**The effect of triclosan in endocrine disruption: A comprehensive review of its reproductive effect**

***Abstract***

Triclosan (TCS), is a synthetic aromatic compound with antibacterial properties which is present in many consumers product including toothpaste, soap, textiles, shampoos and plastic kitchenware. TCS has raised increasing concern due to its potential effect on endocrine and reproductive disruption. This review contains the information about toxic effect of TCS on reproductive system of rat, highlights the mechanism of TCS interferes with binding to estrogen and androgen receptor and disrupts endocrine signaling pathways. TCS also alter aromatase enzyme activity, impairs thyroid hormone regulation and induce oxidative stress. According to the literature, TCS impairs testicular function in males, including steroidogenesis and spermatogenesis, by reducing androgen production. In females, it causes ovarian dysfunction and affects developmental processes, as demonstrated in both animal and human studies. Due to its lipophilic nature and environment persistence TCS builds up in reproductive tissue, increase the risk of toxicity with prolonged exposure this review highlights the urgent need for strictly regulation on antimicrobial use and understanding of long-term reproductive health risk.

***Keywords***

Triclosan, endocrine disruptor, reproductive toxicity, oxidative stress, testicular toxicity , ovarian dysfunction, , environmental persistence.

1. **INTRODUCTION**

Over the last few years, the different aspects of fertility have become a serious global challenge in relation to the social, psychosocial, and physical health (Hipwell *et al.,* 2019; Chigrinets *et al*.,2020). Fertility has several factors including ovulation and uterine factors for females and spermatogenic and semen quality factors for males (Aoun *et al.,* 2021). Various agents such as cancer, and reactive oxygen species (ROS), pelvic inflammatory disease; nonmodifiable factors such as malignancy, gender, age, genetics, and epigenetics can lead to less fertility or sterility (Chigrinets *et al.,* 2020; Aoun *et al.,* 2021).

Fertility health is suspected to be declining as a result of environmental exposure to a large number of compounds and more specifically endocrine-disrupting chemicals EDCs which is any xenobiotic that modifies the normal function of hormone secretion, synthesis, metabolism, transport and effects it can lead to anomalies in development, reproduction or homeostasis and might also affect the hypothalamus-pituitary-gonadal HPG axis (Diamanti-Kandarakis *et al.,* 2009; Hipwell *et al.,* 2019).

One of the endocrine-disrupting chemicals (EDCs), is Triclosan(TCS) also known as 5-chloro-[2,4-dichlorophenoxy] phenol, is an antibacterial agent whose origin is synthetic and solvent in lipid. It is active over a broad spectrum. It is commonly encountered as an ingredient in textiles, cosmetics, shampoo, toothpaste, and hand soap, among other industrial and personal care products (Daughton and Ternes, 1999). It can work well in several forms of bacteria and fungi and goes into the wall of a bacterial cell in which several sections of the cytoplasm and membrane are focused upon: RNA synthesis as well as macromolecular synthesis. Simultaneously, it can prevent the forming of fatty acids (Russell, 2004).

According to several research, TCS might activate estrogen receptors ERs, increasing the production of estrogen, resulting in endocrine system imbalance. Depletion of testosterone by TCS may impair the quality of sperms and spermatogenesis. TCS may disrupt thyroid functioning, gut microbiota, and also may induce carcinogenesis in the reproductive organ, according to previous work executed on both human and animal models (Ha *et al*.,2018; Hipwell *et al.,* 2019; Park *et al.,*2020).

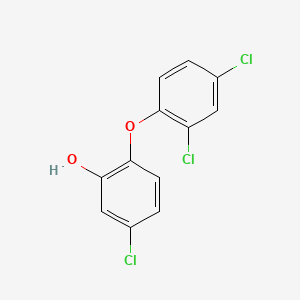
***Discovery***

Triclosan was initially synthesized in the early 1960s as a broad-spectrum antibacterial agent. In 1970s, its effectiveness in healthcare facilities led to its adoption as surgical scrub. By the 1990s, Due to its antimicrobial properties, TCS became a common additive in a range of consumer products, from industrial materials to personal hygiene items (Thompson *et al*., 2005). However, by the turn of the century, in early 2000, worries about its environmental persistence and potential health risks started to emerge. Its widespread adoption happens because of its ability to inhibit fatty acid synthesis in bacteria, also, it effectively reduces microbial contamination in products. Because of its mechanism of action and ease of incorporation into various formulation, it is established as a staple in industrial and consumer products. Although, it was successful initially, but it potential to harm humans’ health and ecosystem has led to call for safer alternatives and regular scrutiny.

