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O 15. IMPORTANCE OF TRICLOSAN FOR ENVIRONMENT AND HUMAN HEALTH

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ABSTRACT: Triclosan (TCS) is the active ingredient used in health and personal care products, especially in the structure of toothpastes, due to its antibacterial properties, and its concentrations are mainly 0.1-0.3% by weight. The use of antimicrobial and antibacterial products is increasing steadily around the world, so there is a constant release of TCS compound into the environment. Recent studies show that the use of antibacterial products is increasing during the corona virus pandemic process, so it is observed that TCS has increased in contact with humans and the environment. TCS is a chemical substance that has the potential for toxic biocide degradation in the environment and may adversely affect the environment and human health. This compound is known as “endocrine disrupting chemicals (EDC)” because it accumulates in aquatic organisms and remains intact in the environmental environment for a long time and is included in a group generally defined as "Emerging Organic Pollutants (EOP)". In this study, the properties of TCS, its contact with the human body and face water, its treatment in the wastewater treatment plant and its effects on the environment and human life are mentioned.

Keywords: Triclosan, Environment, Health, Toxicology

1. INTRODUCTION

Triclosan (TCS: $C_{12}H_{17}Cl_3O_2$; 2,4,4'-trichloro-2'-hydroxydiphenyl ether) is the most common active antiseptic ingredient used in soap. It is used in cosmetics, including soap, toothpaste, lotion and shampoos, and to prevent bacterial contamination in other products such as textiles, kitchenware, furniture, toys. TCS is a phenoxyphenol antimicrobial agent first developed in the early 1960s and has been used as an antibacterial since the 1970s (Kim et al., 2015).

The negative opinions derived from studies with animal models show that TCS is a toxic chemical that has the potential to affect human health. This biocide has been shown to bioaccumulate in aquatic species. TCS has been observed to persist for long periods in the environment, especially under anaerobic conditions. This compound belongs to a group of many known as endocrine disrupting chemicals (EDCs), often described as "Emerging Organic Pollutants" (Chalew and Halden, 2009).

Once in the aquatic environment, TCS undergoes a series of conversion reactions in some cases to decompose into more toxic or bioaccumulative compounds. Sodium hypochlorite (bleach) in tap water or discharged into wastewater sewers by household disinfection products causes oxidation of TCS. This reaction leads to the formation of the relatively unstable tetra and pentachloric diphenyl ethers, which then decompose into dichloro and trichlorophenols (Morales et al., 2005).

It has been shown that when chemical-containing PCPs (Personal Care Production) are used, chemicals enter the human body through percutaneous absorption. It has been reported that TCS enters the human body primarily through oral intake and dermal contact with PCPs. It has been observed that 9% of the applied TCS is biologically penetrated into the human body after 24 hours of dermal exposure (Lu et al., 2018). TCS can be released into the environment as a result of various stages. TCS can be discharged directly into the aquatic environment after wastewater treatment plant treatment. TCS can be adsorbed on organic particles in sewage sludge during wastewater treatment with a high log Kow of 4.76 and is likely to then be transported to soil via sludge application (Guo and Iwata, 2017).

TCS, which draws attention around the world, has been restricted to its concentrations in the product in many countries. TCS concentration is limited to 0.3% in all cosmetic products in Europe (Heisterberg and Menné, 2003), Canada (Goverment of Canada, 2019), South Africa (Lehutso et al., 2017) and Australia (EPA, 2016), and 0.1% in Japan (EPA, 2016).

1.1. TCS Chemical

An estimated 1500 tons of TCS are produced annually worldwide, of which about 350 tons are produced in Europe (Bester, 2005). TCS is an antimicrobial that has been found in a variety of consumer products since its first use in hospital settings in 1972, including soaps, hand sanitizers, toothpastes and mouthwashes. In 1977, TCS production was between 0.5 and 1 million pounds per year. This production increased from 1 to 10 million pounds in 1998. Between 1999 and 2000, 75% of 178 liquid soaps contained TCS and 30% of more than 300 bar soap samples contained TCS. In the late 2000s (2008–2010), TCS was found as an active ingredient in 93% of liquid, gel or foam soaps (Weatherly and Gosse, 2017). Kim et al., (2015), in their study, found that approximately 76% of liquid hand soaps and 29% of bar soaps contained TCS in 2015.

