to p-hydroxybenzoic acid by esterases [21]. For a long time, it has been taught that parabens exhibit negligible toxicity with an excellent safety profile. However, gravest apprehensions have recently been aroused because of the

in vitro as well as in vivo endocrine-disruption activity of parabens. Experimental studies have shown the association of parabens with altering the reproductive system of male animals [22]. Parabens displayed a feeble estrogenic activity in in vitro studies with a substantially lower estrogen receptor binding affinity compared with the diethylstilboestrol [23]. Investigations carried out to evaluate the endocrine-disrupting effect of parabens on aquatic biota revealed that these chemicals are capable of interfering with the vitellogenin plasma level in some aquatic wildlife, such as Japanese medaka fish and rainbow trout [10]. Similarly, many reports have claimed the relationship between the endocrine disruption effect of parabens and breast carcinoma in human species [21]. However, many scientists and international health authorities subsequently negated these investigations, demonstrating no scientific evidence that connects human breast cancer with the toxicity of parabens [24,25]. On the contrary, Pan et al. [26] reported a prominent synergism between epidermal growth factor and parabens, indicating the activity of parabens at very low concentrations than considered toxic in earlier studies. Considering the aforementioned discussion, notable adverse impacts of parabens include DNA damage [27], antiandrogenic activity [28], estrogenicity [29], endocrine disruptors [30], cytotoxic and genotoxic effects on human lymphocytes [31], risk of cancer in humans [32], allergic reactions, and reproductive disorders [33,34].

3. Triclosan Persistence and Ecological Impacts

Triclosan (TCS) is a lipid-soluble, antimicrobial agent that is widely employed as a preservative in a variety of personal care products such as shampoos, toothpaste, detergents, hand soaps, deodorants and sunscreens. It is also extensively used as an additive or stabilizer in textiles, packaging, functional clothing and as an antiseptic in numerous household items and medical devices due to its broad-spectrum antibacterial and antifungal functionalities [35]. However, its extensive consumption in rinsing products results in the release of domestic sewage that is considered as the most crucial source of pollution [36]. The discharge of large amounts of TCS accompanied by ineffective elimination in sewage treatment plants is the primary cause for its substantial occurrence in the environment, with levels often ranging from nanograms to micrograms per liter in waters and sediments [37,38]. This widespread distribution and persistence of TCS in the aquatic environment is schematically represented in Figure 1. Reports have shown the ubiquitous presence of TCS in aquatic systems, as well as in sediments with a prevalent accumulation in sediments because of its lipophilic nature [39]. In terms of concentration and frequency, TCS is amid the top 10 most frequently noticed organic wastewater pollutants [40]. It has been detected in surface water in the United Kingdom, USA, China, South Korea and Europe [41–45].

An experimental study conducted on thirteen places (Kyoto: four places, Saitama: five places, Tokushima: four places) in Japanese rivers contaminated by domestic wastewater, effluent, or industrial wastewater reported the ubiquitous detection of TCS with up to 177 ng/L concentrations [46]. Due to the utilization of sewage sludge on farmland as fertilizer, TCS has also been found in terrestrial surroundings [47]. Although TCS persists in the environment, it can be transformed into other chlorinated compounds during wastewater treatment that are highly poisonous and even more persistent than original compounds. Owing to lipophilicity and high stability, TCS has revealed a potential propensity for bioaccumulation in plants, algae, animals (such as fish, snails, marine mussels, earthworms, amphibian larvae and marine mammals) [48–51]. Likewise, a metabolite of TCS, methyl triclosan, has also been identified in fish from various ponds and lakes in Switzerland [52]. It is essential to mention that TCS present in the marine ecosystem exerts unfavorable environmental consequences such as toxic effects to algae species, alteration in the composition of bacterial communities, disruption of the endocrine system in fish and teratogenicity and mortality in the larvae and embryos of zebrafish [53–56].

