

Benzotriazole UV Stabilizers (BUVSs) in the Environment: Much More than an Emerging Contaminant of Concern

Ankur Khare

CSIR-National Environmental Engineering Research Institute

Pradip Jadhao

CSIR-National Environmental Engineering Research Institute

Atul Narayan Vaidya

CSIR-National Environmental Engineering Research Institute

Asirvatham Ramesh Kumar (✉ ar_kumar@neeri.res.in)

National Environmental Engineering Research Institute CSIR <https://orcid.org/0000-0002-6974-9955>

Research Article

Keywords: Benzotriazoles, Bioaccumulation, Persistent organic pollutants, Toxicity, Ultraviolet stabilizers

Posted Date: January 18th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1202371/v1>

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Abstract

Benzotriazole ultraviolet stabilizers (BUVs) are a group of industrial chemicals used in various consumer products and industrial applications. Due to its large scale production and use, BUVs have been detected in all environmental matrices and in human milk; hence, they attract researchers and regulatory bodies worldwide. BUVs are considered as a new family of emerging environmental contaminants. Due to their persistent organic pollutants (POPs) like properties, they have also been classified as substances of very high concern (SVHC). The current review focuses on the persistence, bioaccumulation, and toxicity (PBT) of several BUVs, as well as their multicompartamental occurrence. Scarcity of scientific data on BUVs properties, occurrence in the environment, exposure levels and effects on organisms poses significant challenges to the policymakers and regulatory bodies in adopting management strategies. The need for a science-based integrated framework for risk assessment and management of benzotriazoles (BZTs) is recommended.

1. Introduction

Benzotriazoles ultraviolet stabilizers (BUVs) are considered as emerging environmental contaminants, even though they have been around us for almost six decades. During recent years, they received a lot of attention as an emerging pollutant because of their potential hazardous impacts on human health and biota (SC 2021). Emerging does not imply that they were not considered pollutants previously, mainly because of lack of monitoring data and the notion among the scientific community as they were 'non-toxic'. United States Environmental Protection Agency (USEPA), back in 2008 has classified BZTs (Benzotriazoles) as Emerging Pollutants (Richardson 2008). All of the synthetic polymeric substances used in our day to day life are exposed to natural degrading agents such as ultraviolet (UV) radiation, numerous pollutants, and moisture. Their cumulative consequences lead to abrasion or weathering of the polymer. To protect polymers from degradation, polymeric formulations are dosed with precise stabilizers which shield them from degradation. BUVs are used as additives in polymers, paints, and several industrial and household products to protect them against the harmful effects of UV radiation.

BZTs (Benzotriazoles) are classified as high production volume (HPV) chemicals in European Union (ECHA 2019b). Commercial manufacture and use of benzotriazoles began in the United States in 1950 to prevent oxidation and corrosion in commercial boilers, radiators for cooling systems (Union Carbide Corporation 1965; Donaldson 1965; Malec 1975). In 1961, phenolic BZTs were granted a patent in the United States for their UV absorbing characteristics (Hansjorg et al. 1961). Since then, additional patents for various classes of BZTs as polymer and plastics additives have been filed worldwide (Cantwell et al. 2015). This had revolutionized the use of BZTs in various other applications, including photographic emulsions, antifogging agents, and color tinting agents in photocopying inks. In order to prevent aircraft corrosion, a US patent on BZTs as aircraft de-icing and anti-icing fluids (ADAFs) was issued in 1990 (Chan et al.1995). National Aeronautics and Space Administration (NASA) also recommended BZTs to protect electronics circuits in spacecraft for their space missions (Downs 1968). **Figure 1** represents the complete timeline of BUVs right from its production, applications, followed by its occurrence in different environmental matrices and legislations.

Each class of BUVs has its own set of implications and concerns for the receiving environment based on the uses and application (US EPA 2009). The potential risk of these emerging contaminants to the environment and human health is still largely unknown, even though they meet the Persistency, Bioaccumulation, and Toxicity (PBT) criteria of Persistent Organic Pollutants (POPs) established by various international agencies (ECHA 2018, 2014; SC 2021). Following the reports of the occurrence of BUVs compounds from Narangsett Bay in the United States (Jungclaus et al.1978), Ariake Sea in Japan (Nakata et al. 2009), Indian rivers (Vimalkumar et al. 2018), and Pacific Oceans (Nakata et al. 2012), it is clear that BUVs research has been limited to ecosystem and watershed level (Cantwell et al.2015).The global transport process of BUVs and their redistribution on a global scale is currently unknown and surprisingly scarce in comparison to their economic importance and environmental flows. Simultaneously, there is an urgent need to comprehend the behavior of BUVs in other environmental compartments. Priority research and strong knowledge are required, particularly for this class of Benzotriazoles, including their sources, environmental fate (transportation and degradation) followed by bioaccumulation potential, and toxicity to aquatic organisms.

We have used the acronyms BZTs for Benzotriazoles and BUVs for "Benzotriazoles ultraviolet stabilizers" in this review article. All the other acronyms have been defined at their first mention and also listed under "list of abbreviations" section. Industrial applications of BZTs and other classic BUVs applications have not been extensively addressed and are available in a variety of

articles, book chapters, and technical reports (Cantwell et al. 2015; NTP 2011). Instead, emphasis is placed on their environmental occurrence; bioaccumulation, toxicity potential and their POPs characteristic have been investigated. There are reviews on environmental fate of BUVs, however, they are limited to single environmental matrices and provide little insight about the persistency, bioaccumulation, and toxicity (PBT) criteria and their significance as an Emerging Contaminant (Alotaibi et al. 2015a). Because of the increase in production and applications of BUVs over the last decade, independent researchers have raised serious environmental concerns, highlighting change in concentrations on regional and global environmental transport from time to time. However, they are limited to a small number of BUVs in an unaltered environmental matrix (Kumar et al.2018; Alotaibi et al.2015b). Because of their light-absorbing and stabilizing properties, use of BZTs and their derivatives in plastic and non-plastic products have increased several folds around the world. BZTs have piqued the interest of many other industries. The compound Benzimidazole and its derivatives have found widespread application in pharmaceuticals, owing to their diverse biological behavior (Barot et al.2013; McKeller and Scott 1990). BUVs are found in many daily use and industrial products as absorbers and stabilizers in concentration ranging from 0.5% to 10% (Hauri et al.2003). According to the cosmetic derivative report, 27 BUVs are listed in Annex VII and 43 other chemicals, as Ultraviolet (UV) stabilizers in various cosmetic products in the European Union (Wahie et al. 2007).

Monitoring data on such newly listed POPs, including sampling methodology, quantification in various environmental matrices, forms the foundation of a harmonized monitoring network and aid in capacity building and knowledge sharing. As a result, in our opinion and in search of a broader frame of reference, an up-to-date review of BZTs as an UV stabilizer is required. This review is based on the information collected from peer-reviewed research articles and documents made public by government agencies on BUVs. All the references that came to our attention till October 2021 have been subsumed in this article. International Union for Pure and Applied Chemistry (IUPAC) name, Chemical abstract Service (CAS) number and 3-D structure of BUVs is presented in **Supplementary Table (S1)** while **Supplementary Table (S2)** presents the Physico-chemical properties of different BUVs reviewed in this article.

