Ecological Toxicity of Triclosan (TCS): A Review

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Abstract. TCS has been detected in water systems and organisms all over the world. TCS in water body mostly exists at ng/L or g/L level. The highest content of TCS is mostly from sewage plant water samples, some of which reach 26.80 g/L. TCS concentration was 0.4-38.0 ng/g in maternal plasma and 0.022-0.95 ng/g in breast milk. TCS has been proved to be toxic to algae, plants, lower animals, amphibians, fish, mammals and other organisms at all levels, mainly in growth inhibition, lethal effect, endocrine interference, reproductive toxicity, DNA toxicity and so on.

1. Introduction
As an important antimicrobial agent, triclosan (TCS) has been widely used in personal care products (such as toothpaste, antimicrobial soap, skin cream and decolorizer), daily consumer products (such as fibre fabrics, Plastic Kitchenware and sports shoes and socks), medical supplies (such as dental consumables, medical preservatives and bactericides) and household cleaning products (such as household detergents and disinfectants) for more than 30 years. The annual use of it in the world is estimated to be over 750×10³ tons [1]. Due to its strong lipophilicity and accumulation ability in organisms, TCS are posing a great ecological threat.

2. TCS in the Environment and in the Organisms
Environmental TCS has been reported worldwide. The Geological Exploration Association of United States (USGS) has studied 139 rivers in 30 states of the United States and found that TCS is the most frequently detected organic pollutant [2]. Van der Ohe et al. detected TCS in 802 sites (representing 572 water systems in Saxony, northern Germany) in the Elbe River Basin, indicating that TCS should be considered as a pollutant of priority concern. Ying et al. monitored TCS in water and sediments of the Pearl River, Yangtze River, Yellow River, Haihe River and Liaohe River in China. TCS showed a high occurring rate in water and sediments, and the high concentration is generally located in the polluted tributaries. The maximum detectable concentrations in water and sediment reached 478ng/L and 1329 ng/g respectively [3]. The detected concentration of TCS in sewage treatment plant is higher, reaching 1.86-26.8 g/L. Through cluster analysis and principal component analysis, it was found that urban domestic sewage discharge was the main source of TCS [4].

TCS has strong lipophilicity and can accumulate in various organisms [5]. According to some reports, TCS in various organisms was 50-400 g/kg in Chaetophyta algae, 50-300g/kg in muscle tissue of freshwater snail, 14000 -80 000 g/kg in bile of Oriental blackbream (male), 0.75-10 g/kg in ocean fish plasma, 0.12-0.27 g/kg in South Carolina Atlantic bottlenose dolphin plasma, 0.025-0.11g/kg in Atlantic bottlenose dolphin plasma in Florida Indian River, and 9.0 g/kg in killer whale plasma in Vancouver Aquarium. Also, TCS has been detected in human urine, breast milk and plasma by American and Swedish scientists. In 2008, American researchers published 2517 urine samples of volunteers, of which the concentration of TCS was about 2.4-3790ng/mL. The plasma TCS
concentration of lactating mothers using TCS products was 0.4-38.0ng/g, and that of breast milk was 0.022-0.95ng/g. The plasma TCS concentration of mothers without TCS products was 0.01-19 ng/g, and that of breast milk was 0.018-0.35 ng/g [6, 7].

3. Toxic Effects of TCS on Various Organisms

3.1. Algae
Among aquatic species, algae are considered to be the most susceptible to TCS, mainly showing acute toxicity. For example, both green algae (freshwater algae) and Dunaliella (an oceanic algae) are very sensitive to TCS. TCS could significantly inhibit the growth of freshwater algae, with a 72h-EC50 of about 2.8 g/L [8]. The toxicity of TCS to Scenedesmus obliquus fluctuates due to the influence of phosphorus concentration. The effects of different phosphorus concentrations (0-50mg/L) and TCS (50, 200 g/L) on the growth, chlorophyll fluorescence characteristics and physiological and biochemical indices of Scenedesmus obliquus were analyzed. Under three phosphorus concentration conditions (0, 2.5, 50.0 mg/L), TCS showed a dose-effect relationship on the growth inhibition of Scenedesmus obliquus, and its chlorophyll fluorescence characteristics indicated a dose-effect relationship. Standard Yield-F/Fo and NPQ were affected to varying degrees. The activities of antioxidant enzymes (SOD, CAT) and phosphorus metabolism related enzymes (ACP, AKP) also changed accordingly [9].

3.2. Plants
TCS also affects the growth and development of plants. Wu et al. found that TCS could accumulate in the root of legumes and transfer to the upper part of legumes in the soil through which organic solid waste and wastewater flowed [10]. TCS in soil can inhibit the growth of many kinds of plants. EC50 of rice seeds and cucumber seeds germination are 57 mg/kg and 108 mg/kg [11]. Amorim et al. confirmed that TCS has an effect on the growth of wheat and Brassica plants [12].

