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# A Comprehensive Study On Benzoic Acid And Its Derivatives

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**Abstract:**

In culinary, cosmetic, hygiene, and pharmaceutical goods, the derivatives of benzoic acid like ester, Hydroxy benzene, benzaldehyde, phenyl esters frequently employed in many areas like they show antibacterial activity, antifungal activities, used as flavouring agents and act as antifungal preservatives. These substances are widely disseminated in the society for their use

Which have profound effect on human health as they are available in air and soil for the manufacture of chemical substances. A naturally occurring organic substance as well as synthetically produced benzoic acid are both available. The study focuses on its numerous biological features, including nematicidal, antiviral, antifungal, antimutagenic, antiestrogenic, hypoglycemic, and anti-inflammatory. It has been shown that several derivatives of benzoic acid have direct effects on the haemoglobin, which can cure odema which is produced by direct use of acetic acid as well as some time also use for the treatment of sickle cell anemia. The biological activities of 4-BHA and its derivatives is thoroughly explained by the current investigation. Consequently, benzoic acid and its derivatives can have a high, frequent, and prolonged human exposure.

**Key words:** *Hypoglycemic, Nematicidal, Antimutagenic, Antiestrogenic, Anti-inflammatory*

## INTRODUCTION:

Benzoic acid ($C_6H_5COOH$) is a naturally occurring compound found in various plants. It plays a crucial role as an intermediate in the biogenesis of secondary products which are called metabolites in these plants. Additionally, benzoic acid and its derivatives have widespread applications in various industries. Salts of benzoic acid, known as benzoates, are commonly used as food preservatives due to their antimicrobial properties. They inhibit the growth of bacteria, molds, and yeasts, particularly in acidic food products. This property make 4-BHA effective in extending the shelf life of processed foods such as pickles, jams and other products. Industrial synthesis relies heavily on benzoic acid as a precursor for the production of numerous organic substances. The esters and salts of benzoic acid, collectively known as benzoates, find applications in various fields. Benzoic acids derivativesare used as ingredients in beauty products and pharma product and

cosmetics. Benzoic acid itself is often present in topical antifungal preparation because it is stable and suppress the growth of fungus.

Gum benzoin, derived from the bark of trees belonging to the Styrax genus, is a common natural source of benzoic acid. However, most of the benzoic acid produced today is synthetic. The first industrial synthesis of benzoic acid involved the hydrolysis of benzotrichloride to form calcium benzoate, which was then acidified to obtain benzoic acid. This method has been largely replaced by the air oxidation of toluene, a process that avoids the contamination issue associated with chlorinated byproducts. The presence of benzoic acid in plants is part of their chemical defence mechanism against microbes. It is classified as a phenolic substance, which encompasses a range of compounds like flavonoids and phenolic carboxylic acids. Phenolic substances are frequently associated with the protection of plants against microbial attacks and act as signaling molecules in plant-microbe interaction. benzoic acid is a versatile compound that occurs naturally in plants and is widely used in various industries. Its salts and esters find applications as food preservatives, while benzoic acid itself is utilized as a preservative in products ranging from processed foods to cosmetics Khadem,S.*et al*.,(2010).

Its significance as a precursor in organic synthesis further highlights its industrial importance. The family of phenolic substances, including benzoic acid, is important in chemical defense mechanisms of plants and their interactions with microbes. Phenolic compounds, including benzoic acid derivatives like 4-hydroxy benzoic acid, have been extensively studied for their antimicrobial properties and their role in allelopathic interactions between plants. These compounds can be classified into two main categories: phytoalexins and phytoanticipins. Phytoalexins are inducible antimicrobial compounds that are synthesized by plants in response to pathogen attack or other stresses. They act as defence mechanisms to inhibit the growth of microbial pathogens. On the other hand, phytoanticipins are constitutive antimicrobial compounds that are present in plants even in the absence of pathogens. They provide a baseline level of protection against microbial pathogens.

Benzoic acid and its derivatives mostly used in preservation of food material which inhibit the bacterial, mould and yeast growth. They are particularly effective in acidic conditions and are commonly found in carbonated drinks, fruit juices, pickles, and condiments. Constitutive phenolics can inhibit the germination of fungal spores, impair fungal hypal growth and reduce the formation of fungal structures such as mycelium and fruiting bodies Lemini C *et al*.,(1997). This can limit the ability of fungal pathogens to establish infection and spread within plant tissues. 4-HBA is able to induce the effect of defence mechanism compounds such as phytolexin, antimicrobial proteins, and enzymes that directly or indirectly inhibit fungal growth. Benzoic acid can strengthen the cell walls and cuticles of plant tissues making them more resistant to fungal penetration.