2. Production And Applications Of Benzotriazoles (Bzts)

The Benzotriazole (BZT) market has grown significantly as a result of factors such as the rise in applications of the compounds in and across several household and industrial application bases such as antifreeze solution, antirust coatings, oil antioxidants, emulators, and so on (Kadar et al. 2009; Rajak et al. 2011). Furthermore, there is a growing emphasis on research and development activities that lead to innovations and significant advancements in a variety of sectors, creating a massive market opportunity for key players in the benzotriazole market. BZTs are widely used in polymers, plastics, inks, paints, and other coating formulations. The concentration of BZTs in various products ranges from 0.1 to 1.0 % w/w (BASF 2016). According to the most recent report by Research and Markets (2021), the global benzotriazole market was estimated at US\$355.5 million in 2020 during the COVID-19 crisis and is expected to reach US\$ 531.8 million by 2027, growing at a 5.9 % compound annual growth rate (CAGR) from 2020 to 2027. Plastics, on the other hand, are expected to grow at a 6.7% CAGR with a market value of US\$ 225.9 million by 2027.

The market for BZTs in the United States is estimated to be \$96.2 million in 2020, while China, with the world's largest population and second largest economy, is expected to reach a market size of \$113.6 million by 2027, with a CAGR of 9.1%. Other countries, such as Japan and Canada, are expected to grow at a CAGR of 3.2% and 5.3%, respectively, from 2020 to 2027. Germany, within Europe, is expected to grow at a rate of 3.8% in the global benzotriazole market. According to the Substance in Products in Nordic Countries (SPIN) database, the total usage of UV-328 in the Nordic group of countries (Finland, Norway, Sweden, and Denmark) since 2006 is <10 tons per annum. UV-328 was included in the high priority chemical list in the United Kingdom due to its PBT characteristics (Brooke and Burns 2010). On the other hand, UV-320 is classified as "Class I specified chemical substances" under chemical control substance law in Japan in 2007 which depicts similar characteristics as that of POPs (Watanabe and Noma, 2010). Much of the BZTs production data is not assessable and is presented in broad weight intervals. The United States environmental protection agency (USEPA) reports non confidential data reporting (CDR) information on some chemicals that are produced and being used in United States in quantities greater than 10,000 lb (Cantwell et al.2015). **Figure 2** represents the global market segmentation of BZTs and its applications in different products.

The import/export tonnage and manufacturing data of BZTs are very hazy. Several BZTs have yet to be registered as high priority or production chemicals in various countries chemical lists. Their manufacturers should be brought under the umbrella act in their respective countries for registration and production, import, and exports data be made available for a detailed estimation of the exact demand and supply chain of BZTs.

BZTs are used as de-icing fluids/anti-icing fluids to preserve snow-free flight surfaces, runways for military operations, and highways in colder nations (Cancilla et al. 1997; Voutsas et al. 2006; Scheurer et al. 2011). At a time in the US, there were nearly 4000 functional aircraft deicing units discharging approximately 80 million liters of ADAFs into surrounding water bodies annually (Cancilla et al. 2003; Breedveld et al. 2003; Cornell et al. 2000). According to estimates, approximately 80 % of the anti-icing solution containing BZTs remains at the site, resulting in environmental contamination (Giger 2008; Sahar et al. 2011). BUVs have been detected in ADAFs in varied concentrations at different airports round the world. At Zurich airport, Switzerland the concentration was around 240µg/g, while at Frankfurt, Germany and Milwaukee airport, USA its concentration was accounted to be 1.425µg/g and 1130 µg/gm respectively (Corsi et al. 2003, 2006; Giger et al. 2006; Kiss and Fries 2009). In some countries with extreme cold conditions like North China and Russia, the production volume and usage of BUVs may be extremely high. The increase in BZT pollution has been documented throughout the winter months, which is consistent with the findings of various researchers (Corsi et al. 2003, 2006; Giger et al. 2006).

Apart from anticorrosive and anti-inflammatory applications BZTs also finds their usage in medical sector for drug manufacturing. The fundamental BZT structure has a wide range of applications in the pharmaceutical and nutraceutical industries (Briguglio et al. 2015). It functions as an electron donor and can thus be employed in the formulation of several medications. Some of the polymers substituted BZTs have also been used as a catalyst for synthesizing the tetrahydroquinoline library (Talukdar et al. 2001). On the other hand, the pharmaceutical sector is looking into other biological features linked with BZTs and their derivatives, such as antibacterial, antiviral (Borowski et al. 2003), antiprotozoal (Lopez et al. 2011), choleric (Pagleitti 1994), antiproliferative (Beauchard et al 2009) properties and its role as plant growth regulator (Davis 1954; Picci 1966).

3. Environmental Occurrence And Distribution Of Benzotriazoles (Bzts)

One of the likely consequences of using chemicals in large quantities is their ultimate entry into environmental compartments. BUVs enter the environment through a variety of pathways. Some of them include: i) through wastewater treatment plant (WWTP) effluents; ii) plastic debris and or *via* weathering of outdoor plastics and products coated with BUVs; iii) personal care products (PCPs) containing BZTs as an additive (Lai et al., 2014a; Braush and Rand, 2011). The first occurrence of phenolic BZTs compounds was reported in the 1980s by Jungclaus et al., (1978) and Avila and Hites, (1980). The key findings of the articles highlighted the release of BZTs and other chemicals from a chemical unit in Cranston, USA that was in operation until 1985. The chemicals produced at this plant were discharged into the Pawtuxet River, eventually reaching Narragansett Bay in the United States. During the study, heavy deposition and accumulation of BZTs were observed in both water bodies. The research findings gave a clear insight of long-term persistence and environmental transport of BUVs after their release from the chemical plant.

Figure 3 represents a complete picture of environmental fate of BUVs upon their release in the environment, while **Supplementary Table (S3)** summarizes overall occurrence of BUVs in different environmental matrices, including biological samples.

3.1 Occurrence in Wastewater treatment plants (WWTPs)

Wastewater treatment plants (WWTPs) are considered to be the main source of BUVs contamination in the environment (Cantwell et al. 2010). BUVs can enter the water treatment units easily via daily “wash-off” from products containing BUVs (Liu et al., 2012). Majority of data on occurrence of BUVs in WWTPs are from Western world, while there exists several findings highlighting its occurrence in Asian countries (**Supplementary Table 3**).

BUVs usually have high detection rates in both influent and effluent of WWTPs with concentrations ranging from hundreds of nanogram to thousands nanogram per liter (Molins-delgado et al., 2015; voutsas et al., 2006). Because of low hydrophobicity of BUVs, sorption does not play key role for elimination which is in accordance with poor removal rates (<80%) of BUVs during treatment in most of WWTPs (Heeb et al., 2012, Herrero et al., 2014a, 2014b; Karthikraj and Kannan., 2017). Removal of BUVs in WWTPs is mainly governed by various factors like wastewater loading time, hydraulic retention time, and treatment factors (with

or without biological units). Nakata and Shinohara (2010) reported individual concentrations of three BUVs (UV-326, UV-327, and UV-328) from 5.6 to 78 ng/L in WWTP of Japan. Study from Portugal and Spain, reported concentration of five BUVs in the range of 24 to 85 ng/L with individual concentration of UV-328 varying from ND to 65 ng/L (Carpinteiro et al. 2012). Liu et al. (2012) reported the presence of UV-326 and UV-329 with mean concentration of 25 ng/L and 310 ng/L respectively in WWTP of Australia.

