Mini-Review on Sodium Benzoate: Its Uses, Adverse Effects, and Environmental Impact as a Pharmaceutical Product

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Abstract

This short overview summarizes sodium benzoate's (SB) dual role as a useful preservative and a possible threat to human and environmental health. This review provides a concise summary of uses, adverse effects, and environmental impact of SB. SB is widely used as a preservative in pharmaceuticals and food products due to its ability to inhibit microbial growth, thus extending the shelf life of various formulations, including syrups and ointments. While generally considered safe, SB can cause allergic reactions and may contribute to conditions like ADHD, particularly in children. It can also disrupt gut microbiota balance. The paper highlights the concerns regarding the environmental persistence of SB. Although it is biodegradable, its degradation rate can vary based on conditions and concentrations. Improper wastewater treatment can lead to its accumulation in aquatic ecosystems, posing risks to both the environment and human health. The review emphasizes the need for awareness regarding the long-term effects of sodium benzoate in ecosystems and suggests that environmentally friendly technologies could mitigate its impact.

Keywords: Sodium benzoate, preservative efficacy, health implications, biodegradation pathways, environmental toxicity, sustainable management

Introduction

Sodium benzoate (SB) is a preservative that is used a lot in the pharmaceutical industry and other areas [1]. Due to its ability to prevent microbes from growing, it is often used to make products last longer like other preservatives [2]. However, SB biodegraded easily [3] and not environmentally persistent pharmaceutical pollutants (EPPPs), referring to pharmaceuticals that stay in the environment for a long time [4-6]. Although SB is generally biodegradable, the rate of degradation is contingent upon the particular circumstances and concentrations present. This generates concern over the potential adverse impacts on both human beings and ecosystems.

Sodium benzoate (C_6H_5COONa) is an organic sodium salt derived from benzoic acid, where a sodium ion replaces a proton from the carboxy group. Additionally, SB is extensively employed as a preservative in packaged foods and beverages. Some studies suggest potential therapeutic

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roles in treating conditions like depression, pain, schizophrenia, and autism spectrum disorders [7-9].

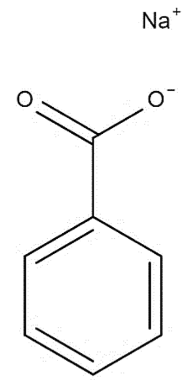

Figure 1. Chemical structure of sodium benzoate

The main reason SB is commonly employed in the pharmaceutical sector is owing to its effective preservative and antibacterial characteristics [10, 11]. It efficiently hinders the proliferation of bacteria, yeast, and fungi [12, 13], which is essential for prolonging the durability of diverse pharmaceutical items like syrups, ointments, and topical creams [14]. The significance of this rests in its capacity to uphold the stability and safety of formulations, especially in liquid pharmaceuticals, by averting contamination and deterioration. In tablet formulations, SB is utilized as an excipient to augment the solubility of active pharmaceutical ingredients, hence enhancing the medication's bioavailability and therapeutic efficacy [15-18].

SB, commonly utilized as a medicinal preservative, studies showed that it has the potential to induce allergic reactions and perhaps contribute to mental hyperactivity like attention deficit hyperactivity disorder (ADHD), especially in children [19-22]. Moreover, it has the potential to disturb the balance of microorganisms in the intestines [23]. Under specific conditions, it decompose into benzene, a well-established carcinogenic compound [24]. Although SB is usually deemed safe, those with allergies or special health issues should get advice from a healthcare practitioner prior to utilizing goods that include this component.

SB's impact on the environment in wastewater can be minimal when the wastewater is not properly treated [25], due to its toxicity it can contribute to pollution and disrupt aquatic ecosystems if not managed effectively [26]. Environmentally friendly technology applied to this field can drastically lower this risk [27].

This mini-review investigates SB in pharmaceutical products, SB is commonly employed preservative in the fields of pharmaceuticals and food industry. The review examines the uses of this substance in different formulations and investigates its possible adverse effects and the potential harm it may do to the environment. The objective of the review is to present an impartial assessment of the advantages and disadvantages of sodium benzoate, taking into account its effects on human health as well as its impact on the environment. The study provides valuable insights into the compound's characteristics, regulatory status, and rising concerns about its long-term presence in ecosystems by combining existing researches.

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Sodium Benzoate Uses, Adverse Effects, and Toxicity

Pharmaceutical companies use SB for many purposes. Mostly used as a preservative in liquid pharmaceuticals like oral suspensions, its antibacterial qualities ensuring product safety [28, 29]. SB can be utilized as a buffer to regulate the pH of pharmaceutical formulations, hence influencing the solubility of the products [30].

The United States Food and Drug Administration (FDA) classifies SB as Generally Recognized as Safe (GRAS) for use in foods, with a maximum limit of 0.1% by weight [31]. SB is commonly employed as a preservative in pharmaceuticals and medications. However, the precise concentration limitations of SB can differ based on the exact formulation and kind of medication. The FDA's guidance primarily focuses on ensuring the safety of the formulation for its intended use, despite the criticism that this assessment has overlooked many studies in related cases [32]. The World Health Organization (WHO), in collaboration with the FAO (Food and Agriculture Organization), sets standards for food additives, including SB. According to the latest recommendation in the ninety-second meeting, the acceptable daily intake (ADI) for SB was established to be up to 20 mg/kg of body weight [33]. Although this ADI has a wide application, it can also serve as a useful tool for assessing medication safety. The European Medicines Agency (EMA) provides guidelines for excipients like SB in pharmaceuticals. In the EU, SB is permitted as a preservative in various pharmaceutical formulations. The concentration of SB in medicines should comply with safety evaluations, which generally align with the maximum limit of therefore recommends a maximum dose of 5 $mg.kg^{-1}$ per day in products, similar to food standards. However, this limit is not exclusively applicable to pediatric populations [18].

While generally recognized as safe (GRAS) by regulatory agencies, sodium benzoate has been associated with several adverse effects. Some individuals may experience allergic and hypersensitivity reactions, including urticaria and asthma-like symptoms [34-37]. Under specific conditions and in the presence of ascorbic acid, SB can undergo a reaction that produces the well-known carcinogen benzene. When using medications that contain both substances or those that contain vitamin C, this reaction becomes much more concerning [38], this reaction is more likely to occur in acidic environments, such as the stomach. Hyperactivity in children: Some studies have suggested a link between sodium benzoate consumption and increased hyperactivity in children, although this association remains controversial [22]. High doses of SB have been shown to induce oxidative stress in cellular studies, potentially leading to DNA damage [39, 40]. Recent studies suggest that SB may modify the composition of the gut microbiota, potentially affecting digestive health [41, 42]. Additionally, some individuals may experience allergic reactions to SB, manifesting as skin irritation or gastrointestinal discomfort [43]. For individuals with liver disease or impaired liver function, the metabolism and excretion of SB may be compromised, potentially leading to adverse effects [44, 45].

Sodium Benzoate Entry to the Environment

SB consumed by humans that utilized in pharmaceuticals and food is disposed of in wastewater. Wastewater treatment plants typically employ a combination of biological and chemical processes to remove SB. The primary method is biological treatment, where microorganisms in activated

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sludge systems break down the compound [46]. These bacteria metabolize SB as a carbon source, converting it into harmless byproducts like carbon dioxide and water [47, 48]. Advanced oxidation processes (AOPs), including UV/hydrogen peroxide treatment, ozonation, Fenton's process, and photocatalysis, can be employed to remove pharmaceutical organic contaminants [49-53], by generating highly reactive hydroxyl radicals that oxidize the organic compounds. that employ oxidative agents to decompose organic contaminants into less toxic ones [54, 55]. When SB makes it to water treatment facilities, it may be disinfected, but there's still a chance it might result in disinfection by products (DBP) [56].

Adsorption techniques using activated carbon, in some processes is combined with biological treatment, can also be effective in removing SB from wastewater [57-59]. In some cases, membrane filtration systems like nanofiltration or reverse osmosis may be employed to separate the compound from the water [60, 61]. The selection of treatment procedure often depends on the concentration of SB and additional pollutants in the effluent.

Contamination of ecosystems is occurring due to the extensive use of preservatives, that containing organic cyclic substances like SB, in pharmaceutical and food products. Preservatives can enter aquatic systems through a variety of direct and indirect routes [62]. The main source of water contamination with organic pharmaceutical pollutants is wastewater that contains residues of these substances [63, 64]. The influents and effluents of wastewater treatment plants were found to include these preservatives like SB often get into aquatic systems without going through the normal steps for treating wastewater [65]. There is a significant amount of these pollutants in the used activated sludge [66]. Biological treatment can get rid of many contaminants, but because these compounds have complicated molecular structures, it may not be able to fully break them down [67]. There are also limits to how well chemical cleaning methods can get rid of these persistent pollutants [68]. Because of this, some of these pharmaceutical residues can end up in rivers, lakes, and other bodies of water, where they could harm aquatic environments and people's health [69]. The use of clean technology in water treatment has the dual benefit of reducing costs and environmental harm while simultaneously optimizing process potentials to minimize pollutants in drinking water [70].

Sodium Benzoate Ecotoxicity

SB may infect aquatic ecosystems via wastewater discharge. Upon entering the environment, it may present hazards to aquatic organisms due to its capacity to induce toxicity when discharged into water bodies [71]. The impact is contingent upon elements like concentration, period of exposure, water quality, and the vulnerability of aquatic organisms [72]. Despite SB is generally considered to possess low toxicity, its persistent release and buildup may adversely impact aquatic environments by changing microbial community balance and compromising the health of fish and invertebrates [73, 74]. Its degradation products, such as benzoic acid, may demonstrate toxicity to fish and other aquatic creatures, affecting their development, reproduction, and survival [75]. Furthermore, SB can facilitate eutrophication, a source of carbon, a phenomenon marked by excessive nutrient enrichment that results in subsequent detriment to aquatic bacteria and organisms [76, 77]. The ecotoxicological consequences of SB may differ, nevertheless it is

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essential to adopt efficient management techniques to reduce its release and investigate alternative preservatives to protect aquatic ecosystems.

SB like other untreated contaminants poses significant risks to aquatic life when it contaminates surface and ground waters [78]. Studies have demonstrated its toxicity to various aquatic organisms, including fish [79]. Exposure to SB may result in acute toxicity, leading to mortality or sub-lethal consequences, including diminished growth rates, compromised reproduction, and behavioral anomalies [80-83]. Extended exposure may lead to lasting consequences, including biodegradation in aquatic ecosystems and modifications of ecological processes. While SB itself is biodegradable, its still or its breakdown products can have harmful effects on aquatic organisms and plants [26, 84]. Moreover, SB can engage with other water pollutants, intensifying their hazardous effects. The presence of SB in aquatic habitats can profoundly affect the health of aquatic ecosystems and its resident organisms.

Conclusion

Sodium benzoate (SB) is recognized for its effectiveness as a preservative in pharmaceuticals, helping to prevent microbial growth and extend product shelf life. This characteristic is crucial for maintaining the stability and safety of liquid formulations like syrups and creams. Despite its benefits, SB has been linked to potential adverse health effects, including allergic reactions and possible contributions to ADHD in children. It may also disrupt the balance of gut microbiota, raising concerns about its long-term safety for consumers. The review highlights that while SB is generally biodegradable, its degradation can be influenced by environmental conditions. If wastewater containing SB is not properly treated, it can lead to pollution and disrupt aquatic ecosystems, emphasizing the need for effective management strategies. The study proposes the development of eco-friendly technology to lessen the impact of SB and seeks for additional thorough research to determine its long-term effects on individuals and the environment.

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