Benzoic acid can strengthen the cell walls and cuticles of plant tissues, making them more resistant to fungal penetration. They can also promote the deposition of lignin and other structural compounds, which can form physical barriers to inhibit fungal infection. Constitutive phenolics can generate reactive oxygen species (ROS) within plant tissues, leading to oxidative stress. Fungal pathogens are susceptible to oxidative damage caused by ROS, which can impair their cellular structures and functions. phenolics against fungal pathogens can vary depending on the specific compound, the concentration, and the fungal species involved. Additionally, some fungal pathogens have developed mechanisms to detoxify or evade the effects of phenolic

compounds, reducing their effectiveness as a sole defence mechanism. Therefore, plant defence against fungal pathogens often involves a complex interplay of multiple defence strategies Horvath et al. (2007)

**Biochemical Properties of Benzoic acid**

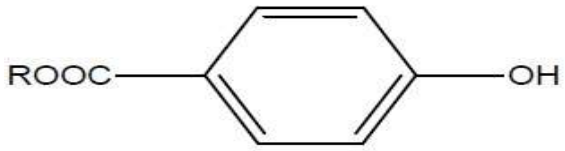
**1.Benzoic acid as antimicrobial inhibitor:** Benzoic acid is a common antimicrobial agent that has been used for many years. It is a white due to its crystalline solid with the chemical formula $C_6H_5COOH$. Benzoic acid has antimicrobial properties and has the ability to inhibit the growth of various microorganism including bacteria, fungi and yeast. Mechanism of Action: Benzoic acid exerts its antimicrobial effects by disrupting the pH balance within microbial cells. It enters the cell and lowers the intracellular pH, causing acidification of the cytoplasm. This acidification interferes with the normal metabolic processes of the microorganisms, ultimately inhibiting their growth and survival. Preservative Properties: Benzoic acid is widely used as a food preservative due to its antimicrobial activity. It inhibits the growth of bacteria, molds, and yeasts, thus preventing spoilage and extending the shelf life of various food products.

Synergy with Other Preservatives: Benzoic acid is often used in combination with other antimicrobial agents, such as sorbic acid or propionic acid, to enhance its effectiveness. These combinations create synergistic effects, providing a broader spectrum of antimicrobial activity.

pH-Dependent Activity: The antimicrobial activity of benzoic acid is pH-dependent. It is more effective in acidic conditions, as the undissociated form of benzoic acid ($C_6H_5COOH$) is more lipophilic and can easily penetrate microbial cell membranes. In neutral or alkaline conditions, where benzoic acid is mostly in the dissociated form, its antimicrobial activity is reduced.

Regulatory Approval: Benzoic acid is approved for use as a food preservative by regulatory authorities such as the FDA. Maximum usage levels are specified for different food categories to ensure safety.

Safety Considerations: Benzoic acid is generally recognized as safe (GRAS) when used in accordance with approved limits. However, some individuals may be sensitive or allergic to benzoic acid, leading to adverse reactions. As with any food additive, it is essential to follow recommended guidance and consider individual sensitivities.




| | R |
|---|---|
| Methyl ester | $-CH_3$ |
| Ethyl ester | $-C_2H_5$ |
| Propyl ester | $-C_3H_7$ |
| Butyl ester | $-C_4H_9$ |

Figure-1: Orsellinic acid structure and its compounds

compound found in certain fungi and lichens. It belongs to the class of compounds called depsides and has been studied for its various biological activities. While it does not have well-documented antimicrobial properties like benzoic acid, orsellinic acid has been investigated for its potential medicinal and pharmaceutical applications. Orsellinic acid is produced by various fungal species, including certain

Aspergillus and Penicillium strains. It is also found in lichens such as Parmelia and Umbilicaria. Orsellinic acid has a chemical structure consisting of a benzene ring with two hydroxyl groups (-OH) and a methyl group (-CH3) attached to it. Its molecular formula is $C_8H_8O_4$, and it has a molecular weight of 168.15g/ml. Orsellinic acid and its derivatives have been investigated for their potential medicinal properties. They have shown promising activities in areas such as anti-inflammatory, antioxidant, anticancer, and antimicrobial effects. Synowiec,A.*et al*., (2021).