The estimated levels of BUVs in WWTPs are generally low, but uniform and similar to other persistent contaminants such as Polybrominated Diphenyl Ethers (Anderson and MacRae 2006). UV-328 levels in effluent and sludge samples from WWTPs in Sweden were measured in tens of ug/kg range. UV-328 had a maximum concentration of 3.1 µg/kg dry weight in effluent suspended particles, while effluent samples from WWTP from Norway reported concentration in the range of 7 to 57 ng/L (Schlabeck et al. 2018). Studies have suggested open air system of lagoons and long HRT (<27 days) which may create favorable conditions like photodegradation, transformation and bioaccumulation for BZT degradation in WWTPs (Liu et al., 2012; Herrero et al., 2013). Negative removal rates of BUVs during wastewater treatment have been reported, which could be attributed with the fact that these compounds are predominant in nature and persist for longer duration in the aquatic environment. Further, the effluent from WWTPs can play a key role in polluting the receiving aquatic ecosystem (Zhao et al. 2017).

3.2 Occurrence in Receiving environment

3.2.1 Water

Incomplete and inefficient removal of BUVs from WWTPs leads to its presence in effluent discharged from WWTPs to the receiving water bodies. Water samples from Narragansett Bay were found to be contaminated with UV-328 at concentrations of 7-85 µg/L respectively during 1978 to 1980 (Jungclas et al. 1978), whereas water samples from San Francisco Bay were reported to contain UV-328 at a concentration of 17 ng/L (Silva and Muir 2015). UV-328 with other sun-blocking agents was detected in freshwater and seawater samples in Okinawa Islands, Japan. UV-328 was predominantly detected in seawater samples (2.8-287 ng/L) (Tashiro et al. 2013). Water samples from heavily polluted river streams in Japan (Saitama prefecture) reported about 4.8×10^3 ng/L of UV-328 (Ciba 1988), whereas in seawater, UV-328 was reported up to the concentration of 287 ng/L (Tashiro et al. 2013). Huge amount of plastic debris was also reported from these areas confirming, plastics as a carrier of these chemicals. Water samples from the Kaveri River in South India were contaminated with several classes of BUVs with UV-329 (31.3 ng/L) being the most prevalent in Indian subcontinent (Vimalkumar et al. 2018). Surface water samples from Oslo and the Alna River, Norway were contaminated with UV-328 at concentrations of 0.8-17 ng/L and 1.0-1.9 ng/L after being characterized for BUVs (Schlabeck et al. 2019). Recently, the St. Lawrence River in Canada was reported to be contaminated by UV-328 at concentrations ranging from 1.2 to 3.0 ng/L (Giraud et al. 2020). Water samples from Philip Bay, Australia were predominantly contaminated with UV-328 with a concentration of 216 ng/L (Allinson et al. 2018). To date only Denmark and Australia are the two countries having explicit drinking water quality standards for BZTs (<20 ng/L for CBT and BTri in Denmark and <2400 ng/L for 5-TTri in Australia) (Dummer, 2014).

3.2.2 Sediments

Reddy et al. (2000) reported a very high concentration of BUVs in Pawtuxet River sediments, with concentrations of 4300 mg/kg for UV-P and 5200 mg/kg for UV-327. In comparison, the concentration in Narragansett Bay sediments ranged from 10 to 25 mg/kg, which is lower than that of Pawtuxet River sediments (Avila and Hites 1980). Pruell and Quinn (1985) reported similar findings in sediment cores throughout Narragansett Bay depicting the spatial and temporal distribution of the two BUVs. Phenolic compounds generally occur in two forms, the free form and bound form, the latter is also known as bound phenolics. Reddy et al. (2000) reported the occurrence of both these forms, indicating the sediment binding potential of BUVs in the bay.

Furthermore, Hartman et al. (2005) found two BUVs, UV-P and UV-328, in sediment samples from Narragansett Bay, indicating their extensive dispersion. Conventional WWTPs were ineffective in the removal of BUVs, as shown by the occurrence in mg/L levels of UV-327 and UV-328 in the receiving water. Finally, Cantwell et al. (2010) found that all other BUV compounds in Narragansett Bay were discharged from the same chemical manufacturing facility. UV-328 was also found in every stratum of sediment core samples, taken from Lake Ontario between 1975 and 2013. These data indicate of the persistency of UV-BZTs in sediments, and

freshwater bodies. Urban streams in Canada reported UV-328 with concentrations up to 240 ng/g of sediment which was ten times higher than the concentration in rural areas of the state (Parajulee et al.2018).

Four BUVs were found in sediment samples from the Ariake Sea in Japan, in range of 1 to 16 µg/kg dry weight (Nakata et al.2009). In silt sample taken from the Omuta River in an industrialized area of Japan, the individual concentration of UV-328 was 320µg/kg. Individual concentration of three BUVs (UV-326, UV-327, and UV-328) in Songhua River, China ranged between 0.31 and 7.12 µg/kg (Zhang et al. 2011), while it ranged from 0.22 to 22µg/kg in two rivers (Detroit and Saginaw) in US (Zhang et al. 2011).

3.2.3 Biometrics

Pruell et al. (1984) were the first to report the bioavailability of two BUVs (UV-327 and UV-328) in bivalve mollusks (*Mercinaria mercinaria*) from Narragansett Bay in the range of 1.0 to 8.5 ug/kg and 7.0 to 61.0 µg/kg wet weight, respectively. Tissue burden of BUVs has been accounted for in numerous marine species in a study done by Nakata et al. (2009). UV-327 and UV-328 concentrations in the porpoise blubber varied from 4.5 to 31µg/kg and 11 to 64µg/kg, respectively. Furthermore, Kim et al. (2011) calculated the concentrations of eight BUVs in marine species from Manila Bay, Philippines ranging from not detected (ND) to 211 µg/kg wet weight. Four BUVs were found in blue green mollusks of eleven Asia-Pacific countries, with individual concentrations ranging from ND to 1500 µg/kg wet weight. UV-326 had the highest concentration (ND-1500 µg/kg wet weight), while UV-328 was predominantly found in the concentration range of ND-830 µg/kg wet weight in most of the sites. UV-320 was only accounted in mollusks samples collected from Japan in the range of 39 to 86 µg/kg wet weight (Nakata et al.2012).

3.2.4 Air and Household Dust

BUVs have been found as particulate and vapor phases of urban and indoor air in several regions (Xue et al.2016; Maceira et al. 2020). Six different BUVs were screened in air samples in Sweden in a study by Brorström-Lundén et al.2012, of which four BUVs (UV-320, UV-327, UV-329, and UV-360) were determined in the background and urban air samples. The highest concentration of phenolic BZTs was found in air samples collected in Stockholm, Sweden. Xue et al.2016 reported an average concentration of BUVs ranging from ND- 9.31ng/m³ in the vapor phase and 2.35-395 µg/gm in the particulate phase in New York, USA. A study by Maceira et al. 2018 reported the average concentration of BUVs in urban air at two different locations in Spain: Constanti (2.8ng/m³) and Tarragona harbor (2.2ng/m³). Constanti harbor had an average range of 0.93-5.5 ng/m³, while Tarragona harbor had a range of 0.69-4.1 ng/m³. Another study (Maceira et al. 2020) found that the average maximum concentration of different BUVs compounds was 962pg/m³ and 2248pg/m³. Inhalation of BUVs in ambient and indoor air can be the primary route of direct exposure to human populations.