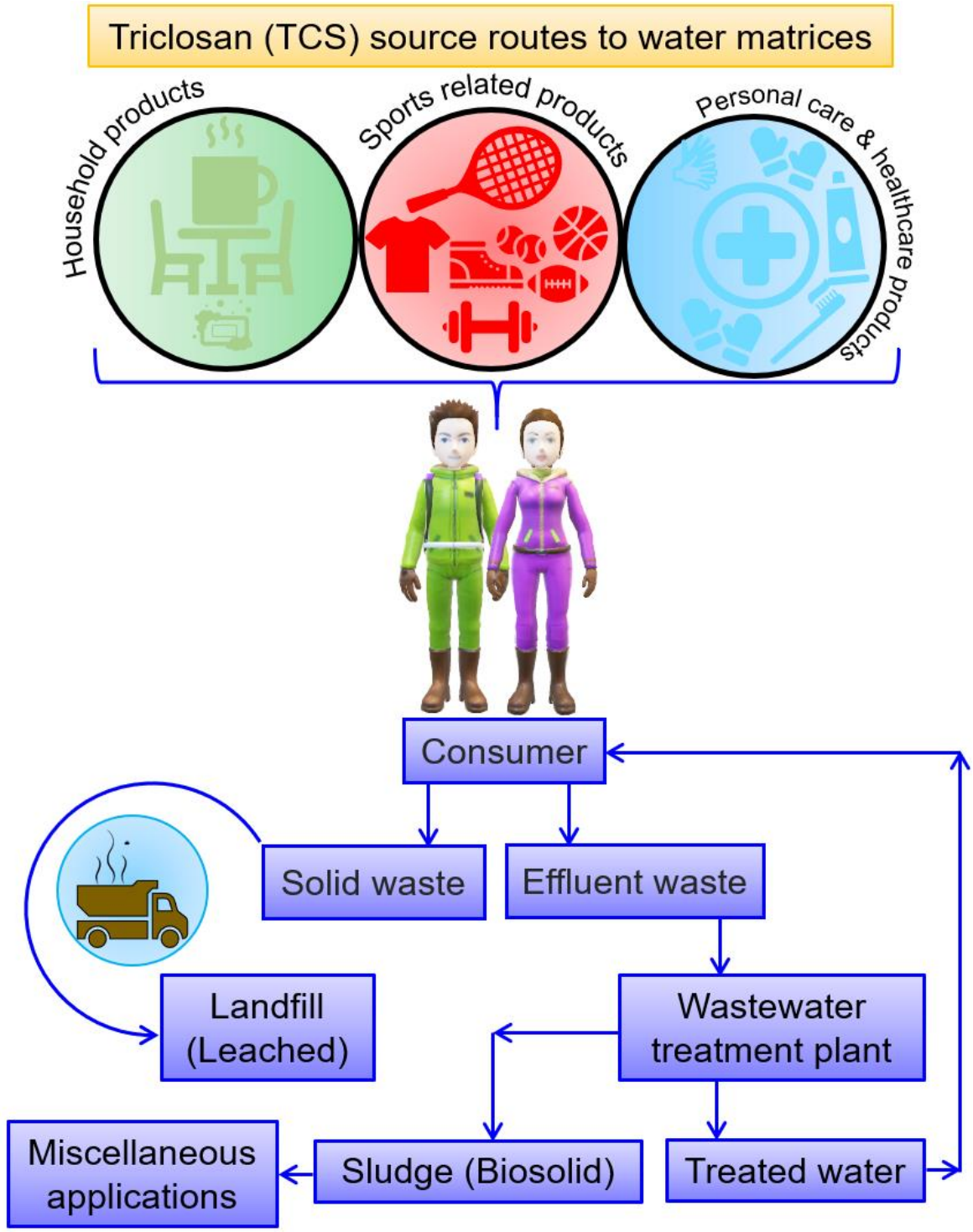

Figure 1. Schematic illustration of the fate and general distribution of Triclosan (TCS) in water matrices.

Epidemiological studies have documented that TCS is present in a more extensive concentration range in human body fluids such as breast milk, blood, and urine [38]. Some researchers have revealed that the TCS in human body fluids is primarily related to the application of personal care products containing TCS. According to some other researchers, oral absorption is a significant source taking into consideration that TCS is identified in drinking water [57,58]. Exposure to this antimicrobial agent can induce an array of adverse impacts on the environment and human health, including contact dermatitis [59], interference with the endocrine system, depression of the central nervous system [60],

decreased sperm production [61], liver carcinogenesis [62], oxidative stress, tumor development and impairment of thyroid functions [38,63–65]. Given all data available in the literature concerning TCS and its transformed by-products in the environment and its health effects, this chemical should be deliberated as a serious concern top-priority contaminant [65].