However, it should be noted that the specific antimicrobial properties of orsellinic acid are not extensively studied or established. Orsellinic acid is synthesized in fungi and lichens through enzymatic reactions involving polyketide synthases and other biosynthetic enzymes. It serves as a precursor in the synthesis of various secondary metabolites, including depsides and depsidones. Some derivatives of orsellinic acid have shown pharmacological activities. For example, usnic acid, which is derived from orsellinic acid, has been investigated for its antimicrobial, antiviral, and anticancer properties. Usnic acid has been used in traditional medicine and as an ingredient in certain topical ointment. Orsellinic acid and its derivatives continue to be subjects of research and development for their potential therapeutic applications. Scientists are exploring their biological activities, mechanisms of action, and potential uses in drug discovery and development. It's important to note that while orsellinic acid and its derivatives show promise in various areas of research, further studies are needed to fully understand their mechanisms of action, efficacy, and safety. As with any bioactive compound, thorough evaluation and testing are required before considering its application in antimicrobial contexts or pharmaceutical formulations, reported by Robbins *et al*., (2003).

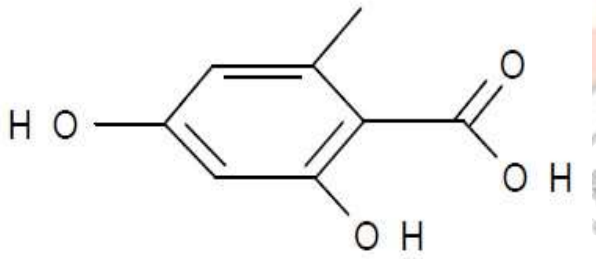



Figure-2: Syringic acid structure

Syringic acid is a natural compound that belongs to the class of phenolic acids. It is derived from the hydroxylation of vanillin or syringaldehyde. Syringic acid is found in various plant sources, including fruits, vegetables and herbs. Syringic acid is present in several plant-based foods, including grapes, strawberries, blackberries, olive oil, coffee, and some spices such as cloves and sage. It is also found in significant amounts in certain medicinal plants like sphagneticola trilobata and Gynura procumbens.

Studies have shown that syringic acid possesses anti-inflammatory properties. It can inhibit the production of inflammatory mediators and reduce inflammation-related markers, making it potentially beneficial in the management of inflammatory conditions. Syringic acid has been investigated for its antimicrobial effects. Research suggests that it may possess antibacterial and antifungal activities against various pathogenic microorganisms. However, the antimicrobial properties of syringic acid are not as extensively studied or established as some other phenolic compounds. : Syringic acid, along with other phenolic compounds found in plants, has been associated with potential health benefits. These include cardiovascular protection,

anticancer effects, and potential antidiabetic properties. However, more research is needed to fully understand its mechanisms of action and therapeutic potential. the bioavailability and absorption of syringic acid can vary, and its effects may depend on factors such as dosage, formulation, and individual metabolism. As with any natural compound, it is important to consult scientific literature and consult with healthcare professionals for specific applications and potential interactions with medications as reported by Chong *et al.*, (2009).

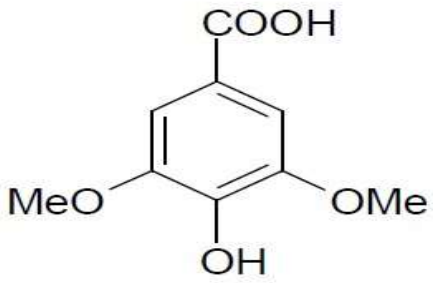



Figure-3: Protocatechuric acid Structure

Protocatechuic acid is a naturally occurring compound belonging to the class of phenolic acids. It is found in various plant sources and has been studied for its potential health benefits. Protocatechuic acid has a chemical formula of C7H6O4 and a molecular weight of 154.12 g/mol. Its structure consists of a benzene ring with two hydroxyl group(-OH) and carboxyl group (COOH) attached to it. Protocatechuic acid exhibits strong antioxidant properties. It can scavenge free radicals and protect cells and tissues from oxidative damage. Antioxidants play a vital role in maintaining overall health and are associated with various health benefits

Studies have shown that protocatechuic acid possesses anti-inflammatory properties. It can inhibit the production of inflammatory mediators and reduce inflammation-related markers, potentially contributing to the management of inflammatory conditions. Protocatechuic acid has been investigated for its antimicrobial effects. Research suggests that it may possess antibacterial, antifungal, and antiviral activities against various microorganisms. However, the extent and specificity of its antimicrobial properties may vary depending on the target microorganism.