Household dust samples and vehicles cabin dust were reported to contain BUVs (UV-326, UV-327, and UV-328) in the range of 22-4880 ng/g. The study also provided evidence of the exposure of BUVs to humans *via* consumer products (Carpinteiro et al., 2010) similar to PBDEs in household dust generated from consumer products. Significantly high quantities of PBDEs were found in WWTPs and household items, indicating their widespread use (Otazo et al.2005). Due to dust inhalation and exposure levels in humans, risk assessment can also be studied in professional drivers, spending eight to twelve hours of duration inside a car.

It is quite certain that BUVs are omnipresent in nature and have been detected in all environmental matrices, as evidenced by the literature. While researchers have documented the release of BUVs, it is clear that BUVs are released post-production, primarily during and after the use of products doped with certain UV stabilizers. What remains uncertain is their transport mechanism in environment through different carriers. The presence of BUVs in various environmental contexts raises legitimate concerns about their potential exposure to the human and animal populations

4. Properties Of Benzotriazoles (Bzts) As Per Persistent Organic Pollutant (Pop) Criteria

4.1. Persistency

Although BUVs have been produced and estimated in the environment for decades, knowledge on its environmental behavior and fate is lacking. However, few modeling studies employing EAWAG-BBD (Bio-catalysis/Biodegradation Database) have made some attempts in this approach. Long-term preservation was predicted for several BUVs, implying that BUVs are preserved for a longer time in sediments and soils (Avila and Hites 1980; Pruell et al.1984; Nakata et al.2009). UV-328 and other BUVs are adsorbed onto sewage sludge and suspended materials due to their high $\log K_{oc}$ and $\log K_{ow}$ values. BUVs are unlikely to undergo hydrolysis, photo-transformation, or oxidation due to their limited water solubility. UV-328 biodegradation was found to be very low in a prediction research conducted by EAWAG-BBD (Bio-catalysis/Biodegradation Database). In a study employing sludge treated soils, UV-328 had a half-life of 179-218 days. Although, there were certain limitations in the study, like only dissipation monitoring was done and, no homogeneous sampling was carried out (Lai et al.2014a). Another finding by the same researcher reported that UV-328 has a disappearing half-life (DT_{50}) of 99-223 days (Lai et al. 2014b). UV-327 has been prohibited in Japan upon having similar characteristics (bioaccumulation and persistency) in common with persistent organic pollutants (POPs) (Nakata 2009).

According to various investigations, UV-327 and UV-328 were detected in sediments in Narragansett Bay, USA, decades after they were released from a chemical manufacturing plant. Hartman et al. 2005 found a similar trend in BUVs concentrations in Narragansett Bay. UV-328 persistency was projected to be 100 days in sediments and 2 days in water by several modelling tools, such as BIOWIN v4.10 and AOPWin v1.92 (EPA 2012), respectively. The metabolite M1 (CAS RN 84268-36-0), which is structurally identical to UV-328 and the major breakdown product of UV-328, showed dissipation time (DT_{50}) in sediments ranging from 238 to 248 days. This investigation was the best-case scenario for determining the DT_{50} for UV-328 (SC 2021).

4.2. Bioaccumulation

The ability of BZTs to persist in multiple environmental compartments has been studied thoroughly (Pruell et al.1984;Nakata et al. 2012). BZTs upon their release in the aquatic environment, becomes readily available for aquatic species and thus pose risk to aquatic organisms. BUVs have been found in biological tissues and organs of numerous life forms, according to various studies (Pruell et al.1984; Nakata and Sinohara 2010; Kim et al. 2019). Researchers have conducted several ex situ studies to determine the degree of bioaccumulation of BUVs in order to determine its bioavailability for different organisms. Bio concentration factor (BCF) (L/kg) is the term for this degree, which is stated as:

Where, (ug/kg) is the concentration of BUVs in the organism and (ug/L) is the concentration in exposure water. The reported BCF values ranged from 370 to 10,000 L/kg for different BUVs in diverse organisms like *Cyprinus carpio*, *daphnia* species, etc. $BCF > 5000$ indicate tendency to accumulate in the organism, rather than present in the surrounding water (SC 2021). **Figure 3A** represents the minimum and maximum BCF values of BUVs reported in different aquatic species. The results of a sixty days bioaccumulation study on *Cyprinus carpio* (ECHA 2014; J-CHECK 2018) done according to OECD test methodology demonstrated accumulation in several internal organs, with the gut accumulating the most, followed by the head, skin, and muscles (**Figure 3B**).

Concentrations of two BUVs (UV-327 and UV-328) were detected in blubbers of five finless porpoises in Ariake Sea, Japan in a monitoring study conducted from 1998 to 2009. Whole-body concentrations of UV-327 and UV-328 were 4.0ng/g and 8.4ng/g, respectively. UV-328 bioaccumulation in aquatic biota and its presence in foodstuffs and in human adipose tissue are depicted in several research findings (Nakata et al.2012). Several Bioaccumulation Factor (BAF) values have been derived using laboratory data and lipid normalized wet weight (Nakata et al. 2009). Still, more research is needed to determine the bioaccumulation of additional phenolic BZTs and their uptake through the food chain. Studying the uptake of BUVs in benthic macro-invertebrates in aquatic ecosystem can be a major breakthrough in this as, they are bottom dwellers and mainly feed on the sediments contaminated by organic contaminants like BUVs. Different ecosystems, such as land and forest, can also be studied in the same way.

For bioaccumulating compounds with $\log K_{ow} > 4$, the introduction of multiple bioaccumulation values derived by lab research is insufficient for estimation *via* dietary intake (Nakata and Shinohara 2010). Metabolic transformation of higher K_{ow} compounds in aquatic organisms is not significant. In aquatic species, there is no major metabolic transformation of compounds with high K_{ow} . As compared to classical POPs, most of the UV stabilizers compounds have $\log K_{ow} > 4$ (**Figure 4**) as a result of which they have been detected in several species and marine wildlife including humans with concentration of several hundred nanograms/gram lipid weight (Nakata et al.2012).

UV-328 and other structurally similar BUVs (UV-326, UV-327, UV-328 and M1), occur in their neutral state and have slower rate of transformation. The metabolic rate constant (K_m) was calculated to be 0.01/day for UV-328 in a 184 gm fish. (Arnot et al.2008a, b). This K_m was considered low as compared with other organic compounds. Due to the sluggish metabolism of UV-328 or similar chemicals, they disperse slowly after they enter a higher trophic level. According to the AQUAWEB model, the estimated BAF value in a mid-trophic level carp was 8.7×10^4 L/kg wet weight in normal conditions.

4.3. Toxicity

BUVs have been regularly monitored and their presence in aquatic environment is a subject of increasing concern owing to their toxicity to aquatic species. Bioaccumulation of BUVs in several aquatic species has been reported in previous section, the more important step is determining the adverse effects in different organisms. There is currently no information on the acute toxicity of BUVs in aquatic species. Although attempts have been made by individual researchers for toxicity assessment, significant research findings are still needed to come on a concrete conclusion.

4.3.1. Acute and repeated dose toxicity

Several classes of phenolic BUVs meet the criteria for Specific Target Organ Toxicity-repeat exposure-sub category 2 (STOT RE2) according to the ECHA Risk Assessment Committee (RAC) (RAC 2013). Sub-acute (49 days) and sub-chronic (90 days) toxicity studies in rats are used to classify the substances. Because the liver is the primary site for xenobiotic transformation, repeated exposure to UV-328 in rats resulted in severe hepatic toxicity as well as harm to other organs. Modeling results indicated that UV-328 gets absorbed into GI (gastrointestinal) tract rather than ionizing in the intestines (Screening Assessment Report 2016). Kidney malfunctioning was also reported as they serve in the excretion of metabolites. Til et al (1968) observed similar results after conducting sub-acute and sub-chronic experiments in male and female rats in response to OECD test protocol TG 408. The liver and kidneys were found to be altered. Increased feeding levels (52.7-98.7 mg/kg bw/day) resulted in renal tubular nephrosis and hepatic necrosis in the liver, which met the requirements for human toxicity evaluation. Toxicity in the liver and kidneys was measured when beagle dogs were fed UV-328 (15-240mg/kg bw/day) for 90 days *via* diet.

According to the STOT-RE classification, animals exposed to > 15mg/kg dose had alteration in serum protein enzymatic activity (RAC 2013;Ciba 1970). In hybrid yeast bio-assays, UV-328 showed strong anti-androgenic enzyme activity towards human androgen receptors after being activated by human CYP3A4 enzyme-hydroxylation (Zhuang et al.2017). BUVs have not been found to have any estrogenic action (Kawamura et al. 2003). Contrary to this, several scientific studies investigated the toxicity of aircraft deicing and anti-icing fluids (ADAFs) on fish and other organisms (Pillard et al.2001; Cancilla et al. 2003;Corsi et al.2006). BUVs from ADAFs upon leaching to water bodies were reported to be toxic to zooplanktons species. Decrease in cellular growth and yield in *Ceriodaphnia dubia* and *Pimephales promelas* were reported by Cornell et al.2000.

4.3.2. Reproductive and geno-toxicity

To the best of our knowledge, and based on a thorough literature review genotoxicity, reproductive, or developmental toxicity of BUVs has not been reported so far. Significant research is needed in this area to estimate the toxicity of BZTs to aquatic organisms because they are more vulnerable and are primarily exposed to BUVs in water bodies.

4.3.3. Eco-toxicity

The eco-toxicity of BUVs is yet to be determined, as research highlighting eco-toxicity of BUVs is very scarce (J-CHECK 2018). Research finding suggests that fish and other organisms contaminated with BUVs upon consumption can pose severe risks to humans and other organisms in the food web (Screening Assessment Report 2016).

4.3.3.1 Short and long term eco-toxicity

At a dosage of 10 mg/L, no substantial toxicity was seen in fish or tiny crustaceans. However, at a lower concentration of 0.1mg/L, the algae *Scenedesmus subspicatus* showed growth inhibition after 72 hours of exposure (ECHA 2014). Another study on *Daphnia pulex* and *Daphnia Magna* that followed the OECD procedure found no adverse effects when concentrations were varied from ug/L to mg/L under static circumstances (Kim et al.2011; Ciba 1988a). At 96 hours of exposure to a dose of 100

mg/L, fish (*Danio rerio*) produced No observed effect concentration (NOEC). However, another fish (*Oryzias latipes*) produced $LC_{50} > 0.08$ mg/L after same exposure time for UV-328 (Ciba 1988 b).

These short-term observations, however, do not provide sufficient proof of toxicity to aquatic organisms. Neither of these pieces of evidence is adequate or convincing for evaluating the risk using appropriate models. Long-term exposure (after 96 hours) to two BUVs (UV-234 and UV-328) on green alga (*Chlamydomonas reinhardtii*) increased lipid peroxidation and reactive oxygen species (ROS) formation for UV-234 and UV-328, respectively. A two- to six-fold increase in glutathione peroxidase (GPX) activity in *Chlamydomonas reinhardtii* implies that a combination of two BUVs accounted for synergistic effects in the alga, alerting the antioxidant defense mechanism (Giraud et al. 2017). Khare et al. 2019 reported similar results in common carps exposed to a pesticide cocktail. Another long-term exposure of UV-328 on carp (*Oncorhynchus mykiss*) resulted in down-regulation of gene and induced ribosomal protein transcription after 28 days of food exposure (Giraud et al. 2020).

5. Long-range Transport (Lrt)

In the late 1980s, the first observation report on Polychlorinated biphenyls (PCBs) detection in human breast milk (Dewailly 1989) revealed evidence of high POPs exposure to Arctic indigenous people. Since then, multiple scientific papers have confirmed the presence of POPs in such pristine environment (Deutch and Hansen 2000; Bjerregaard 2001). In a study it was accounted that Inuit (locals or Eskimo) living in such areas with a stable traditional diet, tends to bio-accumulate contaminants thousand times more than non-native individuals (Czub and McLachlan 2005). Some of the most important factors for LRT of contaminants include i) persistence in air and water, ii) semi-volatile nature, which allows them to be partitioned and travel with aerosols before deposition, iii) the ability to bioaccumulate in organisms and biomagnify in food chain.

Because of low vapor pressure and short half-life in air, it is unclear from the literature if BUVs are capable of long-range atmospheric transfer (Screening Assessment Report 2016; EPA 2012). On the other hand, higher $\log K_{OW}$ and $\log K_{OC}$ values of some BUVs (UV-328, UV-327), indicate strong partition to sediments and organic matter, including its adsorption on aerosols and suspended solids in water. BUVs are photostable, which means they won't degrade when exposed to light. Nonetheless, UV-328 may establish an intramolecular hydrogen bond and become charged under certain environmental conditions, especially in oceans (Waiblinger 2000; Werner 1979). This charged molecule has a high affinity for adsorption on suspended materials and the ability to travel long distances. Overall Environmental persistence (PoV), and Characteristic Travel distance (CTD) of BUVs (UV-328) was plotted with other listed POPs as shown in **Figure 5**. PoV of UV-328 was determined to be 196 days while, CTD was 2800 Km with the transfer efficiency as 12.4%. These values clearly place BUVs in a position similar to those of other listed POP chemicals (SC 2021).

None of the BUVs have been routinely measured in environmental samples from remote areas, and the available data is insufficient. UV-328 has been found in several Swedish background sites, in Lake Superior and the Great Lakes in the United States (Lu et al. 2018), in Canada, and in the Norwegian arctic environment (Schlabech 2018). UV-328 was found in the liver of Fulmars (a sea bird) collected from the Prince Leopold Islands in the Canadian Arctic (Lu et al. 2019). Birds sampled near the Great Lakes seemed to bioaccumulate higher levels of UV-328 than fish, which could be due to their higher trophic status (Lu et al. 2019). Seagulls eat a terrestrial diet, they swallow microscopic creatures mixed with plastic waste polluted with UV absorbers, and a trace quantity of UV-328 was identified in their eggs. Because BUVs were not discovered in blood samples of polar bears from the same location, adipose tissue samples can be assessed for studying bioaccumulation (Schlabech 2018).

6. Regulatory Concerns Associated With Benzotriazoles (Bzts)

As the use of BUVs in commercial applications grows, so does production. Exposure to the general population is increasing, either at work or through the use of various industrial and personal care products (PCPs). BUVs distribution has also been predicted and compared to known POPs on a global scale. UV-328 may get listed under SC POPs, as it meets the POPs criteria after being listed in Annex D. UV-320, UV-327, UV-350, and Metabolite M1 are structurally related BUVs that have been examined and classified by several environmental agencies based on comparable chemical features to UV-328. **Table 1** summarizes the regulations associated with BUVs in different countries.