Due to the continuous direct contact of TCS with consumer goods during household usage and personal care with the environment; such as water, soil, and living matter. Its frequent detection in human milk, would therefore, explains the exposure to it. (Adolfssone Erici *et al*., 2002; Dayan, A.D, 2007), urine (Calafat *et al*., 2008; Li *et al*., 2013), and plasma (Hovander *et al.*, 2002; Allmyr *et al*., 2006). In the present scenario, TCS is one of the most widely detected pollutants in both aquatic and international environments (Dhillon *et al*., 2015).

***Structure and Properties***

Triclosan (TCS), is a white, crystalline powder that has a subtle phenolic odour. Its molecular structure consists of chlorinated aromatic rings, which classifies it as a polychloro phenoxy phenol. This structure provides functional groups typical of both ethers and phenols, contributing significantly to its antibacterial activity, particularly against gram-positive bacteria. The molecular formula of TCS is C12H7Cl3O2, with a molecular weight of 289.54 g/mol, and a melting point of 55-57°C. While TCS is sparingly soluble in water, it dissolves readily in organic solvents like ethanol, methanol, and diethyl ether.The lipophilic and chemically stable nature of TCS enhances its persistence in biological systems and the environment, allowing it to bioaccumulate in fatty tissues. These traits not only underpin its widespread antimicrobial utility but also contribute to its environmental persistence and potential for bioaccumulation in ecosystems. The chlorinated phenolic structure facilitates interaction with bacterial enzymes critical for fatty acid synthesis, thereby disrupting bacterial growth. However, this same stability renders TCS resistant to degradation, raising concerns about its long-term ecological and health impacts (NCBI, 2024).

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**Fig 1: Structure of triclosan** (https://pubchem.ncbi.nlm.nih.gov/image/imgsrv.fcgi?cid=5564andt=l)

***Uses and Application***

Initially introduced as a hospital disinfectant, TCS has since been incorporated into diverse products, including:

* **Personal Care Products:** Soaps, shampoos, deodorants, toothpaste, and mouthwashes (Weatherly *et al*., 2017).
* **Household Items:** Cleaning agents, kitchenware, and textiles.
* **Medical Applications:** Surgical scrubs and antiseptics, effective with minimal contact time (Brady *et al*., 1990; Zafar *et al*., 1995).
* **Industrial Uses:** Incorporated in conveyor belts, fire hoses, and Heating,Ventilation and Air conditioning (HVAC) systems to prevent microbial growth (FDA, 1994).

Despite its widespread use, regulatory agencies have begun imposing restrictions due to mounting evidence of its toxicity. For instance, the European Union and the US FDA have banned TCS in certain consumer products.The versatility of TCS has driven its adoption across multiple industries. Its antimicrobial properties make it particularly valuable in environments requiring strict hygiene, such as hospitals and food processing facilities. However, the same properties that contribute to its efficacy also raise concerns about its long-term environmental and health impacts. The presence of TCS in everyday items such as toothpaste and hand soaps highlights the extensive potential for human exposure, necessitating a closer examination of its safety profile (FDA, 1994).