Protocatechuic acid has been associated with potential health benefits, including cardiovascular protection, anticancer effects, neuroprotective properties, and potential antidiabetic activity. However, it is important to note that further research is needed to fully understand its mechanisms of actions and critical significance. the bioavailability and absorption of protocatechuic acid can vary, and its effects may depend on factors such as dosage, formulation, and individual metabolism. As with any natural compound, it is important to consult scientific literature and healthcare professionals for specific applications and potential interactions with medications or existing health conditions.

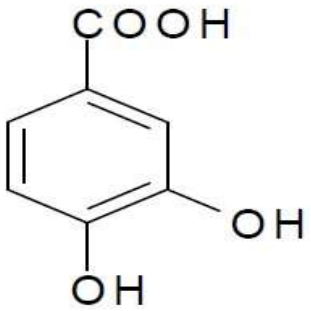



Fig-4: 3,3-dihydroxy benzoic acid Structure

**2.Benzioc acid anf its derivative as antisickling agent**

Antisickling agents are substances that are used to prevent or treat sickle cell disease, a genetic blood disorder characterized by abnormal, crescent-shaped red blood cells. The primary goal of antisickling agents is to inhibit the formation of sickle hemoglobin and promote the production of normal healthy red blood cells. Hydroxyurea is the most widely used antisickling agent and has been approved by the U.S. Food and Drug Administration (FDA) for the treatment of sickle cell disease. It works by increasing the production of fetal hemoglobin, which can inhibit the polymerization of sickle hemoglobin and improve red blood cell deformability. While benzoic acid is an organic compound with various applications, it is not recognized as an effective antisickling agent. It is commonly used as a food preservative, fragrance ingredient, and in the production of other chemicals. However, in the context of sickle cell disease, there are more specific and targeted medications available, such as hydroxyurea, that have been extensively studied and proven to be effective in managing the condition. If you or someone you know has sickle cell disease, it is important to consult with a healthcare professional for appropriate diagnosis and treatment options

Gamaniel *et al*, 2019.

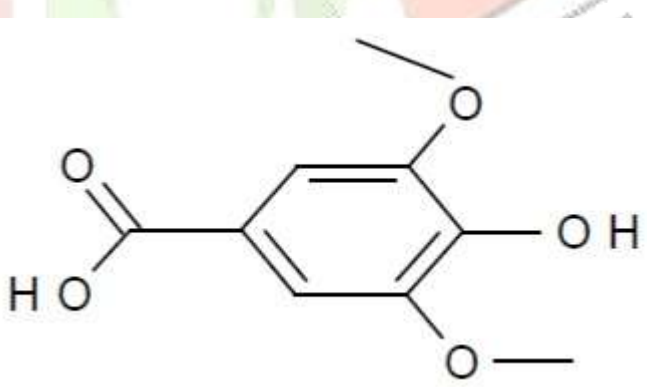



Figure-5: Vanillic acid Structure

It also possess analgesic and anti-inflammatory response. Qin et al., studied that vanillic acid

Is a derivative of 4-HBA. It also exerts anthelmintic activity and produce protective action against hepatotoxicity.

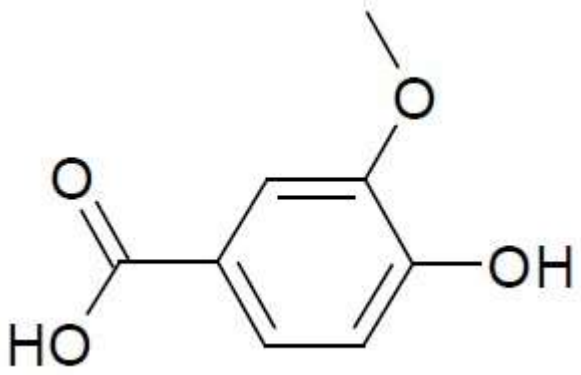



Figure-6:3-oxo-4-hydroxy benzoic acid structure

**3. Benzoic acid and its derivative as antialgal agent**

Benzoic acid is primarily known for its antimicrobial properties rather than its effectiveness as an antialgal agent. While it may have some inhibitory effects on certain types of algae, its efficacy and specific mechanisms of action against algae are not extensively studied or established.

In aquatic environments, various methods and compounds are used to control and manage algal growth, including algaecides specifically designed for this purpose. These algaecides often contain specific active ingredients that are known to effectively target and control algae growth.

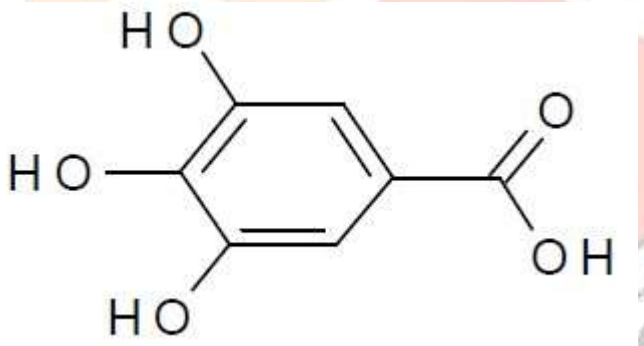



Figure-7: Structure of 3,4,5-tribenzoic acid

Wang et al., studied that 4-HBA and its derivatives trihydroxy benzoic acid inhibit the growth of few algal stains like *Microcystis aeruginosa.* This stain is more sensitive to 4-HBA. Nakai et al., reported that hydroxyl group and Carboxylic group present at benzene ring have more analytic effect of phenolic acids and have antifungal group.

**4.Benzoic acid as mutagenic agent:**

Birsovaa *et al*., (2005) studied the carcinogenic effect of caffeic acid and vanillic acid. These are phenolic compounds possess anticarcinogenicity by inhibiting 4-Nitroquinoline-1-oxide. It can induce tongue cancer in rats. Benzoic acid is primarily known for its role as a preservative in food and cosmetics due to its antimicrobial properties. Antimutagenic agents are substances that can reduce the frequency or occurrence of mutations in DNA. These agents can be beneficial as they help prevent or reduce the risk of genetic damage and the development of disease such as cancer.

While there is limited research on the specific antimutagenic effects of benzoic acid, some studies have investigated its potential genotoxic and mutagenic properties. In certain circumstances, benzoic acid can undergo metabolic activation to form reactive intermediates that have the potential to cause DNA damage and induce mutations. However, it's worth noting that these effects are typically observed at high concentrations or under specific condition. Moreover, several studies have demonstrated that benzoic acid, when used at concentrations commonly found in food and cosmetic products, does not possess significant genotoxic or mutagenic properties. This suggests that the potential risk associated with benzoic acid exposure in normal usage is minimal. It is important to note that the antimutagenic effects of substances can vary depending on various factors such as concentration, exposure duration, and the specific mutagen being tested. Therefore, further research is required to determine the exact antimutagenic properties of benzoic acid and its potential application. There are other compounds that have been more extensively studied and recognized for their antimutagenic properties. Some examples include certain antioxidants,

Flavonoids and polyphenols found in fruits, vegetables and herbs.

$$\% \text{ mutagenicity} = 100-(X1/X2) \times 100$$

Where, X1= number of colonies per plate of mutagens

X2=number of colonies per plate in absence of antimutagen

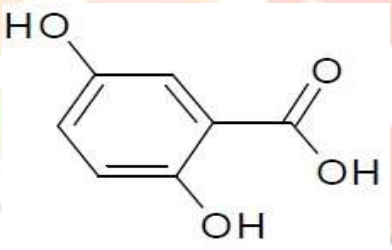



Figure-8: 2,5-dibenzoic acid structure

**5. Benzoic acid as estrogenic agent**

Benzoic acid is not typically considered an estrogenic agent. Estrogenic agents are substances that can mimic or interact with the hormone estrogen in the body, leading to estrogenic effects. These effects can include the activation of estrogen receptors and the potential to influence various physiological processes. While benzoic acid itself does not possess inherent estrogenic activity, there is limited evidence suggesting that certain derivatives or metabolites of benzoic acid may exhibit weak estrogenic effects. One example is parabens, which are esters of benzoic acid (such as methylparaben and propylparaben) commonly used as cosmetics and pharmaceuticals industries and in food industries as a preservative. Some parabens have been found to weakly bind to estrogen receptors and exert estrogenic activity in laboratory studies.

However, the estrogenic activity of parabens is significantly weaker compared to natural estrogens, and their potential effects on human health are a topic of ongoing scientific debate and research., FDA have concluded that parabens used in cosmetic products are safe at current levels of exposure, although some countries have imposed restrictions on their use in certain product.

It's worth mentioning that the potential estrogenic activity of benzoic acid or its derivatives is a complex topic, and the specific compound, its concentration, and the context of exposure are all important factors to consider.