3.3. Lower Animals
TCS is toxic to various lower aquatic and terrestrial animals, including daphnets, snails, tetrahedrons, earthworms and so on. The toxic effects include growth inhibition, reproductive inhibition and lethal effects. TCS was recognized as RED insecticide by the U.S. Environmental Agency and is hazardous to lower organisms [13]. TCS showed acute toxicity to Daphnia magna, with a 48h-EC50 of 390 g/L [8]. TCS at µg/L level caused growth inhibition on Tetrahymena, with 24h-EC50 of 141µg/L, minimum ineffective response concentration of 2µg/L and minimum effective concentration of 4µg/L. In addition, when the concentration of TCS reached 1000 µg/L, the cell membrane of Tetrahymena was damaged obviously. TCS also affected the lysosomal activity in Tetrahymena. Treatment with TCS of 1 µg/L for 2 h resulted in a 88.62% lysosomal activity [14]. TCS of 1.0 µM/L significantly decreased the sperm activity of sea urchin, and 2.0µM/L led to sperm inactivation. TCS of 0.5µM/L significantly reduced the fertilization rate and 1.5 µM/L TCS resulted in totally failed fertilization [15]. Four weeks exposure TCC (TCS analogues) to a freshwater snail confirmed that the lowest effective concentration (LOEC) and the lowest ineffective response concentration (NOEC) were 0.2µg/L and 0.05µg/L respectively, and EC50 were 2.5µg/L [16]. Chronic exposure to 50-300 mg/kg TCS significantly reduced the reproductive capacity in earthworms, and the EC50 was 142.11 mg/kg. Comet assay showed that TCS caused DNA damage with EC50 value of 8.85 mg/kg. The expression level of Hsp70 gene in 50 mg/kg group was up-regulated, which was 2.28 times higher than that in control group. EC50 value based on Hsp70 biomarker was 1.79 mg/kg [17].

3.4. Fishes
When exposed to TCS solution, especially at high concentration, the incubation time of fish embryos was significantly delayed and teratogenic effects were produced on larvae and adults. TCS showed acute toxicity to Pimephales promelas, with a 24h-LC50 of 360 g/L [8]. TCS and its derivatives have an effect on the secretion of male hormones in fish, and belong to newly recognized endocrine interferons. Also, It may cause many problems including cancer, reproductive dysfunction and
developmental abnormalities [18]. The 96h-EC$_{50}$ to Brassica brasiliensis was 10-13 g/L, and 96 h-LC$_{50}$ to blue mumps and rainbow trout was 97µg/L and 180µg/L respectively [19]. The effects of TCS on the reproduction of blue gill fish were also confirmed. Fourteen days of exposure to 313 g/L TCS resulted in the decrease of hatching ability of fertilized eggs and the prolongation of hatching time [20].

3.5. Mammals
Thirty days exposure to TCS (40 to 632 mg/kg) in rats caused hepatotoxicity, nephrotoxicity, damaged immune system. The observed effects included decreased weight gain, spleen-body ratio, and increased liver-body ratio, male-kidney-body ratio, serum alanine aminotransferase, urea nitrogen and creatinine [21]. TCS exposure showed effects on the pregnancy outcome of pregnant rats. The pregnant rats had abnormal feeding and weight gain ability, blood sugar, serum malondialdehyde, serum protein and other indicators. The composition of live fetus and absorbed fetus of pregnant rats also changed [22]. TCS caused DNA damage in human hepatocytes. DNA breakage in normal human hepatocytes cultured in vitro was observed, with a significant dose-effect relationship and time-effect relationship [23]. After short-term intake of TCS in male mice, TCS was detected in testis, epididymis and prostate. It was found that TCS tended to accumulate in epididymis, showing a significantly longer half-life and accumulation time. High dose of TCS (200 mg/kg) was also shown to reduce sperm production and cause sperm malformation in rats [24]. A short time exposure to TCS in male rats indicated that the expression levels of several important proteins such as testosterone emergency monitoring protein, androgen receptor and so on were significantly decreased. The levels of luteinizing hormone, follicle stimulating hormone, cholesterol, progesterone and testosterone in serum were significantly decreased, showing a significant impact on sex hormones [25].

4. Discussion
As mentioned above, TCS has been widely detected in the environment and organisms worldwide, and its toxic effects on organisms have been confirmed. While, most studies are conducted in recent years, and the research of TCS is not deep or systematic enough. For example, the following questions are worth discussing: (1) Most studies focused on acute and subacute experiment, while chronic toxicity are poorly studied. In fact, people and animals are generally exposed to TCS substances via long-term low-dose exposure. The negative effects of this contact mode are quite different from that of acute mode. Therefore, chronic toxicity studies over six months should be strengthened to reflect its toxic effects better. (2) There have been many studies on TCS itself, while less attention is paid to its derivative or degradation products. TCS has been confirmed to undergo photolysis. When exposed to sunlight or ultraviolet radiation, about 12% of dissolved TCS can be converted to dioxins. In addition, TCS can react rapidly with manganese oxides such as δ-MnO$_2$ and MnOOH. TCS partially degrades or derives many toxic by-products, such as phenoxyphenol, chlorinated phenol, trihalomethane and dioxins. The toxicity, persistence and enrichment of degradation products of TCS may be higher than that of TCS. Therefore, attention should be paid to the mechanism, conditions and influencing factors of the transformation and degradation of TCS. (3) There have been more studies on lower organisms than on higher animals and human beings. Because TCS is used as a product of direct contact with human body, its threat to human health should be taken as an important concern. Such problem as the potential carcinogenic effect of TCS, which is widely concerned, has still no certain conclusion. (4) There are many observational studies on toxic effects of TCS but too few mechanism studies. The toxic mechanisms observed in many studied are still poorly understood. (5) There has been much detection in water but too less in other environmental medium like soil and air.

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