Antimicrobial agents in consumer products: Dark side of Triclosan

Microorganisms tend to degrade and decrease the shelf life of many consumer products such as hand lotions, mouthwashes, toothpaste etc. To increase the shelf life of consumer products, antimicrobial chemicals are frequently added to stop the growth of unwanted microorganisms. One such chemical is Triclosan (5-chloro-2-(2,4-dichloro phenoxy) phenol), which is frequently added to the consumer products available in India and worldwide such as soaps, toothpaste, deodorants etc. Now one can find triclosan even in the kitchenware and clothes, although, its initial use in the 1960s was restricted to medical care products. In very low amounts, triclosan may be well tolerated by humans, but given the widespread use of triclosan in personal care products, it is getting bioaccumulated in human tissues and organs (Geens et al., 2012).

An emerging public health concern points out that unregulated and extensive use of triclosan may lead to proliferation or emergence of harmful microorganisms that are resistant to clinically proven antibiotics (Carey and McNamara, 2015). Recent studies have found that environmentally relevant concentrations of triclosan can affect many developmental processes (Wirt et al., 2018). However, our understanding of the molecular targets and mechanisms of triclosan induced toxicity is very limited. In the absence of scientific mechanistic data, it is nearly impossible to propose a ban or restriction on the use of such chemicals. Over the last few years, we got interested in understanding the mechanisms of toxicity / adverse effects caused by chemicals such as triclosan. To understand the mechanisms of toxicity in our lab, we use an excellent, versatile vertebrate animal model, the Zebrafish. Zebrafish is a well-validated model for toxicity research, results from which have been reliably extrapolated to humans. Using a combination of molecular biology, biochemistry and behaviour analysis tools, we observed that triclosan even at sublethal concentrations can induce potent neurotoxic effects. We have recently published our results in Chemosphere (Pullaguri et al., 2020). In our study, prolonged exposure (up to 4 days) of 0.6 mg/L (50% Lethal concentration, LC50, 96 h) and 0.3 mg/L (<LC50, Sublethal) triclosan produced aberrations in motor neuron innervations (loss of structural integrity of motor neurons) in skeletal muscles and reduced touch-evoked escape response in zebrafish larvae. Touch-evoked escape response is a behavioural assay to assess locomotor behaviour. Locomotor behaviour in zebrafish is primarily regulated by the activity and integrity of motor neurons, therefore the results of this assay can be used to assess motor function. Along with other genes that are involved in synaptic transmission, the ache gene was downregulated upon exposure to triclosan.

The ache gene encodes for acetylcholinesterase enzyme that catalyzes the breakdown of the neurotransmitter acetylcholine at neuronal and neuromuscular junctions. Together with other results, our data support the hypothesis that even sublethal triclosan concentrations are potent enough to interfere with the motor neuron structure and function. The potential underlying mechanisms include down-regulation of genes involved in synaptic transmission and direct inhibition of acetylcholinesterase enzyme (see figure). Our study suggests caution in the use of triclosan based products and perhaps it's time that triclosan use in India is restricted or banned?

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(Arranged in the alphabetical order of author's name)

References:

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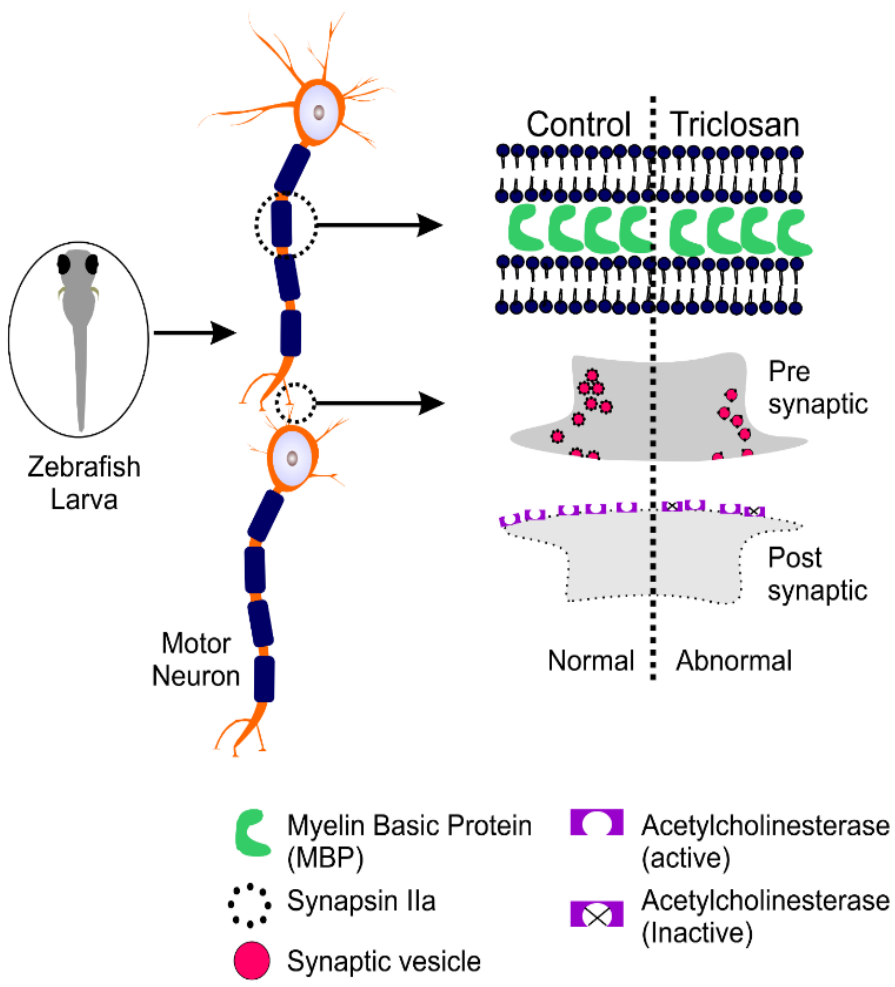

Figure 1: Potential mechanisms of triclosan induced neurotoxicity in developing zebrafish embryos. Downregulation of ache gene and inhibition of acetylcholinesterase enzyme activity may result in the abnormal cholinergic transmission caused by aberrant signaling mediated through acetylcholine receptors. Downregulation of synapsin IIa gene may result in the interference in vesicle trafficking at the presynaptic terminals. Overall, this aberrant neuronal signaling may have resulted in the abnormal motor function in zebrafish larvae. Figure reproduced from Pullaguri et al., 2020.

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