Table 1. Products Containing the Chemical TCS

Category	Product	Reference
Personal care products	Soaps, detergents, shaving gels, face washes, wet wipes, skin cleansers, toothpastes, mouthwashes, cosmetics, deodorants	(Weatherly and Gosse, 2017)
Household products	Kitchenware, dishwashing liquid, toys, computer equipment, furniture, humidifiers, helmets, wall coverings, air filters, blankets, mats, handrails, paints, earplugs, coolers, drinkers, feeders, vacuum food containers	(Dhillon et al., 2015)
Textile	Clothes, shoes, sandals, towels	(Zhao et al., 2016)
First aid	Antiseptics, Burn creams, Medicated sprays	(Dhillon et al., 2015)
Office and school products	Calculators, scissors, paper, glue, cutting tools, notebooks, pens	(Dhillon et al., 2015)

2. TCS IN THE AQUATIC ENVIRONMENT

TCS, which is included in personal care and health products and has antibacterial properties, penetrates into the aquatic environment through sewage after consumption and poses a potential threat to existing organisms in the water or to the environment. In many studies and researches, varying concentrations of TCS have been detected in surface or underground waters in various parts of the world.

Surface waters with high concentrations of TCS in China are generally found in or near urban areas. The TCS concentration in Liao River was 27.4 ng/l, 6.89 ng/l for Hai River, 8.7 ng/l for Yellow River, 95.7 ng/l for Zhujiang River and finally 26.4 ng/l for Dongjiang River (Zhao et al., 2013). TCS an endocrine disrupting phenol, was found to be highly present in river water in China, with a TCS concentration of 35 – 1023 ng/l. The cause of the TCS concentration in river water is thought to be mainly due to random discharge or seepage of municipal wastewater (Peng et al., 2008).

The presence of chemical substances in surface waters is important for humans and the environment. Because surface waters have been the main source of drinking water for people from past to present and are home to many living things. Drinking water is the primary source of dietary intake of the pollutant. For this, the control of chemicals or pollutants in surface waters is an important issue. TCS concentrations of 2.6 ng/l and 8 ng/l were found in the lake waters of Mead and Las Wegas Wash in the USA. TCS is thought to be adversely affected by Las Wegas Wash as the lake water is a habitat for various wild animals, including birds and fish. It is also thought that the concentration detected in Lake Mead may have long-lasting effects on human health because Lake Mead is the primary source of drinking water for local residents (Bai and Acharya, 2017).

In another study conducted in the North American continent, TCS was determined in the Mississippi river in New Orleans, Louisiana, USA. TCS was detected in the range of 8.8 to 34.9 ng/l in the river water in the determination (Zhang, Zhang, Darisaw, Ehie and Wang 2007). It is estimated that TCS passes into ground waters with the leakage of surface waters. TCS concentrations in groundwater have been found to be 12-53 ng/l in the USA (Karnjanapiboonwong, 2011). This study demonstrates the presence of endocrine disrupting chemicals even in groundwater.

Table 2. TCS Concentration in the Aquatic Environment on Earth

Sample Region	Location	TCS Concentration	Reference
River water	China	0,035-1.023 µg/l	Peng et al., 2008
River water	India	5.14 ng/l	Ramaswamy et al., 2011
River water	USA	8.8-34.9 ng/l	Zhang et al., 2007
Lake water	USA	0,0026-0,008 µg/l	Bai and Acharya, 2017
Canal water	Japan	0,011-0,031 µg/l	Nishi et al., 2008
Tap water	Taiwan	14 ng/l	Li et al., 2010
Drinking water	Taiwan	8 ng/l	Li et al., 2010
Drinking water	USA	1.4 ng/l	Padhye et al., 2014

When we look ahead, the demand for water increases with the increasing population and the current water scarcity emerges. Studies are needed to increase water resources, recycle and reuse water. Recently, due to the developing technology and changing needs, the use of chemicals has increased, and it has become easier for the increased chemicals to enter the water environment with discharge. As a result of discharges, water, soil and nature are directly polluted. Therefore, the treatment and control of wastewater becomes important. To obtain a reliable estimate of TCS removal in sewage treatment plants (WWTP), the concentration of the main pollutant and its conversion products must be determined in both the water phase and the solid sludge.

TCS which comes to the wastewater treatment plant, goes through the primary treatment after entering the wastewater treatment plant, but the efficiency of this treatment method remains low compared to the secondary, that is, biological treatment. Removal of pharmaceuticals and personal care products (PPCDs) in physical and chemical treatment processes is limited (28%), but it has been observed that the majority of PPCDs are removed in secondary treatment (biological processes) (Behera et al., 2011).

