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AN OVERVIEW ON PARABENS USED AS PRESERVATIVES IN DIFFERENT AREAS AND PARABEN IMPACT ON ENVIRONMENT

Dr.K.Radha*
Assistant Professor, Department of Biotechnology,
Arulmigu Kalasalingam College of Arts and Science, Krishnankoil

Abstract

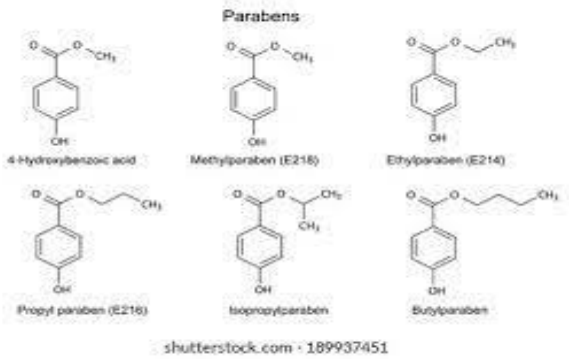
Parabens like preservatives are generally used as additives in pharmaceutical products, food and make up items. A preservative is a natural or chemical substance added to a range of products which helps to avoid microbial decomposition. For many years scientist have been attentive of the must to protect their commodities against microbial contamination but it is only during the last one or perhaps two decades the serious thought of has been applied to the science of preservation. Some of them mainly fluid preparations are susceptible to microbial contamination because of the composition of the cosmetics. Such products are protected by preservatives which avoids degradation and change of the product. Present article deals with the study of supreme properties, categorization, mode of action, applications and its effects on health of Parabens.

Key words: Paraben: Preservative: Mode of action: natural: chemical: contamination.

Introduction:

Parabens are alkyl ester derivatives of p-hydroxybenzoic acid, where the ester functional group is located at the 4- carbon of the aromatic ring (Ley *et al.*, 2006). Parabens are odorless, colorless, non-volatile, low costs of production and they do not change consistency or color of formulations (Bledzka *et al.*,2014). Methyl, ethyl, propyl, butyl and benzylparaben are some of the commercially available parabens. Among them, methylparaben and propylparaben are the most commonly used and are often present in the products together (Xue and Kannan, 2016). Although parabens are generally considered as safe ingredients, several studies have raised concerns on the safety of parabens (Xue and Kannan, 2016). With the increased use of pharmaceuticals and personal care products for the human population, various anthropogenic substances are continuously released into aquatic environments (Terasaki *et al.*, 2012). Through domestic and industrial wastewater (Bledzka *et al.*, 2014). As the sewage treatment plants in most countries do not have an effective removal of parabens, they can be found in surface water samples at concentrations ranging from 0.001 to 52.1 μg L^{-1} (Czarczyńska- Goślińska *et al.*, 2017) and may cause toxic effects on non-target organisms, representing a threat to aquatic ecosystems functioning. Recent reports indicate that exposure to parabens through ingestion, inhalation, or dermal

absorption may modulate or disrupt the endocrine system and induce oxidative stress, which may cause deleterious effects in animals and humans (Kang *et al.*, 2013).



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S.no	Name of the compound	Chemical Name	Empirical formula and Molecular weight	Characters	Function	Applications
1.	Methyl paraben	Methyl-4-hydroxybenzoate	$C_8H_8O_3$; 152.15	colorless crystals or a white crystalline powder. It is odorless or almost odorless and has a slight burning taste	Antimicrobial preservative	Cosmetics, food products, and pharmaceutical formulations.
2.	Ethyl Paraben	Ethyl *para*-hydroxybenzoate	$C_9H_{10}O_3$: 166.17	odourless, small, colourless crystals or a white, crystalline powder	Antimicrobial preservative	Antifungal preservative and Food additives in food.
3.	Propylparaben	Propyl 4-hydroxybenzoate	$C_{10}H_{12}O_3$: 180.20	colorless crystals or white powder or chunky white solid	Antimicrobial preservative	Typically found in many water-based cosmetics, such as creams, lotions, shampoos and bath products. Also used as a food additive.

4.	Butyl paraben	Butyl 4-hydroxybenzoate	$C_{11}H_{14}O_3$: 194.23	Odourless white crystals or crystalline powder and Tasteless	Antimicrobial preservative	Flavouring agent in Foods
5.	Benzyl paraben	Benzyl 4-hydroxybenzoate	$C_{14}H_{12}O_3$:228.24	Odourless white crystals	Antimicrobial preservative	cosmetics and pharmaceuticals
6.	Isobutyl paraben	Isobutyl 4-hydroxybenzoate	$C_{11}H_{14}O_3$: 194.23	Odourless white crystals	Antimicrobial preservative	Personal care(skin cream to body lotion to deodorant.) and House hold products

Applications of Parabens:

In the cosmetics industry, parabens are used as kinds of preservative in products that are exposed to decompose and are easily reachable to bacteria, as well as in products that should last for a long time after opening. These include:

1. creams,
2. lotions,
3. oils,
4. tonics,
5. glosses,
6. lipsticks,
7. other wet cosmetics,
8. powders and foundations and other cosmetics that are used for a long time,
9. antiperspirants and perfumes.

As a result of the addition of parabens, the usefulness of products is extended by up to several months, the products do not become covered with mould and are protected against other fungi and bacteria that are dangerous to health(Roden,2010).

Parabens (*p*-hydroxybenzoic acid) are an important class of preservatives extensively used in the cosmetic and pharmaceutical industries for preparing shampoos, commercial moisturizers, shaving gels, personal lubricants, topical/parenteral pharmaceuticals, spray tanning solutions, and toothpaste. Although effective as antibacterial and antifungal agents, these compounds are supposed to possess hepatotoxic effects (Verma and Asnani, 2007).

The **FDA, the European Community,** and the Joint **FAO/WHO** Expert Committee on Food Additives (JECFA) have been approved the use of parabens in food, and they are generally recognized as safe (GRAS). Parabens are rapidly metabolized without accumulating in the body, are relatively non irritating and non sensitizing, and present low toxicity. Recent studies have raised concerns about the use of parabens, with special focus on propylparaben as possibly having estrogenic potential; however, no conclusive evidence suggests any risk to people under current used levels.

In 1984, **CIR** reviewed the safety of parabens used in cosmetics and concluded that they were safe, even in extremely large doses. Typically parabens are used at levels ranging from 0.01 to 0.3 percent, and the CIR concluded they were safe for use in cosmetics at levels up to 25 percent. In 2012, the CIR reopened its safety report on parabens to consider all new data. As it did in 1984, the expert panel reaffirmed the safety of cosmetic products in which parabens preservatives are used.

Plants such as blueberries, carrots, olives, strawberries and others produce parabens (mainly methylparaben) for its presumed antimicrobial activity. Overall, the concentration of parabens within the environment are low with water concentrations of around 7 ng/L and effluent concentrations of up to 6 µg/L, soils concentration range from 0.5 to 8 ng/g while house dust contains up to 2,400 ng/g (Kucińska and Murias,2013) .

Methylparaben was detected at a maximum concentration of 920 ng/L. Heptyl- and benzylparaben were found in influent waters of a STP in the Albany area in New York at maximum concentrations of 0.31 and 0.27 ng/L respectively(Wang and Kannan, 2014).

Bioaccumalation of Soil and Water:

A team of environmental chemists has discovered that methyl paraben, a compound widely used as a preservative in personal care and pharmaceutical products, can bioaccumulate in marine food chains. The compound is a suspected endocrine disruptor, but has not previously been flagged up for its bioaccumulative properties (Philip lightowlers, 2017).

Parabens are widely used in different industries as preservatives and antimicrobial compounds. The evolution of analytical techniques allowed the detection of these compounds in different sources at _g/L and ng/L. Until today, parabens were already found in water sources, air, soil and even in human tissues. The impact of parabens in humans, animals and in ecosystems are a matter of discussion within the scientific community, but it is proven that parabens can act as endocrine disruptors, and some reports suggest that they are carcinogenic compounds. The presence of parabens in ecosystems is mainly related to wastewater discharges(Joao *et al.*,2021).

Parabens are also linked to ecological harm, as low levels of butylparaben can kill coral, according to laboratory tests (Danaovaro 2008). Parabens have been detected in surface waters, fish and sediments (Haman 2015). When parabens are combined with chlorinated tap water, a number of chlorinated paraben byproducts can form (Canosa 2006). Little is known about the toxicity of these byproducts, which may be more persistent (Haman 2015).

several authors have reported in in vitro studies that parabens show weak estrogenic effects (Bledzka *et al.*,2014) but other studies suggest that PP, BuP and BeP can cause adverse effects in aquatic organisms and elicit low estrogenic activity(Brausch and Rand, 2011). Additionally, other studies mention that the exposure of

fish to low concentrations of paraben compounds can cause vitellogenin (VTG) synthesis, so with this, can cause estrogenic effects (Brausch and Rand, 2011).

Similar conclusions were reported in studies reviewed by Bledzka et al., 2014. The effects of endocrine disruptors, namely xenoestrogens, were already noticed in alligators and fishes (Sumpter, 2013 and Renz *et al.*, 2013). Renz et al.,2013 did not find evidence of bioaccumulation of parabens in fishes.

The directive (European Union) N_ 75/2010(Directive (European Union) No 75/2010 of 24 November 2010 on Industrial Emissions (Integrated Pollution Prevention and Control)) indicates some guidelines for industrial emissions and presents the Paraben compounds that are considered as air and water pollutants. Parabens are not directly considered as pollutants but are indirectly considered, since carcinogenic substances and substances that alter chemical oxygen demand (COD) and biochemical oxygen demand (BOD) are considered as pollutants. This directive also indicates that the substances present in directive N_ 60/2000. Directive of the European Community (EC) (which was already updated by directive (EC) N_ 105/2008 and directive (EU) N_ 39/2013 are considered as water pollutants, but once again, the paraben family are not part of it.The directive (EU) N_ 39/2013 regulates and classifies some priority substances in water policy(Lincho *et al.*,2021)

The aggregation concentrations of bisphenol analogues, parabens, and paraben metabolites were 106 ng/L, 4.53 ng/L, and 231 ng/L in aqueous samples, 868 ng/g, 173 ng/g, and 9320 ng/g in SPM samples, 41.6 ng/g, 6.46 ng/g, and 460 ng/g in marine organisms, respectively. This study identified significantly higher concentrations of paraben metabolites than their parent parabens in the marine environment, which has not yet been reported in previous studies. These findings call for greater attention on the contamination of paraben metabolites in marine environments(Zhao *et al.*,2019).

Limitations of using Parabens:

A number of commonly used parabens have had the **U.S. Food and Drug Administration's (FDA)** Generally Recognized as Safe (GRAS) classification since the early 1970s. The **GRAS** designation means the substance is generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use. Other examples of compounds that are considered GRAS include vitamin A, wheat starch and sugar.

FDA also participates on the **Cosmetic Ingredient Review (CIR)**, an independent panel of medical and scientific experts that meets quarterly to assess the safety of cosmetic ingredients based on data in the published literature, as well as data voluntarily provided by the cosmetics industry. FDA takes the results of CIR reviews into consideration when conducting a safety assessment.

- In 1984, CIR reviewed the safety of parabens used in cosmetics and concluded that they were safe, even in extremely large doses. Typically parabens are used at levels ranging from 0.01 to 0.3 percent, and the CIR concluded they were safe for use in cosmetics at levels up to 25 percent.
- In 2012, the CIR reopened its safety report on parabens to consider all new data. As it did in 1984, the expert panel reaffirmed the safety of cosmetic products in which parabens preservatives are used.

The European Scientific Committee on Consumer Safety (SCCS) reiterated in 2013 that methylparaben and ethylparaben are safe at the maximum authorized concentrations (up to 0.4% for one ester or 0.8% when used in

combination). The SCCS concluded that the use of butylparaben and propylparaben as preservatives in finished cosmetic products is safe to the consumer, as long as the sum of their individual concentrations does not exceed 0.19%. Isopropylparaben, isobutylparaben, phenylparaben, benzylparaben and pentylparaben were banned by **European Commission Regulation (EU) No 358/2014.**

Parabens effect on normal flora Microorganism and Pathogenic Microbes:

Human skin is the front line of defenses against external infectious or toxic substances, and is an environmental habitat that various microorganisms, including bacteria, fungi, yeasts, and viruses, can colonize (Schommer and Gallo, 2013). Human skin is a complex ecosystem with various microenvironmental conditions, and thus, skin microbial communities are very diverse and complex (Oh *et al.*, 2014;Schommer & Gallo, 2013). Skin structures such as hair follicles, sebaceous glands, eccrine and apocrine sweat glands as well as subepidermal skin compartments, provide distinct biological niches that are colonized by their own unique skin microbiota (Nakatsuji *et al.*, 2013; Oh *et al.*, 2014).

Besides them, various factors, including the use of antibiotics, cosmetics, soaps, personal care products, and living conditions such as life styles and alimentations can have influence on the skin microbiome (Perez *et al.*, 2016). Skin microbial communities have been reported to be site-, individual-, and race-specific and are largely stable over time, despite the human skin's exposure to different external environments such as climates (Leung, Wilkins, & Lee, 2015; Oh, Byrd, Park, Kong, & Segre, 2016; Oh *et al.*, 2014). It was also reported that the skin microbiome was clearly different depending on the ethnic races, which may be because endogenous (immune status, genetic characters, and skin properties) and exogenous (foods and life styles) factors are different depending on ethnicity (Alexis & Alam, 2012; Pappas, Fantasia, & Chen, 2013; Perez et al., 2016).

Cosmetics typically consist of substances that are an excellent medium for micro-organisms (bacteria and fungi), e.g. amino acids, peptides, protein hydrolysates, polysaccharides, plant extracts and vitamins. Cosmetics that have not been protected by a preservative quickly spoil, resulting in a change in the aroma and appearance of the product (Pawlik *et al.*,2013).

The mechanism of the antibacterial action of parabens has not been fully explained. They are suspected to be inhibitors of the synthesis of DNA and RNA nucleic acids or to inhibit the enzymes necessary for the proper functioning of bacterial cells (Doron et al.,2001).

Parabens can also act by interfering with membrane transport processes. In addition, they can inhibit the influx of amino acids, such as alanine, serine, and phenylalanine, into the vesicles of bacterial cell membranes without altering glucose transport. It is also likely that they have antibacterial effects consisting in the denaturation of bacterial proteins, which increase in the acidic environment. All phenol derivatives work analogously (Terasaki *et al.*,2009).

Effects of Paraben on Human Health:

Most of the available paraben toxicity data are from single-exposure studies, meaning one type of paraben in one type of product. According to paraben research this is relatively safe, posing only a negligible risk to the endocrine system. However, since many types of parabens in many types of products are used commonly,

further assessment of the additive and cumulative risk of multiple paraben exposure from daily use of multiple cosmetic and/or personal care products is needed(Karpuzoglu *et al.*,2013). FDA states that they have no information that use of parabens in cosmetics has any effect on health. They continue to consider certain questions and evaluate data about parabens' possible health effects (U.S. Food and Drug Administration,2018*)*.

Allergic reactions:

Parabens are, for the most part, non-irritating and non-sensitizing. Among people with contact dermatitis or eczema, less than 3% of patients were found to have a sensitivity to parabens(Hafeez and Maibach, 2013*)*. At least one case has been reported of an allergic reaction to parabens (Nagel *et al.*,1977).

Breast cancer:

The American Cancer Society mentioned a 2004 study that found parabens in the breast tissue of mastectomy patients but did not find parabens to be a cause of the cancers. Michael Thun of ACS stated that the effects of parabens would be minuscule compared to other risks "such as taking hormones after menopause and being overweight". A 2005 review concluded "it is biologically implausible that parabens could increase the risk of any estrogen-mediated endpoint, including effects on the male reproductive tract or breast cancer" and that "worst-case daily exposure to parabens would present substantially less risk relative to exposure to naturally occurring endocrine active chemicals in the diet such as the phytoestrogen daidzein."

Estrogenic activity:

Animal experiments have shown that parabens have weak estrogenic activity, acting as xenoestrogens(Byford *et al.*,2002). In an *in vivo* study, the effect of butylparaben was determined to be about 1/100,000th that of estradiol, and was only observed at a dose level around 25,000 times higher than the level typically used to preserve products(Edwin J. Routledge *et al.*, 1998). The study also found that the *in vivo* estrogenic activity of parabens is reduced by about three orders of magnitude compared to *in vitro* activity.

The estrogenic activity of parabens increases with the length of the alkyl group. It is believed that propylparaben is estrogenic to a certain degree as well,(Cashman and Warshaw 2005*)* though this is expected to be less than butylparaben by virtue of its less lipophilic nature. Since it can be concluded that the estrogenic activity of butylparaben is negligible under normal use, the same should be concluded for shorter analogs due to estrogenic activity of parabens increasing with the length of the alkyl group.

The effect of parabens in the Terrestrial environment:

In the most recent years, make-up items, as well as pharmaceuticals and many other products for personal care that do not fall within cosmetic regulation (disinfectants, insect repellents, dietary supplements), have raised major concerns as one of the most significant types of up-and-coming pollutants. This is as a result of them being continually released into the water environment; their ecological and environmental collision is connected with large amounts being used and with the reality that sometimes they are environmentally constant, bioactive, and potentially capable to bioaccumulate (Chunyang et al.,2013).

Effects on Aquatic Life:

The chemicals in this group range from slightly to highly toxic in aquatic organisms (Terasaki *et al.*,2013). The measured median lethal concentration (LC50) and median effective concentration (EC50), as well as the no observed effect concentration (NOEC) and the lowest observed effect concentration (LOEC) values for model organisms across three trophic levels for methylparaben (MeP), ethylparaben (EtP), propylparaben (PrP), butylparaben (BuP), benzylparaben (BzP), heptylparaben (HeP), and octylparaben (OcP) have been reported (Yamamoto *et al.*,2011).

Calculated data for long-chain parabens indicates higher levels of toxicity than for short-chain parabens. This trend is consistent with previous studies, which demonstrated that the toxicity of parabens is proportional to their lipophilicity(Yamamoto *et al.*,2011). This indicates that the acute toxicity of parabens is likely to occur through the non-specific disruption of the cell membrane function(Terasaki *et al.*,2009). Calculated and measured toxicity values for the short chain parabens were fairly consistent therefore the calculated ecotoxicity endpoints for the long chain parabens appears to be reliable. Reliable values for acute ecotoxicity endpoints for laurylparaben cannot be calculated (Barabasz *et al.*,2019).

Conclusion:

parabens are also good but study has reported that they cause many health troubles as almost all are cancer causing in nature. Hence these must be used allowing for highest safety border for the preservatives used in pharmaceuticals as well as cosmetics. The number of rising pollutants released in the surroundings as a result of human movement is rising day by day and reflects the increasing utilization of a broad range of products, including cosmetics and personal care products. In some times, Parabens are separated in wastewater treatment plants, they can escape usual treatment processes, continue in the surroundings at unpredicted amounts, undergo bioaccumulation, and even react with other pollutants to form new volatile contaminants. prohibition the products answerable for these problems is an impossible option, except in particular circumstances only. Generally parabens are the most commonly used preservatives. They are relatively active against a broad spectrum of microorganisms. Parabens are commonly used as antimicrobial preservatives in household products, cosmetics, pharmaceuticals, and food and beverage processing, and are environmental compounds with oestrogenic activity.

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