4. Benzalkonium Chloride and its Cytotoxic Effects

Benzalkonium chloride (BAC) is one of the most extensively used preservatives in cosmetic products. BAC belongs to a cationic family detergent and surfactant preservative. It is also known as a quaternary ammonium compound (QAC) and commonly used as a potential constituent of various cosmetics, household items, pharmaceutical products, personal care products and also used as a surface disinfectant. In a report published in 1986, BAC was considered as one of the important components of 83 well-known cosmetic products at concentrations varying from ≤0.1% to 5%. In 2013, the use of BAC increased up to 567 cosmetic items, which carry the 0.46% weightage as compared to other compounds used in cosmeceutical items. [66]. In addition, BAC is the most active ingredient and widely used as a preservative in ophthalmic solutions [67]. Nevertheless, the usage of BAC has been linked to inducing considerable adverse consequences in humans. Reports have documented the cytotoxic effects of BAC in vivo and in vitro models that induce toxicity in corneal and conjunctional epithelial cells. Similarly, continuous and excessive exposure to BAC may cause Dry Eye Disease (DED) [2,68,69]. BAC is also used in the pharmaceutical industry. Medications containing BAC result in increased chances of peripheral ocular disorders including itching, irritation, stinging, burning, foreign body sensation (FBS), redness, blurred vision, sensitive to light and sometimes may cause more severe conditions such as failure of glaucoma surgery, conjunctival hyperemia and blepharitis [70,71]. Moreover, a large number of studies have been conducted on ophthalmic toxicities such as corneal injury and irritation and intranasal damage of mucosal membranes [72]. Experimental results of a study conducted to analyze the effects of BAC in a dose-dependent manner showed neurites concentration decrease in corneal nerves and also induction of oxidative stress that leads to cholinergic neurotoxicity [73]. Recently, a study showed that the overproduction of ROS results in the destruction of caspase-8 expression, a result, the cell viability waned, when rat neural progenitor cells (NPCs) were exposed to a higher concentration of BAC [74]. Previous data have shown that cosmetic products with a high concentration of BAC have high potency to induce the severe ROS-mediated neurotoxicity in rats that leads to apoptosis in later stages. Toxicological metadata analysis results revealed that nasal and oral medication containing BAC causes pulmonary toxicity [75]. Similarly, human nasal epithelial cell viability was used to analyze the toxicological assessment of the gradient concentration of BAC; results showed that 14%–19% of cells were viable after treatment [76]. Electron microscopic analysis envisaged that the variable concentration of BAC also induces the demolition of the lipid bilayer structure; changes the configuration of cytoskeleton and microvilli destruction [75]. It has also been documented that a BAC concentration of 10 µg/mL and 1.0 mg/L, and 3.0 mg/L significantly increase the micro-nucleated cell colonization when exposed to human lymphocytes and *Vicia faba* [77]. In addition, BAC concentration also increases the lap of cell division. BAC-mediated induction of DNA damage has also been reported in marine organisms *Ceriodaphniadubia* and *Daphnia magna*, which are widely used organisms to study the genotoxicity [56].

5. 1,4-Dioxane, Uses and Adverse Impacts

1,4-Dioxane ($C_4H_8O_2$, dioxane) is a synthetic chemical that has been previously used as a fixative agent in a chlorinated solvent, but nowadays, is traced in many commercially available products especially food items. 1,4-Dioxane is an organic solvent (ether), which is commonly used as an emulsifying agent and as a detergent. For this reason, it is commonly used in personal cleaning and household products including baby lotion, shower gel, body lotion, toothpaste, mouthwash, and shampoo [78]. It is taken by aerosol, by means of inhalation, by physical contact with skin or cutaneous exposure and ingestion of dioxane-contaminated food. The chemical structure and

physical properties allow 1,4-Dioxane to reach underground water reservoirs and as a result, drinking water is contaminated once released in the environments [79]. It is used to enhance the foaming texture in personal care products such as shampoo, shower gel, soaps and also minimize the adverse effects of chemicals especially sodium lauryl sulfate. 1,4-Dioxane is produced during ethoxylation steps in the manufacturing process of other cosmeceutical constituents such as polyethylene glycol, polyoxyethylene, and polyethylene, hence that is why it is not listed as a cosmeceutical component [80].

Previous studies revealed that overconsumption or exceeding the threshold level of 1,4-Dioxane causes severe effects on animal life, for example, skin cell carcinoma, breast, and hepatocellular carcinoma. A study revealed that chronic intake of 1,4-dioxane via drinking water in mice and rats induced hepatocellular toxicity, and long term exposure (more than 3 months) prompted Piecemeal necrosis, progression of pre-neoplastic lesions and Rhinitis or nasal cavity irritation [81]. In vitro studies on both prokaryotes and eukaryotes concluded that 1,4-dioxane has not been involved in genotoxicity. In vivo analysis of genotoxicity has shown negative results but only a few studies reported that a high dose of 1-4-Dioxane induced genotoxicity but this dose was much higher than the environmental exposure. However, there is still a need to uncover the genotoxicity of human systems especially the reproductive system. 1-4-Dioxane also interferes with transportation, biosynthesis, metabolism and disruption of endocrine components [82,83].

6. Microplastic Particles

The plastic pollution of aquatic systems represents an emerging environmental apprehension. According to Moore [63], microplastic is considered any plastic material that is less than 5 mm in length. Most small plastic materials or particles stem from the disintegration of larger substances; nevertheless, microplastics can also directly incorporate into the marine environment by various sources, such as clothing, cosmetic products, and industrial processing [84]. Plastic microbeads are widely used as abrasive cleaners or scrubbers in a plethora of cosmetic and personal care products, including toothpaste, hand-cleansers, soaps, shampoos, bubble baths, and scrubs [85]. In all these products, plastic microbeads are used as a replacement for natural exfoliating compounds (apricot husks, oatmeal and pumice). Apart from the deep cleansing and dead skin removal functions, these microbeads also have a decorative and ornamental role in numerous personal-care products [86]. Due to the extremely small size, micro-plastic beads incorporated in cosmetic products are trapped in sewage treatment plants and enter into water streams through domestic drainage systems and are finally channeled into oceans and seas [87]. After entering the environment, high-density micro-plastics such as polyester and polyvinyl chloride settle out of the water system and tend to accumulate in the sediment, whereas the microbeads composed of low-density micro-plastics (polystyrene, polyethylene) float on the surface of the sea [88]. Aquatic organisms can ingest micro-particle pollutants from the marine environment due to the lack of effective methods for the removal of micro-plastic and high degradation resistance. Extensive reports have described the ingestion and accumulation of micro-plastic materials in various marine entities, including fish, seabirds, bivalves, and copepods [89–93]. Polystyrene microparticles are known to affect adversely the marine biota following their exposure. A worrying concern is the microplastics capacity in aiding the delivery of persistent organic pollutants such as alkylphenols, organochlorine pesticides, polychlorinated biphenyls, polycyclic aromatic hydrocarbons, incorporated during the manufacture of plastics, which subsequently is transferred along the food chain and can potentially damage organisms [94,95]. Figure 2 shows possible bioaccumulation and biomagnification of microplastics in the environment.

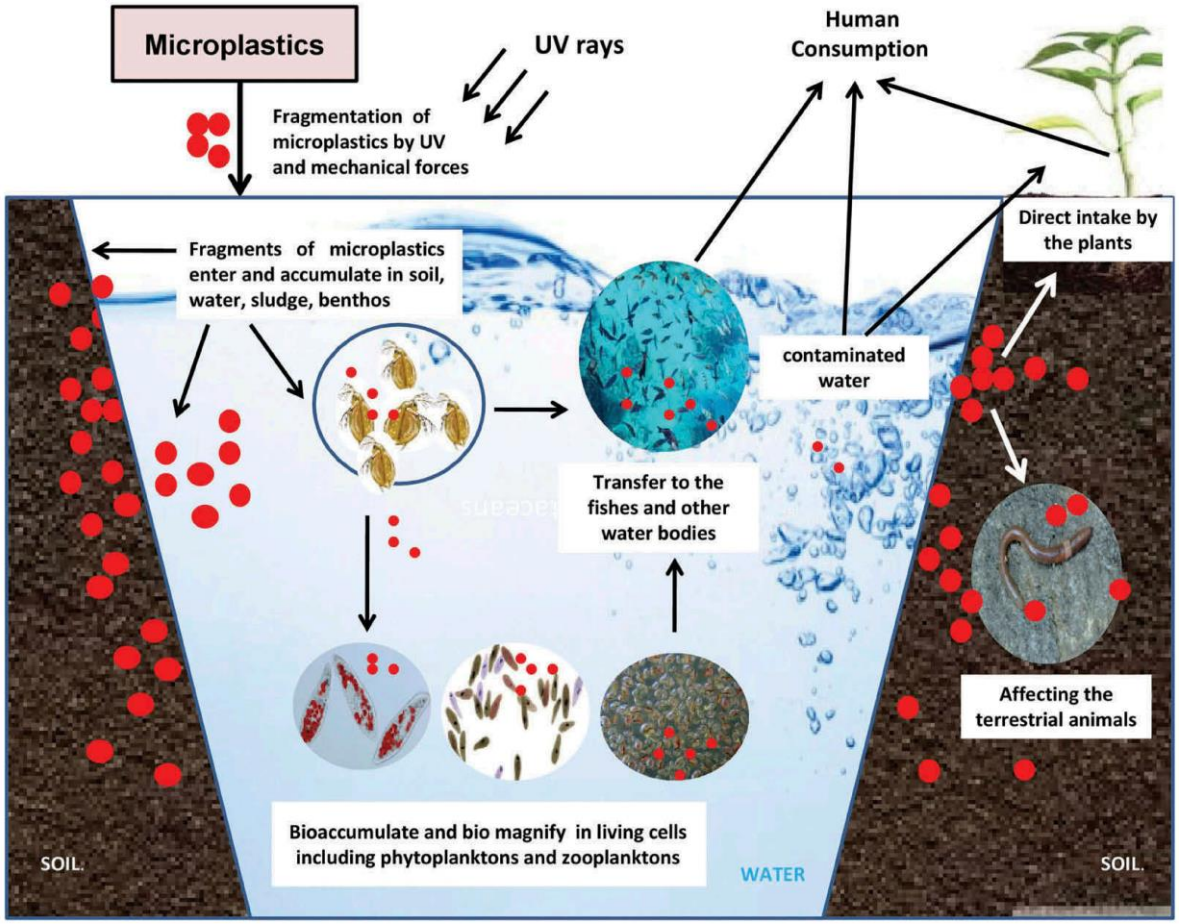

Figure 2. Schematic illustration of possible bioaccumulation and biomagnification of microplastics in water matrices. Reprinted from [86] with permission from Taylor & Francis. Copyright (2019) Informa UK Limited, trading as Taylor & Francis Group.

7. Formaldehyde, Transmission Routes and Health-Related Effects

Formaldehyde (FA) is another organic compound that is widely employed as a stabilizing or protective agent in various household, cosmeceutical products and personal care products. Formaldehyde or formalin (37% v/v solution of formaldehyde) or oxymethylene are an important class of additives used in a broad range of cosmetic industries in the formulation of shampoo, liquid soap, body shower gel, skincare lotion and many other products [96]. In USA, the most commonly used preservatives are quaternium-15, imidazolidinyl urea, diazolidinyl urea, 2-bromo-2-nitropropane-1, 3-diol and 1,3-bis(hydroxymethyl)-5,5-dimethylimidazolidine-2,4-dione (DMDM)-hydantoin, that released FA [2,97,98].

Formaldehyde follows the various routes of transmission to human bodies such as cutaneous, nasal route and ingestion. However, research has revealed that the nasal route or inhalation is the most common and prominent route of FA exposure, because most indoor contaminants have been found in gaseous form in the air [99]. The continuous and delayed exposure with FA is associated with a broad range of serious health concerns such as various types of cancers including cutaneous carcinoma and sinus carcinoma, causes allergy, and also produces a mutagenic effect [100]. Moreover, long-term exposure with a high intensity of FA led to increasing the risk of myeloid leukemia progression [101]. Various studies have shown that FA exposure is involved in inducing the cytotoxic effects on human lymphocytes, natural killer cells, bronchial epithelial and endothelial cells [2,102,103]. A study conducted on rabbits to show the impact of FA on corneal epithelial cells showed that an FA level of 0.5 and 1.0 ppm could elicit the ophthalmic irritation that includes increased blinking frequency and

conjunctival redness. On the other hand, nasal and throat irritation happen above the level of 1.0 ppm concentration [104].

8. Imidazolidinyl Urea and Diazolidinyl Urea—Adverse Effects

Imidazolidinyl urea and diazolidinyl urea are widespread antimicrobial fixative agents used in cosmetics and household products [105]. A 0.01%–1% concentration of imidazolidinyl urea, when applied to human peripheral cultured blood cells for 24 h, results in ascetically induced cytotoxicity. A similar result has been shown after 3 h of exposure with a 0.1%–0.5% concentration of diazolidinyl urea [106]. However, the clinical trial study revealed imidazolidinyl urea as a causative agent as a skin allergen that causes dermatitis and skin hypersensitivity [107,108]. Human fibroblast cells, when exposed to a variable concentration of imidazolidinyl urea led to the inflammatory response and steered toward the substantial loss of cell viability [109].

Since 1982, diazolidinyl urea is being used as an antimicrobial fixative agent in cosmeceutical industries and personal-care products, especially skincare products, childcare products, hair treatment products, skin and face makeup, and nails. In Europe, 0.5% diazolidinyl urea can be used in cosmetic products, because many studies have confirmed that dermal exposure to the high concentration of diazolidinyl urea causes an allergic reaction. Besides, it is also reported as a carcinogenic and genotoxic agent because of releasing formaldehyde [110]. Upon the hydrolysis of diazolidinyl urea, formaldehyde is released that may cause itching, skin redness, and irritation. Ryu et al. [74] reported different types of cosmetic preservatives such as diazolidinyl urea, benzalkonium chloride, and imidazolidinyl on rat NPCs cell culture. In this study, they assessed the ROS released by treated cells at different concentrations of 1–50 μM diazolidinyl urea or imidazolidinyl urea and 1–1000 nM benzalkonium chloride at different time laps. The results showed that cellular viability and count severely decreased after 24 h of treatment with imidazolidinyl or diazolidinyl urea and ROS production and apoptosis significantly increased. These results also showed that imidazolidinyl urea and diazolidinyl urea induce oxidative stress in mitochondria [74]. However, there is still ambiguity because these compounds can also be involved in cell death followed by autophagy. Due to the triggering properties of ROS and formaldehyde-releasing agents, use of these chemicals or diazolidinyl urea and imidazolidinyl urea-based cosmetics are strictly prohibited during pregnancy [105].

9. Organic and Inorganic UV-Filters/Absorbers

UV-filters, chemicals that absorb or scatter UV radiation in sunlight, are increasingly employed in a plethora of personal care and cosmetic products for skin protection from UV-triggered impairment and as a stabilizer of fragrance and color of cosmetic preparations. These filters are referred to as broad-spectrum since they are believed to provide protection against different UV rays such as UV-A (400–320 nm), UV-B (320–280 nm), or both UV-A and UV-B rays. At present, active sunscreen elements are categorized into organic (chemical) or inorganic (physical) filters or absorbers. Organic filters first absorb radiations, followed by efficient dissipation of the absorbed energy by several photochemical and photophysical pathways. On the other hand, inorganic filters partially absorb and reflect UV rays [111]. It is documented that UV filters account for approximately 20% of sunscreen products [112], but are considered as emergent contaminants because of their ubiquitous occurrence in the environment. These chemicals can enter the aquatic system either directly or through wash-off from the skin surface during recreational activities [113]. Studies have reported the detection of UV filters in wide environmental compartments such as surface waters, oceans, seas, coastal waters, groundwater, lakes, rivers, and sediments [114,115]. The most commonly detected organic filters in sediment are octocrylene (OC), Ethylhexyl methoxycinnamate (EHMC), octyl dimethyl-p-aminobenzoic acid (OD-PABA), butyl methoxydibenzoylmethane (BMDM), and benzophenone derivatives [116,117]. Likewise, sun blockers including homosalate, Ethylhexyl salicylate, isoamyl p-methoxycinnamate, and 4-methylbenzyliden camphor have been identified in surface waters but are not detected or recovered in sediment presumably due to their limited consumption in sunscreen products or decomposition by

microbial strains [118]. Recent investigations have reported the presence of organic UV filters in water samples in many countries, including USA, China, Thailand, Switzerland, Japan, Hong Kong, Taiwan, Korea, and Norway [119–121].

A large number of studies have documented the toxic effect of organic UV filters in various aquatic organisms; in particular, some widely consumed UV filters have been found to be very toxic to protozoa, crustaceans, and microalgae [122]. Similar to other xenobiotics, the endocrine-disrupting tendencies of some organic UV filters have been noticed in both in vivo and in vitro models. For illustration, BP-3 exhibited a potent anti-androgenic along with weak estrogenic activities in murine models. Besides, this compound has also shown destructive effects on the reproductive outcome of aquatic organisms [43]. With a receptor-based test, Faass et al. [123] assessed the estrogenicity of a series of organic UV filters on fish both in vivo and in vitro. Two UV filters explicitly, 3-BC and 4-MBC, are known to have an estrogenic-like effect and were capable of impairing female sexual outcome in a rodent model [123]. Schlumpf et al. [124] analyzed human milk samples and found that they consisted of UV filters in higher than 75% of the tested cases that indicated a probable exposure to the suckling infants or neonate to these toxic substances [124].

ZnO and TiO_2 are among the important inorganic UV filter compounds that were authorized as a sunscreen by European Regulation. Both oxides (ZnO and TiO_2) are increasingly utilized as nanoparticles in sun blockers because of the improved consumer's acceptance, skin retention, and UV reduction attributes in comparison to their bulk equivalents [125]. In recent years, the toxicological influences of nano-TiO_2 on fish, algae, and marine invertebrates have been described in many reports [126]. Although some researchers have demonstrated the negligible impacts of nano-TiO_2 on various aquatic organisms, its toxic effects were dramatically increased in the presence of UV radiation or strong sunlight due to ROS generation [127,128]. Likewise, nano-ZnO is also categorized as "extremely toxic", and the toxicity of ZnO is well recognized towards aquatic entities such as including sea urchins, marine algae, zebrafish, and many other organisms [127,129,130]. The elevated toxicity of ZnO might be ascribed to the release of Zn^{2+} ions and oxidative damage because of the elevated ROS production [131].

10. Trace Metals and Their Adverse Effects

Many chemicals including natural mineral mica, shine, dyes, coloring agents, and different trace metals, are used as additives in cosmetics formulation to augment their brightness and realize superior quality with boosted effects [4]. Incorporation of high contents of trace metals including arsenic, antimony, chromium, cadmium, copper, cobalt, manganese, lead and nickel into lip cosmetics is a major issue in cosmetics application because of their potential adverse consequences [132,133]. These trace metals used in cosmetic formulations can accumulate in the skin, and some metals including aluminum, lead, cadmium, and mercury, are capable of diffusing across the skin barrier and thus entering blood vessels [134]. Reports have revealed the elevated level of heavy metals in the individual's blood with wide exposure to these heavy metals due to extensive consumption of cosmetics [135–137]. High concentrations of toxic metals in the bloodstream results in the accumulation of these elements in various parts of the body, and consequently, leads to dysfunctioning and damaging of vital multi organs i.e., the kidneys [138]. The ophthalmic related adverse consequences of heavy metals have been widely documented in different reports since heavy metals can bind with retinal epithelium pigments and accumulated at higher concentrations [139–141]. It is reported that prolonged exposure to copper, lead, cadmium, arsenic, chromium and nickel are associated with an improved menace of numerous cardiovascular and neurologic disorders [142,143]. Particular exposure to arsenic, lead, cadmium, and mercury with vital organs can result in nephrotoxicity, neurotoxicity and hepatotoxicity. Additionally, a combination of lead, mercury, arsenic, and cadmium can generate synergistic effects leading to cognitive damage and dysfunction [144]. Introduction of antimony, commonly used in skin creams, face powder, lipsticks, eyeshadows, and eye pencils, can cause severe respiratory complications such as altered pulmonary functions, emphysema, bronchitis, and pneumoconiosis

as well as hostile gastrointestinal related disorders including abdominal pain, ulcers, vomiting, and diarrhea [145]. Prolonged contact with cadmium provokes kidney damage, skin tumors, and bone brittleness and breakages. Increasing the use of mercury exerts potential risk to human health by causing gastrointestinal, nephro- and neurological ailments [146]. Allergic contact dermatitis may occur by the inhalation of nickel and cobalt metals, which are widely used in eyeshadow, lipstick, hair cream and face paint cosmetics. Consumption of lead in large amounts interrupt the synthesis of calcium and heme channels, which are very critical for transmitting nerve signals [142,147]. Furthermore, lead also interferes with the functionality of central nervous system in children [148].

11. Synthetic Musk Compounds

Synthetic musk compounds (SMCs) are semi-volatile cyclic organic compounds that are added to various consumer products including shampoo, soaps, body lotion, deodorants, cleansing agents, fish bait. These compounds are also used as food additives and fragrance materials such as air fresheners and perfumes [149]. Based on their physiochemical properties, SMCs are categorized into four group's namely polycyclic musks, nitro-musks (first-ever commercially available SMCs), alicyclic musks and macrocyclic musks [150]. SMCs have been used as a food additive in various personal care products such as shampoo, soaps, body gels and lotion, deodorants and perfumes, household products like cleaning agents and air fresheners [151]. First-ever synthetic musk was commercialized in the early 20th century and was the derivative of nitro-musk called dinitro and trinitrobenzene [152]. The production of polycyclic musk fragrances has exponentially increased over the last fifty years, for example, galaxolide is one important polycyclic musk [153] and musk ketone and musk xylene are also widely used SMCs [151]. Synthetic musks can bioaccumulate in the aquatic environment due to its lipophilic nature and thus can be easily detected in dust, indoor air, human adipose tissue, blood and breast milk [154].

12. Siloxanes and Silicones

Siloxanes (silicones) constitute a group of low molecular weight compounds, which are used in various cosmetics to soften, smooth and moisten. They make hair products dry faster and improve the spreadability of deodorant creams. They are most often used in moisturizers and facial treatments [155]. It should be noted that the worldwide siloxanes production in 2002 amounted to 2,000,000 tons, and currently, it is more than 8,000,000 tons [156]. The highest consumption of silicones was noted in China, North America and Western Europe [157]. Currently, nearly 50% of new skincare products contain at least one type of silicone [158]. The commonly used siloxane i.e., cyclopentasiloxane and cyclopentasiloxane are toxic and have the potential of bioaccumulating in aquatic organisms. Cyclotetrasiloxane is a type of endocrine disruptor that interferes with human hormone function. As a possible reproductive toxicant, it may also impair human fertility [159].

13. Conclusions and Outlook

In recent times, a large number of chemical compounds are being incorporated into the manufacture of cosmetic, beauty and personal care products as additives, fragrances, preservatives, stabilizers, surfactants, stains and shine to potentiate their quality, performance, and shelf life. However, based on the cosmetics-related literature assessment and this study, it is not unsurprising to comprehend that many of these substances are bioactive, environmentally persistent, and exhibit a potential bioaccumulation ability, thus can exert a serious threat to the environment and human health because of indiscriminate, widespread and prolonged exposure. Prohibiting the use of cosmetic products associated with environmental problems is not a practicable choice. Different novel strategies and approaches are required to address this issue realistically. Although the worldwide cosmetic regulation authorities and management are keenly concerned about this context, they should be more stringent and meticulous in incorporating new ingredients/substances with health hazard effects in the manufacture of cosmetics to circumvent undesirable environmental and health damages. Further comprehensive

studies should be done on the acute or chronic intoxication of these pollutants of high concern allowing a more accurate monitoring and explicit inspection of their tangible health and ecological risks. Finally, information concerning the environmental and health influences of cosmetic products on their packaging would reassure consumers and encourage informed and more responsible employment of these products.

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