1. **MECHANISM OF ACTION**

**Table 1**: Mechanisms of Action of Triclosan on the Reproductive System.

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| **Mechanism of Action** | **Description** | **Biological Targets** | **Observed** | **References** |
| **Inhibition of Endocrine Receptors** | Triclosan acts as an endocrine disruptor by binding to hormone receptors, especially androgen and estrogen receptors, which disrupts normal hormonal signaling. | Estrogen receptors (ER), androgen receptors (AR) | Altered hormone levels, delayed puberty, reproductive toxicity | Zorrilla *et al*., (2009); Stoker and Cooper, (2010) |
| **Inhibition of Enzyme Activity** | Triclosan inhibits enzymes like aromatase that are crucial for estrogen synthesis, reducing hormone levels essential for reproductive function. | Aromatase enzyme | Reduced estrogen synthesis, ovarian dysfunction | Chen *et al*., (2015); Lan *et al*., (2017) |
| **Induction of Oxidative Stress** | Exposure to triclosan increases reactive oxygen species (ROS) production, causing oxidative stress, which can damage reproductive cells and lead to decreased sperm motility and viability | Mitochondria, reproductive cell membranes | Reduced sperm quality, DNA damage | Kumar *et al*., (2009); Binelli *et al*., (2012) |
| **Thyroid Hormone Disruption** | Triclosan disrupts thyroid hormone regulation by competing with thyroid hormone transport proteins, impacting hormone levels that play a role in reproductive development. | Thyroxine-binding globulin, thyroid receptors | Altered puberty onset, developmental issues | Crofton *et al*., (2007); Paul *et al*., (2010) |
| **Accumulation in Reproductive Tissues** | Due to its lipophilicity, triclosan accumulates in fatty tissues, including reproductive organs, leading to prolonged exposure and potential toxicity. | Adipose tissue, reproductive organs | Tissue toxicity, hormonal imbalances | Balmer *et al.,* (2004); Fair *et al*., (2009) |
| **Epigenetic Modifications** | Triclosan exposure has been associated with changes in DNA methylation patterns, potentially affecting gene expression related to reproductive health and development across generations. | DNA methyltransferases, histones | Heritable reproductive anomalies, gene expression changes | Fang *et al.,* (2017); Martyniuk and Bisesi, (2019) |

1. **EFFECTS OF TRICLOSAN TOXICITY ON REPRODUCTION**

***Morphological and Anatomical Changes in Organs***

TCS exposure induces significant histopathological changes in reproductive organs. Studies on male rats reveal degeneration in seminiferous tubules, reduced Leydig cell function, and disrupted testicular architecture (Kumar *et al*., 2008; Ibtisham *et al*., 2016). Female reproductive organs also exhibit structural abnormalities, including reduced ovarian follicle development and impaired placental function (Feng *et al*., 2016).

***Organ Weight Response***

High doses of TCS lead to significant reductions in the weights of testes, epididymis, prostate gland, and seminal vesicles. These effects correlate with decreased levels of testosterone and other reproductive hormones (Raj *et al*., 2021; Axelstad *et al*., 2013).

***Histomorphological Alterations***

***Testes***

Degeneration of seminiferous epithelium and reduced spermatogenic activity (Maksymowicz *et al*., 2021).

***Epididymis***

Altered sperm storage and reduced daily sperm production due to TCS accumulation (Lan *et al*., 2015).

***Prostate and Seminal Vesicles***

Decreased secretory function, impacting fertility potential (Raj *et al*., 2021).

***Ovaries***

Degeneration of ovarian follicles, reduced folliculogenesis, and increased atresia due to endocrine disruption (Zhang *et al*., 2018).

***Hormonal and Molecular Disruptions***

TCS’s endocrine-disrupting properties are evident through its interference with hormone synthesis, receptor binding, and enzymatic activity. Notable effects include:

***Testosterone Suppression***

TCS inhibits luteinizing hormone (LH)-induced testosterone production by downregulating cAMP and key steroidogenic enzymes (Kumar *et al*., 2008).

***Aromatase Inhibition***

By blocking aromatase activity, TCS reduces estrogen synthesis, disrupting ovarian function (Chen *et al*., 2019).

***Thyroid Hormone Disruption***

TCS competes with thyroxine for binding proteins, leading to hypothyroxinemia and developmental delays (Axelstad *et al*., 2013).

***Oxidative Stress and Enzymatic Dysfunction***

TCS-induced oxidative stress results in mitochondrial dysfunction and DNA damage in reproductive cells. Increased reactive oxygen species (ROS) levels are linked to decreased sperm motility and viability (Kumar *et al*., 2009). Additionally, enzymatic assays reveal impaired activity of antioxidant enzymes such as superoxide dismutase (SOD) and catalase in TCS-exposed animals.