If you have concerns about the estrogenic effects of a particular product or ingredient, it is advisable to consult relevant scientific literature and consult with regulatory agencies or healthcare professionals for the most up-to-date and accurate information.

**6. Benzoic acid as nematicidal agent:**

4-HBA and *p*-caumaric acid are purified from the Italian and Algerian azedarach. It is also known as chinaberry. Its fruits and other parts like seeds, woods and kernals shows paralytic effect on the juvenile of nematode like *Meloidogyne incognita*.

**7. Benzoic acid as antiviral agent**

The tiniest known diseases with a global reach are viruses. Currently, viruses are responsible for about three-quarters of all infectious illnesses worldwide. According to reports, hydroxybenzoic acid ester derivatives are frequently used to treat human and animal illnesses brought on by the hepatitis B virus, human papilloma, herpes simplex virus, condyloma acuminate, cervicitis, and cervical erosions. Gallic acid, which is primarily found in wines and green tea, has also been reported to have antioxidant and antiviral properties against HIVPR (0.8-0.05 microgram) by kinetic analysis, Zhang- Poormans method, a complementary assay, and fluorescent probe binding method using 8-anilino-1-naphthalene sulfonic acid (ANS), chemopreventive, antibacterial, anti-inflammatory, and antimutagenic chemical. Human skin mucosa viral infections and hepatitis B were both treated with 3, 4, and 5-trimethoxy benzoic acid. A hydroxy benzoic acid ester has more antiviral activity than the equivalent acid. For instance, propyl gallate has approximately one times the antiviral activity of gallic acid.

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**8. Benzoic acid as antiplatelet factor:**

Gallic acid ester, specifically 3,4,5-trihydroxybenzoic acid ester, which is commonly referred to as propyl gallate, has been found to inhibit the synthesis of thromboxane A2 (TXA2). Thromboxane A2 is a potent platelet aggregator and vasoconstrictor, and its inhibition helps prevent platelet aggregation and the formation of blood clots. Studies have shown that propyl gallate exhibits stronger and faster antiplatelet effects compared to aspirin (ASP), which is a well-known antiplatelet medication. Propyl gallate has been used in solution for Effectiveness and potential therapeutic use.

However, it is important to note that while propyl gallate has shown promise in inhibiting platelet aggregation and may have potential applications, further research is still needed to fully understand its effects, mechanisms, and potential side effects in different contexts and patient populations. As with any medication or compound, it is essential to consult with healthcare professionals for appropriate guidance and recommendation.

**9. Benzoic acid as antioxidant /preservative agent:**

Benzoic acid itself is not typically considered a strong antioxidant. Antioxidants are substances that can help prevent or slow down the oxidative damage caused by free radicals in the body. They accomplish this by

donating electrons or hydrogen atoms to stabilize and neutralize free radicals, thus reducing their potential harmful effects.

While benzoic acid has some antioxidant activity, it is generally regarded as a weaker antioxidant compared to other compounds with well-established antioxidant properties, such

As vitamin C, E or certain phenolic compounds.

However, it's important to note that the antioxidant activity of benzoic acid can be enhanced when it is present in combination with other compounds or when it undergoes chemical modifications. For example, some esters of benzoic acid, such as butylated hydroxybenzoate (BHA) and butylated hydroxytoluene (BHT), are commonly used as synthetic antioxidants in various industries, including food preservation and cosmetics. These derivatives exhibit stronger antioxidant activity than benzoic acid alone.

It's also worth mentioning that the effectiveness of an antioxidant can depend on several factors, including the concentration used, the specific reactive species being targeted, and the physiological environment in which it is applied. Different antioxidants may also have different affinities for specific types of oxidative stress. while benzoic acid itself has some antioxidant activity, it is generally considered to be a weaker antioxidant compared to other compounds. However, certain derivatives of benzoic acid, such as BHA and BHT, are more commonly used as antioxidants due to their enhanced antioxidant properties

**Conclusion:**

Many studies have shown benzoic acid and derivatives to have positive benefits on the human body, but there is also evidence of its negative consequences. Knowing the proper amount of the antioxidant and how the body metabolises it is crucial for preventing the unfavourable side effects of administration. Benzoic acid and its derivatives are powerful antioxidant against superoxide radicals, according to our findings. The antioxidant effects are enhanced by an increase in concentration. At various pH levels (range 6.5 to 8), its structure- and concentration-dependent antioxidant activity very minimally alters. Understanding the activity of naturally occurring substances and how they should be used is highly dependent on knowledge of their antioxidant, antimicrobial, antiviral and others activities.

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