It has been stated that a significant portion of water pollutants are pharmaceuticals and personal care products. In the research of pharmaceuticals and personal care products in the inlet water of the wastewater treatment plant that treats urban wastewater, the treatment efficiency was found to be 74.5%. It has been observed that ozonation after biological treatment is effective in the purification of TCS (Rosal et al., 2010). It has been observed that anaerobic treatment, one of the wastewater treatment processes, is more efficient than the aerobic process to treat TCS in the water in the system. From this point of view, it is understood that TCS chemical decomposes in an oxygen-free environment and some of it is separated from the aquatic environment. In the study, it was understood that the treatment sludge absorbs TCS (Best, 2003).

3. EFFECTS OF TCS EXPOSURE ON HUMAN HEALTH

With the increasing consumption of TCS recently, it has become easier to contact environmental factors, and as a result, people's lives are also affected. Guo and Iwata (2017) stated in their study that consumption of TCS contaminated fish in drinking water or food chain are two different ways for humans to be exposed to TCS. The absorption of TCS into the human body after dermal application of a hydrophobic cream containing 2% TCS to humans was studied. They calculated that after 12 hours of exposure, TCS is absorbed into the human body and most of it is excreted through the urine within 24 hours, and the half-life of TCS in the human body is 10.8 hours (Queckenberg et al., 2010).

TCS is included as an antibacterial agent in many toothpastes sold worldwide. Individuals are chronically exposed to chemicals once or twice a day along with tooth brushing. TCS reaches the systemic circulation by absorption through the mucous membranes of the oral cavity and gastrointestinal tract, thereby initiating a systemic exposure. The antibacterial properties of TCS have been shown to be exerted by inhibition of an enoyl-reductase involved in fatty acid synthesis in bacteria. The lipophilic properties of TCS also increase its dermal absorption and percutaneous penetration of TCS is quite high

(Sandborgh-Englund et al., 2006). TCS, which penetrates the skin and enters the human body, is known to accumulate mainly in the liver. In the TCS study on adipose tissue (adipose tissue), liver and brain samples from human cadavers, concentrations were detected in almost all livers (10/11), most adipose tissue (7/11) and only one brain sample. Total TCS concentrations were 3.92 ng/g in adipose tissue, 0.23 ng/g in brain and 29.03 ng/g in liver. He found that the human liver was the organ with the highest concentration of TCS (Geens et al., 2012). In another study that mothers were divided into those who use TCS-containing personal care products and those who use products that do not contain TCS that TCS has been found in a wide range of concentrations in both mothers using and not using TCS-containing products. TCS has been found in a wide range of concentrations in both mothers using and not using TCS-containing products. TCS has been detected at levels of 20-300 ng/g in breast milk and in the range of 0.01-38 ng/ml in plasma samples. Breastfed infants (daily TCS intake 11-570 ng/day) have been observed to be exposed to very low doses of TCS through breast milk (Allmyr et al., 2006).

In a study conducted on urine, nail and toenail samples of healthy volunteers aged 19-32 years living in Beijing and Sichuan provinces of China, TCS was detected in 80% of urine samples, 79% of fingernails and 69% of toenail samples. Mean concentrations of TCS were 0.36 µg/L in urine, 5.67 µg/kg in fingernails and 13.57 µg/kg in toenails (Yin et al., 2016). In another study, TCS analysis was performed from male and female urine samples collected from seven Asian countries, Greece and the USA; Urine TCS concentration in China 2.38 µg/l, India 4.64 µg/l, Korea 0.7 µg/l, Kuwait 2.5 µg/l, Japan 0.9 µg/l, Saudi Arabia 0.44 µg/l, Vietnam 0.42 µg/l, Greece 1.94 µg/l and finally USA 7.84 µg/l (Iyer et al., 2018).

4. ENVIRONMENTAL HEALTH EFFECTS OF TCS EXPOSURE

Surface water, which is the final destination of many wastewater, is one of the environmental elements most affected by chemicals. Studies show that living creatures living in the aquatic environment are affected by chemicals and accumulate in their bodies. The fact that fish are in an important position in the food chain increases the importance of knowing the chemical concentrations in the aquatic environment for future studies (Zhao et al., 2013).

It has been shown that the antibacterial effects of TCS are mediated, at least in part, through its membranotropic effects, leading to unstable structures that compromise the functional integrity of cell membranes without inducing cell lysis. TCS interferes with the stabilization and integrity of the sperm membrane, which may be the possible cause of sperm death (Villalaín et al., 2001). Sea urchin (Strongylocentrotus nudus) exposed to TCS Fertilization rate was affected at 0.5 µM TCS and no fertilization occurred at concentrations higher than 1.25 µM TCS. It was observed that fertilization occurred in 97.4±1.21%, 92.9±1.8%, and 82.7±1.57%, respectively, when exposed to 0.1, 0.5, and 1.0 µM TCS. The EC_{50} value of the TCS concentration was determined as 1.49 µM (Hwang et al., 2014).

LC_{50} values of TCS on medaka Oryzias latypes were determined at 96 hours, 602 µg/l for 24-hour larvae and 399 µg/l for embryos. Embryonic development, hatchability, and hatching time of medaka eggs were affected by TCS exposure. The hatchability of fertilized eggs exposed to TCS was significantly reduced in the treatment groups compared to controls at concentrations above 313 µg/l, and the hatching time was also significantly delayed (Ishibashi et al., 2004). In adult zebrafish exposed to TCS, it was determined that the total distance traveled and movement speed decreased as the concentration increased, and an increase in freezing and suspending behaviors was observed (Pullaguri et al., 2020). In the study, adult mice were chronically exposed to TCS. It was determined that body weights were affected and memory formation was impaired in female mice affected by the TCS compound, while male mice caused a decrease in social interaction. (Hao et al., 2022)

Table 3. Effect on Reproduction, Hatching, Behavioral and Physical Development of Aquatic Organisms Exposed to TCS

Organism	Scientific name	TCS concentration	Major Results	Reference
Frog	Peleophylax perezi	0.25–2.5 mg/l; 72 s	70% decrease in hatching rate after 72 hours.	(Martins et al., 2017)

Mosquito fish	Mosquitofish	100–350 nM;35 g	Decrease in sperm count.	(Raut et al., 2010)
Zebra Fish	Danio rerio	0.1–0.9 mg/l;24–144 s	Irregular swimming and loss of balance at high TCS concentrations.	(Oliveira et al., 2010)
Zebra Fish	Danio rerio	0.4-40 µg/l; 5 g	Foraging and foraging efficiency decreased with increasing concentration.	(Wirt et al., 2018)
Zebra Fish	Danio rerio	0.2-0.8 mg/l	Prolonged incubation time and decreased heart rate.	(Kim et al., 2008)

5. DISCUSSION

The main exposure of TCS to the environment is due to the discharge of wastewater from people's personal care products after use or from the wastewater of factories producing TCS. Studies show that the presence of TCS in many surface waters around the world is an important component that has a worldwide impact on human and environmental health. TCS, which can penetrate the aquatic environment, also threatens the health of living things in the aquatic ecosystem. It was observed that zebrafish exposed to TCS chemical had behavioral changes as the concentration increased (Pullaguri et al., 2020).

In the study conducted by Allmyr et al. (2006), chemical concentrations were found in the blood of people who declared that they did not use TCS-containing products. It is proof that we are unwittingly in contact with endocrine disrupting chemicals. TCS concentrations were detected in the plasma of the babies in the examination, and it is thought that the reason for this is that the mother's milk is contaminated with the chemical and passed to the baby. TCS is mainly found in many disinfectant products as antibacterial (Weatherly and Gosse, 2017). It was reported that the use of hand sanitizer increased from 14.6% before COVID 19 to 89.8% after COVID 19, and the number of consumers carrying hand disinfectants increased from 4.1% before COVID 19 to 39.3% after COVID 19 (Choi et al., 2021).

Studies show that all individuals, from infants to the elderly, are exposed to TCS. Recently, the amount of hand disinfectants or soaps containing TCS that people use for defense against viruses has been increasing. With this increase, TCS production increases and the waste water generated as a result of use directly affects environmental health. In the research conducted in urban wastewater treatment, it was found that the treatment efficiency of TCS in personal care and disinfectant products was 74.5%, which shows that the treatment of TCS in the water environment is insufficient (Rosal et al., 2010). These studies show that the production of TCS, which is used as an antibacterial, is increasing day by day. At the end of the consumption of cosmetic or antibacterial products, the compound that comes to the treatment plant is released into the environment because it is not purified at full efficiency. TCS reaching the aquatic environment affects aquatic organisms and contaminates them. The water or fish consumed by people pose a threat to human health. To protect against the chemical TCS concentration restrictions should be imposed on products or they should be banned. It is important to research the chemical TCS for the future of human and natural life.

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