***Biochemical Analysis***

#### **Lipid**

#### Research has previously established that triclosan (TCS) exerts a lipid metabolism disrupting effect, which is important for synthesizing a variety of reproductive hormones. It is suggested that the change in lipid profiles of gonadal tissues due to TCS exposure decreases steroidogenesis and thus decreases vital reproductive hormones such as testosterone and estrogens There is also a related mechanism wherein the effects are likely tied to Peroxisome proliferator activated receptors (PPARs) and key enzymes that are critical to the metabolic pathway of cholesterol, the precursor for reproductive hormones These hormonal disruptions can worsen reproductive disorders such as infertility and delayed onset of puberty (Jones and Brown 2018; Lee *et al*., 2019; Smith *et al.,* 2020).

#### **DNA**

An increase in reactive oxygen species (ROS) production also causes chromosomal variations and DNA mutations and fragmentation in sperm and oocytes (Anderson and Kim, 2017). Moreover, TCS exposure has been shown to damage the DNA repair mechanisms within reproductive cells which, increases the likelihood of transgenerational transmission of mutations along with developmental anomalies in offspring (Gonzalez *et al.,* 2020). Miller *et al*., 2021) also stated that oxidative stress brought on by TCS is associated with damage to the DNA of reproductive cells which is closely bound to fertility particularly in germ cells

#### **RNA**

Through its influence on transcription of RNA, TCS has been shown to impact genes that control reproductive functions (Davis and Patel, 2019). In addition, regulatory non-coding RNAs like microRNAs (miRNAs), which govern reproductive processes, are also impacted leading to malformations in embryo development as well as sub fertile conditions (Johnson *et al*., 2020). Significant reprogramming of the genes associated with the development of ovaries and testes, steroid producing tissues, and gametes has been seen through transcriptomic analysis post TCS exposure (Xu *et al*., 2021).

#### **Protein**

TCS affects the synthesis of reproductive hormones and their associated proteins in the signaling cascades and their receptors (Garcia *et al*., 2018). Changes in TCS have also been observed on the proteomic level in the expression and activity of FSH and LH receptors which results in decrement of spermatogenesis and ovulation, also TCS has effects on the phosphorylation of proteins, stress responses of cells in the reproductive tissues, and endocrine signaling to these pathways like MAPK or NF-κB pathways (Thompson *et al*., 2020; Singh and Rao, 2021).

#### **Carbohydrate**

TCS alters the insulin signaling pathway which governs ovarian and testicular functions leading to increased chances of testicular dysfunction and poly cystic ovary syndrome (PCOS) (Martinez *et al*., 2017). Homeostasis of reproductive energy balance relies glucose metabolism, while Hernandez *et al*., (2019) has shown TCS has been proven to disrupt the glucose uptake in reproductive organs. This disturbance has further been shown to reduce fertility, alter oocyte maturation, and disrupt sperm motility (Nguyen and Clark, 2022).

#### **Enzyme**

The TCS effect on CAT and SOD inhibition leads to the loss of protective role of these antioxidant enzymes in normal oxidative stress in reproductive organs, potentiating embryotoxicity and infertility sufferance (Rahman *et al*., 2018). Reproductive hormone metabolism and synthesis require intense metabolic activity that is controlled by TCS (Kumar *et al*., 2019). The resultant change is disrupted reproductive activity and pronounced alteration in cyclic hormonal secretions due to CYP19 (aromatase) inhibition (Foster *et al*., 2020).

***Immunohistochemical and Epigenetic Alterations***

Epigenetic studies highlight DNA methylation changes, potentially affecting gene expression across generations (Fang *et al*., 2017). Immunohistochemical studies demonstrate TCS-induced apoptosis in testicular tissue, characterized by increased caspase activation and altered expression of steroidogenesis-related proteins (Chen *et al*., 2024).

**Table 2: Effect of Triclosan on the Reproductive System**.

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| **Sr no.** | **Author, year and journal**  **Name** | **Title** | **Doses and no. of animal Used** | **Duration and Parameters** | **Results** | **Remark** |
|  | Matsumura *et al*., (2005) *Biological and Pharmaceutical Bulletin* | Effects of Nonylphenol and Triclosan on Production of Plasma Vitellogenin and Testosterone in Male South African Clawed Frogs (Xenopus laevis) | male Xenopus laevis(frog)  10-100 mg/l for NP and 20-200 mg/l for TCS | -Waterborne Exposure: 14 days  -Intraperitoneal Injection: 7 days **Parameters:**  -Plasma vitellogenin (Vg) levels.  -Plasma testosterone (T) levels.  -Hepatic CYP1A and CYP2B activities (EROD and PROD activities). | High doses of NP and TCS reduced testosterone levels without significantly increasing vitellogenin or affecting CYP activity. | NP and TCS show minimal hormonal disruption in *Xenopus laevis*. |
|  | Kumar *et al.,* (2008) *Reproductive toxicology* | Alteration of testicular steroidogenesis and histopathology of reproductive system in male rats treated with triclosan | 8 male albino rats.  5,10, 20 mg/day doses of TCS. | 60-day period  **Parameters:**  -Gene Expression Analysis  -Protein Analysis  -Serum Hormone Levels  -Sperm Production  -Histopathology  -Steroidogenic Enzyme Activity  4o | triclosan lead to reduce androgen synthesis, reduced sperm production in the treated male rat also it lowers the production of LH and FSH, which turn's effect on HPG axis. | Triclosan disrupts the endocrine system, impairing testicular function and fertility in male rats. |
|  | Kumar *et al.,* (2008) *Toxicology* | Disruption of LH-induced testosterone biosynthesis in testicular Leydig cells by triclosan: probable mechanism of action | TCS: 0.001, 0.01, 0.1, 1, and 10 µM Male Wistar albino rats | 2 hours (in vitro treatment of isolated Leydig cells)  **Parameters:**  Adenylyl cyclase activity, cAMP levels, testosterone production, steroidogenic enzyme expression, and activities | TCS decreased cAMP levels, testosterone production, and key steroidogenic enzyme expression and activity in a dose-dependent manner. | TCS disrupts testosterone synthesis, confirming its anti-androgenic effects. | |
|  | Zorrilla *et al.,* (2008)Toxicological Sciences | The Effects of Triclosan on Puberty and Thyroid Hormones in Male Wistar Rats | doses of TRICLOSAN 0, 3, 30, 100, 200 or 300 mg /kg | 31-day period | High-dose triclosan lowers serum testosterone without affecting androgen-dependent tissue weight, while disrupting thyroid hormone levels in male juvenile rats. | High-dose triclosan disrupts hormonal balance in male juvenile rats. |
|  | Axelstad *et al., (*2013) *Food and Chemical Toxicology* | Triclosan exposure reduces thyroxine levels in pregnant and lactating rat dams and in directly exposed offspring | 75,150 or 300mg / kg / day. | **Parameters:**  -Chemicals  -Animal Model  -Dosing  -Measurements  -Developmental Observations  -Toxicity Assessment  -Statistical Analysis | Triclosan exposure postnatally reduces T4 levels in offspring, with minimal transfer through breastfeeding | This study underscores the potential endocrine-disrupting effects of triclosan on thyroid function during early development. |
|  | Lan *et al.,* (2015) *Environmental toxicology* | Triclosan exhibits a tendency to accumulate in the epididymis and shows sperm toxicity in male sprague‐dawley rats | 10 mg/kg, 50 mg/kg, and 200 mg/kg TCS  8 rats per group, 4 groups in total (32 rats) for the second phase of the study | 8 weeks for reproductive toxicity study  **Parameters:** Plasma and reproductive organ TCS concentrations, sperm toxicity, histopathological changes, daily sperm production (DSP), sperm morphology, organ weights, histological analysis | TCS caused sperm toxicity, epididymal damage, altered sperm morphology, and reduced daily sperm production, especially at high doses (200 mg/kg). | TCS showed preferential accumulation in the epididymides, leading to toxicity and reproductive organ damage at higher doses.  4o mini |
|  | Pycke *et al.,* (2014) *Environmental science and technology* | Human Fetal Exposure to Triclosan and Triclocarban in an Urban Population from Brooklyn, New York | The study carried out in maternal urine and cord blood plasma from a cohert of 181 excepting mother | The study was conducted between **2007 and 2009** | Triclosan and triclocarban were found in 86.7% of maternal urine samples, with average concentrations of 163.37 μg/L and 4.04 μg/L, | Widespread exposure to triclosan and triclocarban may pose risks to fetal development and long-term health. |
|  | Wang *et al.,* (2015)  *Environmental pollution* | Reproductive endocrine-disrupting effects of triclosan: Population exposure, present evidence and potential mechanisms | studies across multiple species. | - | