



## A REVIEW ON SYNTHESIS OF PARABEN AND APPLICATIONS OF PRESERVATIVES

SD. Haseeb<sup>1</sup>, S. Asma Parveen<sup>2</sup>, Y. Prapurna Chandra<sup>3</sup>.

1. B. Pharmacy, IV Year, Ratnam Institute of Pharmacy, spsr Nellore, Andhra Pradesh.

2. Associate professor, Department of Pharmaceutical Analysis, Ratnam Institute of Pharmacy, spsr Nellore, Andhra Pradesh.

3. Principal of Ratnam Institute of Pharmacy, spsr Nellore, Andhra Pradesh.

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### Abstract

Parabens are a class of widely used preservatives in pharmaceutical, cosmetic, and food industries. Despite their efficacy, concerns over their safety and toxicity have led to increased interest in alternative preservatives. This review provides a comprehensive overview of the synthesis of parabens, their properties, and applications. We discuss the different methods of paraben synthesis, including chemical and enzymatic approaches. The review also covers the use of parabens as preservatives in various industries, including pharmaceuticals, cosmetics, and food. Furthermore, we examine the safety and toxicity concerns associated with parabens and discuss alternative preservatives that are being developed. This review aims to provide a thorough understanding of parabens and their applications, as well as the current state of research on alternative preservatives.

**Keywords:** parabens, preservatives, synthesis, applications, safety, toxicity, alternative preservatives.

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### \*Corresponding Author

S. Asma Parveen

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### 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. Parabens are odorless, colorless, non-volatile, low costs of production and they do not change consistency or color of formulations. 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. Although parabens are generally considered as safe ingredients, several studies have raised concerns on the safety of parabens. With the increased use of pharmaceuticals and personal care products for the human population, various anthropogenic substances are continuously released into aquatic environments. Through domestic and industrial wastewater. 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 and may cause toxic effects on non-target organisms, representing a threat to aquatic ecosystems functioning [1].

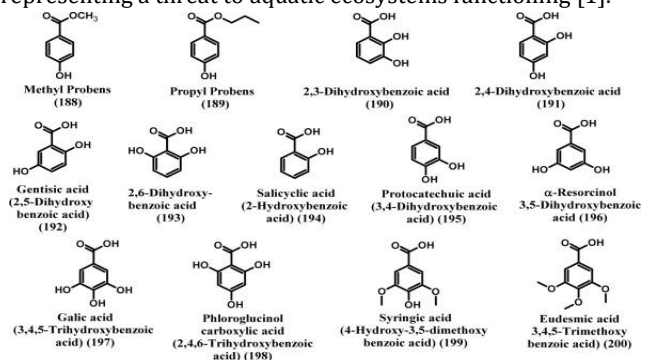


Fig:1 Parabens

### Importance of Parabene in Various Industries:

Parabens play a crucial role in various industries due to their antimicrobial properties, stability, and low toxicity. Here is some of the importance of parabens in different industries.

#### Pharmaceutical Industry

1. **Preservation of formulations:** Parabens are used to prevent microbial growth in pharmaceutical products,

such as ointments, creams, and injectables.

- 2. Stability and shelf-life extension:** Parabens help maintain the stability and shelf-life of pharmaceutical products by preventing degradation caused by microorganisms.
- 3. Protection of active ingredients:** Parabens protect active pharmaceutical ingredients from degradation caused by microorganisms, ensuring their potency and efficacy [2].

#### Cosmetic Industry:

- 1. Preservation of personal care products:** Parabens are widely used in personal care products, such as shampoos, conditioners, lotions, and creams, to prevent microbial growth.
- 2. Prevention of spoilage:** Parabens prevent spoilage and extend the shelf-life of cosmetic products.
- 3. Maintenance of product texture and appearance:** Parabens help maintain the texture and appearance of cosmetic products by preventing microbial growth and degradation.

#### Food Industry:

- 1. Preservation of food products:** Parabens are used as preservatives in food products, such as baked goods, beverages, and dairy products.
  - 2. Prevention of spoilage:** Parabens prevent spoilage and extend the shelf-life of food products.
  - 3. Protection of food quality:** Parabens protect the quality of food products by preventing microbial growth and degradation [2].
- To review the synthesis methods of parabens
  - To explore the applications of paraben
  - To evaluate the benefits and safety concerns of parabens
  - To discuss regulatory guidelines and alternatives
  - To provide comprehensive overview on parabens

### Synthesis of Parabens

parabens are widely 'synthesized' and 'utilised' as preservatives in nature, some plants can produce parabens to keep their fruit fresh. A microorganism, bacterium, produces parabens in its calcareous sponge. A marine bacterium biosynthesizes parabens in preventing the growth of yeasts, molds, and gram-positive bacteria. The synthesis of parabens from p-hydroxybenzoic acid. R represents CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>, C<sub>3</sub>H<sub>7</sub>, C<sub>4</sub>H<sub>9</sub>. The process to synthesize parabens in lab or industrial scale has been known for hundreds of years. It is a simple 'acid-base' reaction in the presence of a suitable catalyst such as montmorillonite K10 clay, thionylchloride, and dodecatungstophosphoric acid. Successful synthesis requires p-hydroxybenzoic acid as the starting material, mixed with an appropriate amount of alcohol, and produce parabens as the main product and water as a by-product. The traditional method is considered as a simple and robust process; while new technologies have been explored to improve the synthesis efficiency and cost-effectiveness by introducing microwave radiation and inorganic salt ZnCl<sub>2</sub> as catalysts. There is also a trend to develop more green methods as alternatives to save power and energy consumption during the manufacturing process [4].



Fig:2 Synthesis Of Paraben

### Properties of Paraben

#### Physical Properties

- 1. Appearance:** Parabens are white or off-white crystalline powders.
- 2. Odor:** Parabens have a characteristic sweet or fruity odor.
- 3. Melting Point:** The melting points of parabens vary depending on the specific compound, but they typically range from 120°C to 160°C.
- 4. Solubility:** Parabens are generally soluble in water, ethanol, and other organic solvents.
- 5. Density:** The density of parabens ranges from 1.2 to 1.4 g/cm<sup>3</sup>.

#### Chemical Properties

- 1. Chemical Structure:** Parabens are esters of p-hydroxybenzoic acid (PHBA) with a general chemical structure of:  
p-Hydroxybenzoic acid + Alcohol → Paraben + Water
- 2. pH:** Parabens are stable over a wide pH range, typically between 4 and 8.
- 3. Hydrolysis:** Parabens are susceptible to hydrolysis, which can lead to the formation of p-hydroxybenzoic acid.
- 4. Oxidation:** Parabens are generally resistant to oxidation, but they can undergo oxidation reactions in the presence of strong oxidizing agents.
- 5. Thermal Stability:** Parabens are thermally stable and can withstand temperatures up to 200°C without undergoing significant degradation.

#### Other Properties

- 1. Antimicrobial Activity:** Parabens exhibit antimicrobial activity against a wide range of microorganisms, including bacteria, fungi, and yeast.
- 2. Toxicity:** Parabens are generally considered to be non-toxic and non-irritating, but they can cause skin irritation and allergic reactions in some individuals.

### Effects of Ph and Temperature on Paraben Properties

#### Effects of pH on Parabens

- 1. Stability:** Parabens are stable over a wide pH range, typically between 4 and 8.
- 2. Solubility:** The solubility of parabens can vary depending on the pH of the solution. At low pH, parabens are more soluble, while at high pH, they are less soluble.
- 3. Hydrolysis:** Parabens can undergo hydrolysis at high pH, resulting in the formation of p-hydroxybenzoic acid and the corresponding alcohol.
- 4. Antimicrobial Activity:** The antimicrobial activity of parabens can be affected by pH. At low pH, parabens are more effective against microorganisms.

#### Effects of Temperature on Parabens

- 1. Stability:** Parabens are thermally stable and can withstand temperatures up to 200°C without

undergoing significant degradation.

2. **Solubility:** The solubility of parabens can increase with temperature, making them more soluble in water and organic solvents.
3. **Hydrolysis:** Parabens can undergo hydrolysis at high temperatures, resulting in the formation of phydroxybenzoic acid and the corresponding alcohol.
4. **Antimicrobial Activity:** The antimicrobial activity of parabens can be affected by temperature. At high temperatures, parabens may be less effective against microorganisms.

#### 8.3. Combined Effects of pH and Temperature on Parabens

1. **Increased Hydrolysis:** High temperatures and high pH can increase the rate of hydrolysis of parabens.
2. **Decreased Antimicrobial Activity:** High temperatures and high pH can decrease the antimicrobial activity of parabens.
3. **Increased Solubility:** High temperatures and low pH can increase the solubility of parabens [6].

### Applications of Parabens

#### Pharmaceutical Applications

##### Topical Preparations

1. **Creams and Ointments:** Parabens are used as preservatives in topical creams and ointments to prevent microbial growth.
2. **Gels and Lotions:** Parabens are used in topical gels and lotions to provide antimicrobial protection.
3. **Transdermal Patches:** Parabens are used in transdermal patches to prevent microbial growth and maintain the stability of the active ingredients.

##### Ophthalmic Preparations

1. **Eye Drops:** Parabens are used as preservatives in eye drops to prevent microbial growth and maintain the sterility of the product.
2. **Ointments and Gels:** Parabens are used in ophthalmic ointments and gels to provide antimicrobial protection.

##### Parenteral Preparations

1. **Injectable Solutions:** Parabens are used as preservatives in injectable solutions to prevent microbial growth and maintain the sterility of the product.
2. **Implants and Inserts:** Parabens are used in implants and inserts to provide antimicrobial protection and maintain the stability of the active ingredients.

##### Other Pharmaceutical Applications

1. **Tablets and Capsules:** Parabens are used as preservatives in some tablet and capsule formulations to prevent microbial growth.
2. **Suspensions and Emulsions:** Parabens are used as preservatives in suspensions and emulsions to prevent microbial growth and maintain the stability of the product.
3. **Veterinary Products:** Parabens are used as preservatives in some veterinary products, such as topical creams and ointments.

Overall, parabens are widely used in various pharmaceutical applications due to their antimicrobial properties, stability, and low toxicity [7].

### Cosmetic Applications

#### Skin Care Products

1. **Moisturizers and Creams:** Parabens are used as preservatives in moisturizers and creams to prevent microbial growth and maintain the stability of the product.
2. **Facial Cleansers and Toners:** Parabens are used in facial cleansers and toners to provide antimicrobial protection and prevent the growth of bacteria and other microorganisms.
3. **Sunscreen and After-Sun Products:** Parabens are used in sunscreen and after-sun products to prevent microbial growth and maintain the stability of the product.

#### Hair Care Products

1. **Shampoos and Conditioners:** Parabens are used as preservatives in shampoos and conditioners to prevent microbial growth and maintain the stability of the product.
2. **Hair Masks and Deep Conditioning Treatments:** Parabens are used in hair masks and deep conditioning treatments to provide antimicrobial protection and prevent the growth of bacteria and other microorganisms [8].

#### Makeup and Color Cosmetics

1. **Foundations and Concealers:** Parabens are used as preservatives in foundations and concealers to prevent microbial growth and maintain the stability of the product.
2. **Eye Shadows and Mascaras:** Parabens are used in eye shadows and mascaras to provide antimicrobial protection and prevent the growth of bacteria and other microorganisms.

#### Other Cosmetic Applications

1. **Deodorants and Antiperspirants:** Parabens are used as preservatives in deodorants and antiperspirants to prevent microbial growth and maintain the stability of the product.
2. **Fragrances and Perfumes:** Parabens are used in fragrances and perfumes to provide antimicrobial protection and prevent the growth of bacteria and other microorganisms.

Overall, parabens are widely used in various cosmetic applications due to their antimicrobial properties, stability, and low toxicity.

### Safety and Toxicity of Parabens:

#### Safety Concerns

1. **Endocrine Disruption:** Parabens have been shown to mimic the effects of estrogen in the body, which can lead to hormonal imbalances and other endocrine-related problems.
2. **Breast Cancer:** Some studies have suggested a link between paraben use and an increased risk of breast cancer, although the evidence is still limited and inconclusive.
3. **Reproductive Issues:** Parabens have been shown to affect reproductive health in animal studies, including reduced sperm count and decreased fertility.
4. **Skin Irritation and Allergic Reactions:** Some people may experience skin irritation, allergic reactions, or

contact dermatitis due to paraben exposure.<sup>10</sup>

### Toxicity Concerns

- 1. Acute Toxicity:** Parabens are generally considered to be low-to-moderate acute toxins, with LD50 values ranging from 2-8 g/kg.
- 2. Chronic Toxicity:** Long-term exposure to parabens has been linked to various health problems, including endocrine disruption, reproductive issues, and cancer.
- 3. Environmental Toxicity:** Parabens have been detected in environmental samples, including water and soil, and have raised concerns about their potential impact on ecosystems.

### Effects on Environment

Some of parabens are causing the most of the environmental problems including water along with some of the effects.



FIG: 3 EFFECTS ON ENVIRONMENT

### REGULATORY GUIDELINES FOR PARABEN USE:

#### FDA Guidelines (USA)

- 1. Cosmetic Products:** The FDA allows the use of parabens in cosmetic products, but requires that they be listed on the ingredient label.
- 2. Food Products:** The FDA allows the use of parabens as food preservatives, but sets limits on their concentration in certain products.
- 3. Pharmaceutical Products:** The FDA requires that parabens be used in accordance with good manufacturing practices (GMPs) and that their concentration be limited to the minimum amount necessary to achieve the intended effect [12].

#### EU Guidelines (Europe)

- 1. Cosmetic Products:** The EU bans the use of certain parabens, including propylparaben and butylparaben, in cosmetic products.
- 2. Food Products:** The EU sets limits on the concentration of parabens in food products, including beverages, dairy products, and meat products.
- 3. Pharmaceutical Products:** The EU requires that parabens be used in accordance with GMPs and that their concentration be limited to the minimum amount necessary to achieve the intended effect.

### Conclusion

Parabens are a group of preservatives widely used in various industries, including cosmetics, pharmaceuticals, and food. They have been used for decades due to their effectiveness in preventing microbial growth and extending product shelf life. The applications of parabens are diverse, ranging from cosmetics and pharmaceuticals to food and veterinary products. In cosmetics, parabens are used as preservatives to prevent microbial growth and extend product shelf life. In pharmaceuticals, parabens are used as

excipients to improve the stability and bioavailability of active ingredients. In food, parabens are used as preservatives to prevent spoilage and extend shelf life. In conclusion, parabens are a widely used group of preservatives with diverse applications. While their synthesis and applications have been well-established, their safety concerns and regulatory guidelines must be carefully considered.

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