The Organization for Economic cooperation and development (OECD) recognized four phenolic BUVs compounds (UV-P, UV-234, UV-328, and UV-329) as HPV in 2015 and continued funding for future research work under the Cooperative Chemical Assessment Program (CoCAP) (OECD 2015). Furthermore, Japan funded the evaluation of three compounds from this group (UV-326, UV-327, and UV-350) in 2015, with UV-328 being identified as a possible candidate for further research (OECD 2015).

The EU designated four compounds (UV-320, UV-327, UV-328, and UV-350) as SVHCs under REACH regulations based on persistence and bioaccumulative properties. UV-320 and UV-328 have also been classified as PBT substances and have been reported to be hazardous to human health (ECHA2016a). Under the SVHC, four new chemicals (UV-P, UV-234, UV-326, and UV-329) are being investigated as subjects for informal risk assessment and risk management (ECHA2016b). Currently, UV-328 is under the review of POPs review committee (POPRC). Listing in Annex A of the SC will lead to phase out from production and use, thus will affect the BZT market. This will have implications on socio-economic front in both developed and developing countries.

Environmental contamination from BUVs can be an area of significant concern after listing of UV-328 by the SC in the near future. This can be regarded as a wakeup call for the entire globe to take a concerted action for sound management of BUVs. For instance, several countries of the western world have categorized and listed BUVs in different categories in accordance to their chemical and waste management policy. Asian countries, especially China are on top in terms of production and usage of BUVs as described in section 2. Till date, apart from Japan, none of the Asian countries has classified neither regulated the production and usage of BUVs which could be due to lack of scientific evidences. It's high time when both developed and developing nations should come together and formulate a common management plan (usage and sound disposal) for BUVs in light of the available scientific findings to check further environmental contamination.

7. Conclusion

BZTs have been detected in all environmental matrices, including human samples. Due to its widespread applications and continued use, BUVs are released into the environment. The majority of current BUVs research is concentrated at watershed or aquatic ecosystem level. Constant circulation of plastic waste, which acts as a primary source of transport of phenolic BUVs in water bodies, exacerbates their long-range environmental transport. Following the initial reporting of BUVs, particularly UV-328, decades after its distribution was stopped, demonstrates their long-term persistence. The presence of UV-328 in human milk and adipose tissues indicates its bioaccumulative potential. Absorption of BUVs in the GI tract followed by the transformation in liver, and excretion, resulting in hepatic and renal toxicity has been demonstrated via modelling studies. Genotoxicity, reproductive, mutagenic, or carcinogenic effects of BUVs are yet to be explored, followed by their degradation and transformation behavior in different conditions. Following the inclusion of UV-328 in "Annex D" of the SC, after meeting the POPs screening criteria, phenolic BZTs should be prioritized for research (SC 2021). Regulatory agencies should consider the entire group of BUVs due to their similar PBT properties rather than phasing out or restricting a single chemical.

Declarations

Ethical Declarations:

Ethics approval and consent to participate:

"Not applicable."

Consent for publication:

"Not applicable."

Author(s) Contribution statement:

Conceptualization and original drafting was done by AK. Data collection was done by PJ. Revision and editing was done by ARK and ANV. All authors read and approved the final manuscript.

Funding:

"The authors declare that no funds, grants, or other support were received during the preparation of this manuscript." Partial financial support was received from Council of Scientific and Industrial Research (CSIR) to the first author in terms of monthly fellowship (31/0016(11375)/2021-EMR-I).

Competing interests:

"The authors have no relevant financial or non-financial interests to disclose."

Availability of data and materials:

All the data referred in this paper have been extracted from peer reviewed journals available in public domain.

Acknowledgement- All the authors gratefully acknowledge Director CSIR-NEERI, for granting permission to publish the paper. The first author thanks Council of Scientific and Industrial Research (CSIR) for providing financial assistance in terms of monthly fellowship (31/0016(11375)/2021-EMR-I).

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Tables

Table 1- Regulations and Categorization of BUVs in different countries

Country/Union	Chemical Name	Classification/Categorization	Reference
Canada	UV-234, UV-326, UV-328, UV-329 and UV-350	Bioaccumulative (B) and inherently toxic to the environment, but not persistent (P).	Environment Canada, 2013a
	UV-327	Categorized as P, but not B	Environment Canada, 2013b
	UV-P and UV-320	not P and not B	
European Union (EU)	UV-320, UV-327, UV-328, and UV-350	Substances of Very High Concern (SVHC) under the Registration, Evaluation, Authorization, and Restriction of Chemicals (REACH)	ECHA, 2016a
	UV-320 and UV-328	STOT RE2, Persistent, Bioaccumulative and Toxic (PBT) substances	ECHA, 2016b
	UV-P, UV-234, UV-326 and UV-329	Put on SVHC Roadmap for consideration as PBT	ECHA, 2016c
USA	UV-P, UV-234, UV-328 and UV-329	Low to high bioaccumulation potential and high persistence	US EPA, 2009
Japan	UV-320	Chemical Substances Control Law (CSCL) Class I Specified Substance (Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture; Substances that are persistent and extremely bioaccumulative, offering a long-term toxicity risk to humans or top predator animals.	NITI, 2016
Japan	UV-327 and UV-350	Chemical Substances Monitoring under the CSCL, Persistent and bioaccumulative, with long-term effects in humans and top predator animals unknown.	METI, 2010
UNEP	UV-328	Annex D of the convention after meeting PBT and long-range environmental transport	SC, 2021

Figures

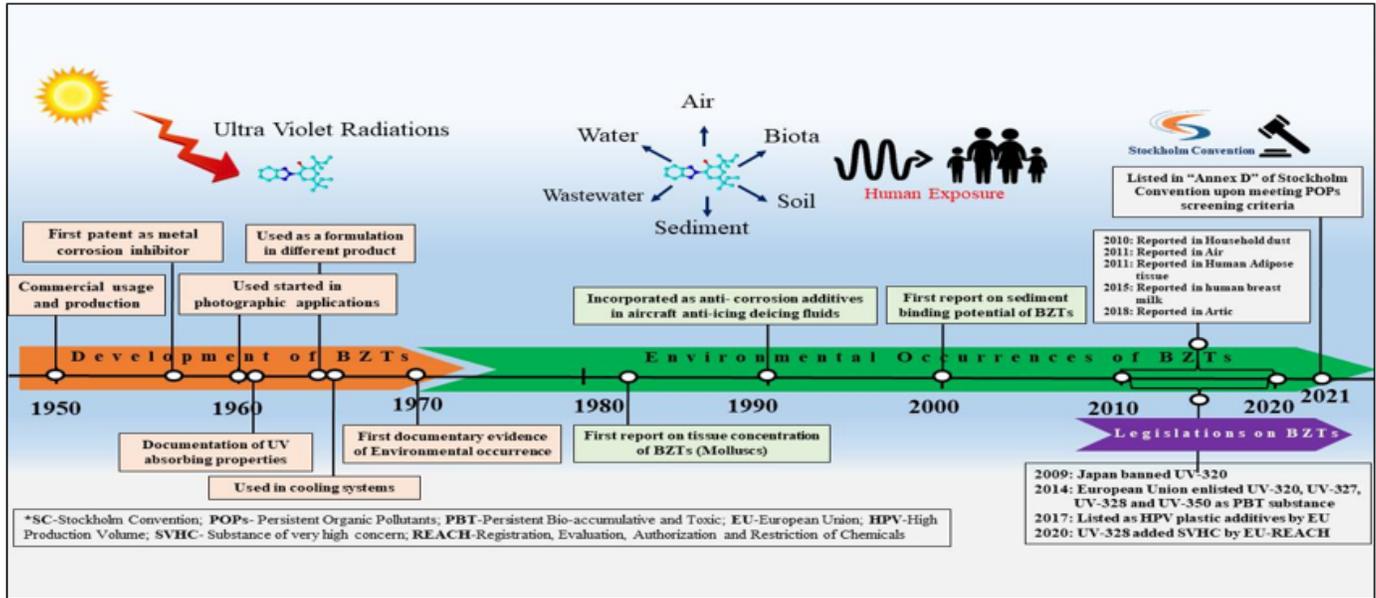


Figure 1

Timeline of UVs

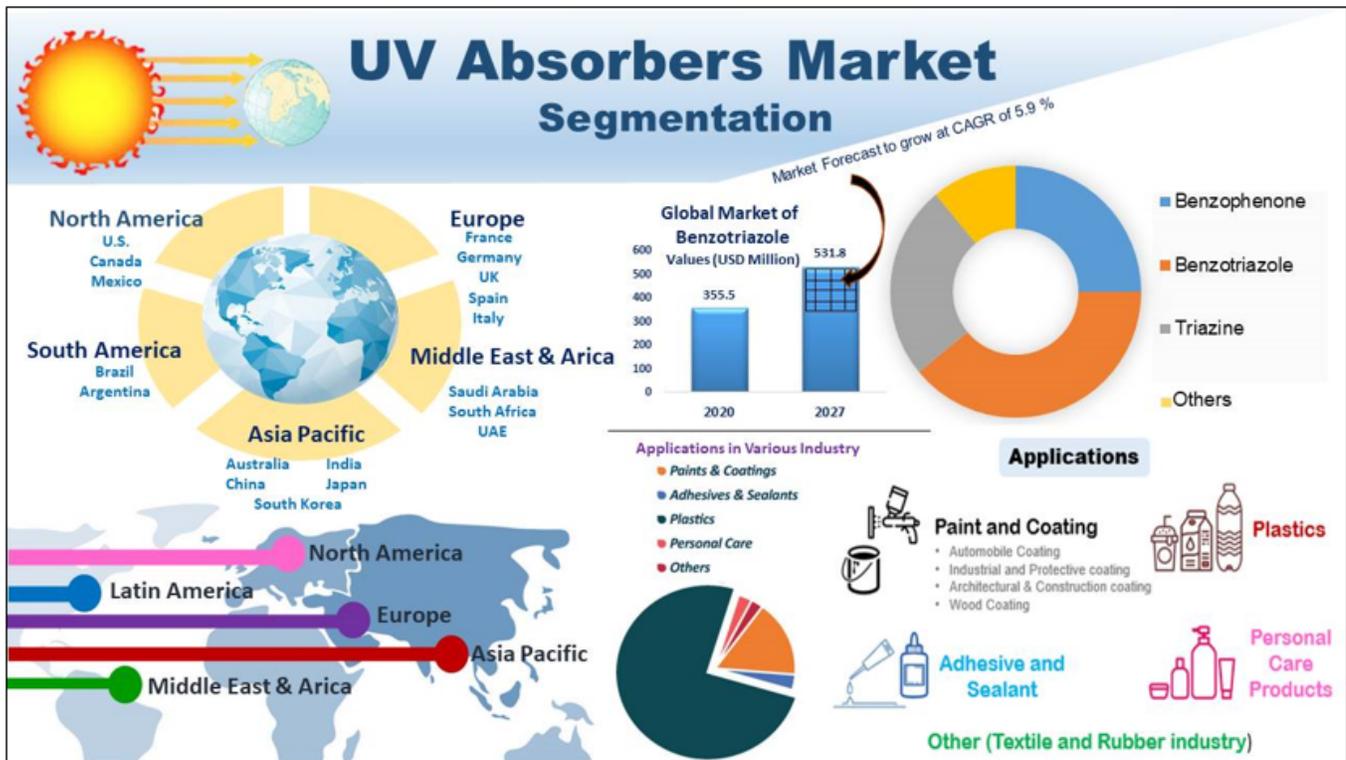


Figure 2

Market share and Application of Benzotriazole UV absorbers

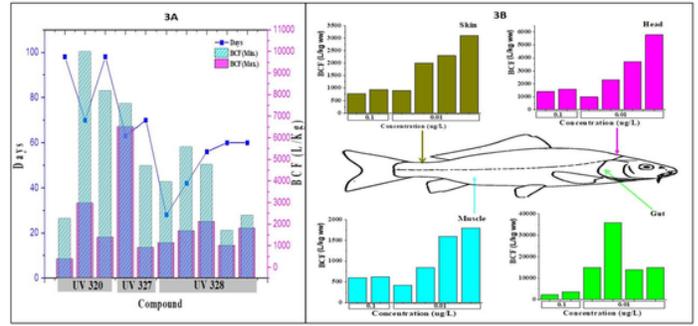
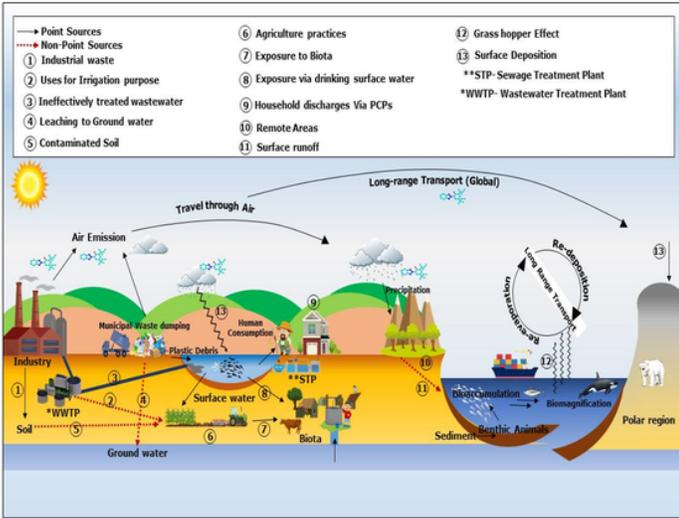


Figure 3

Environment Fate of BUVsS

A- Minimum and Maximum BCF values of different BUVs in fish (Nakata et al., 2009; Canada report, 2014; ECHA, 2018);

B- BCF in different organs of fish based upon nominal concentration of test substance (SC, 2021)

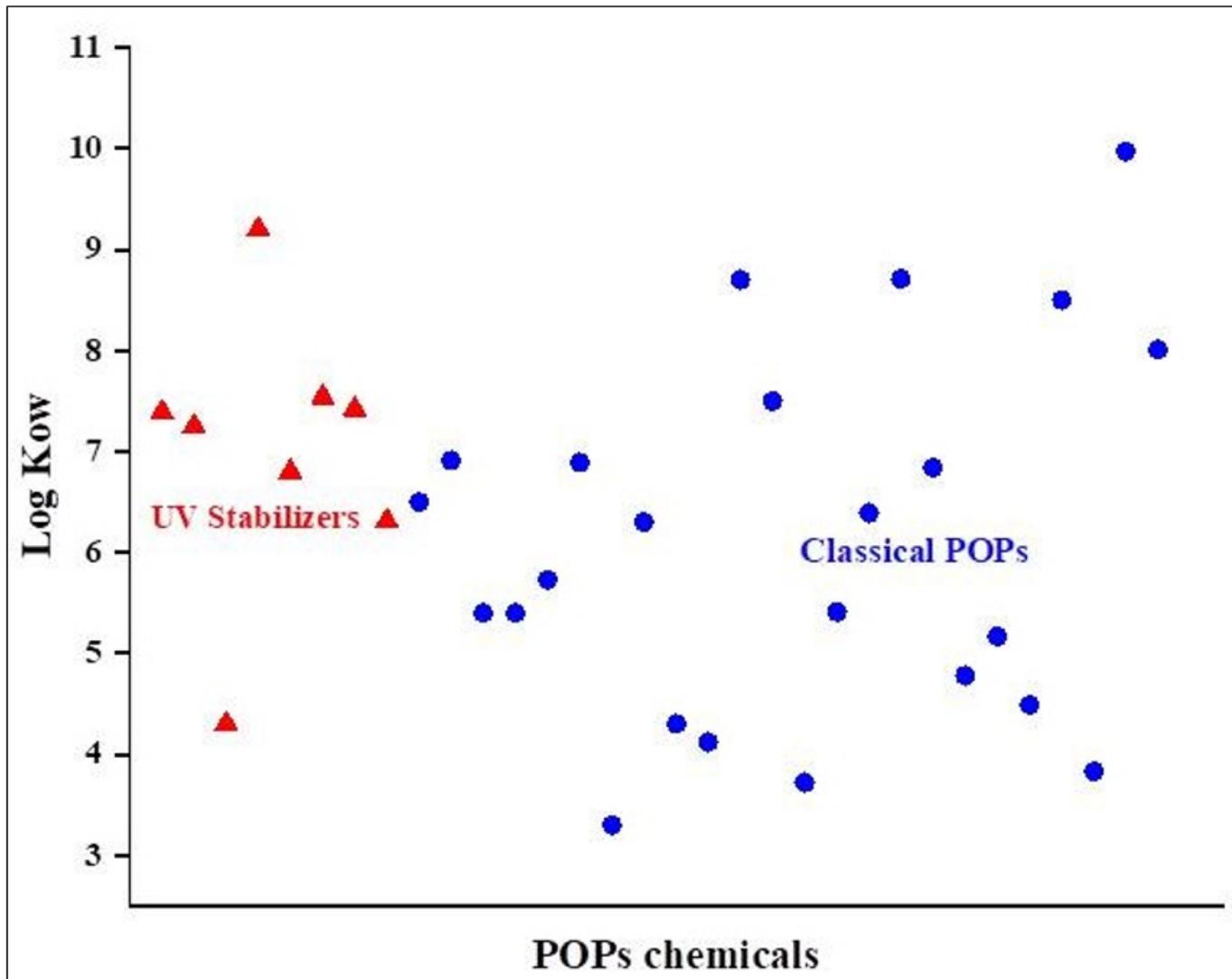


Figure 4

Plot comparing K_{ow} values of UV absorbers (in red) with other classical POPs (in blue)

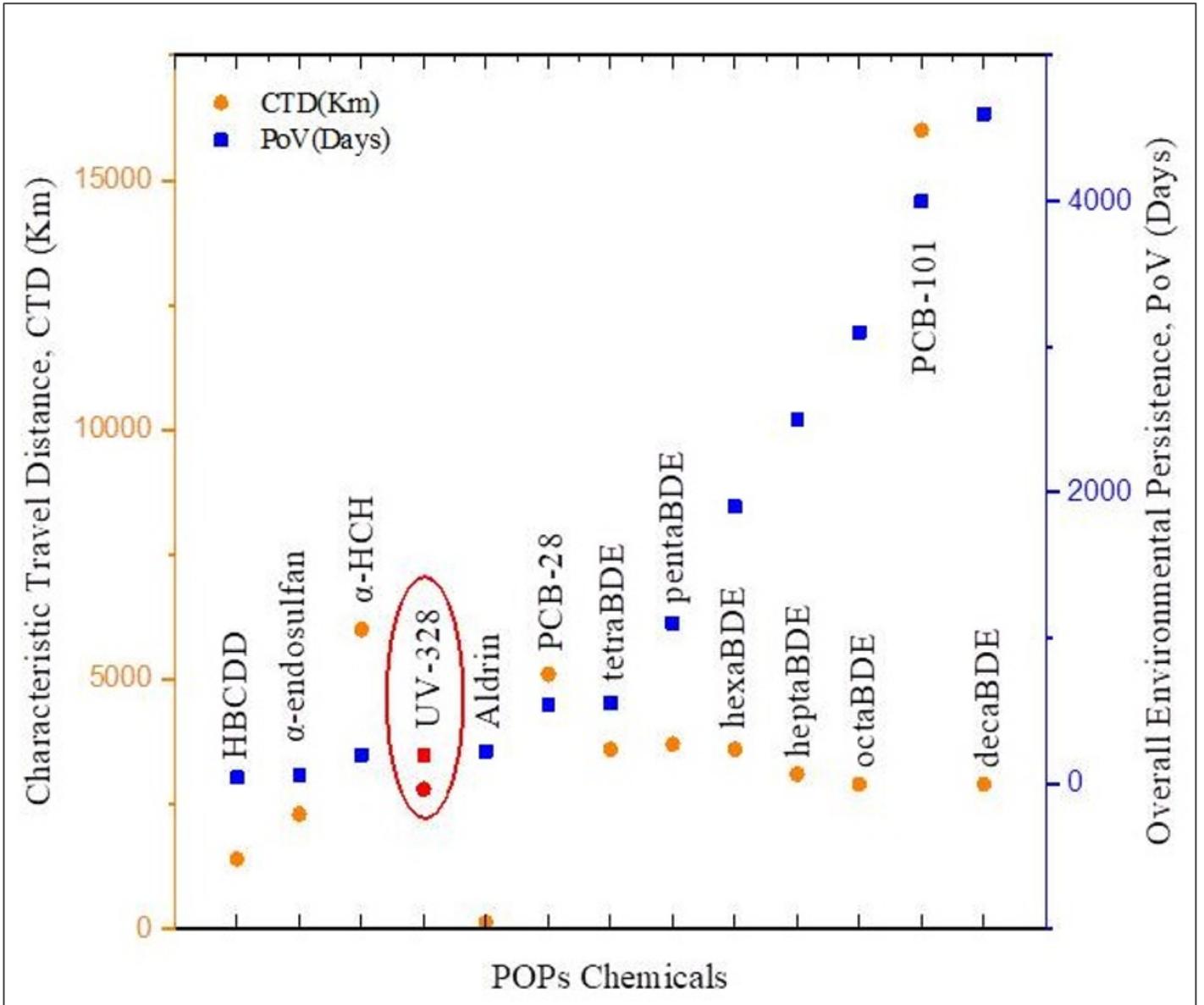


Figure 5

Plot comparing Benzotriazole (UV-328) in red dot to other listed POP chemicals for Overall Environmental Persistence (PoV) and Characteristic Travel Distance (CTD).

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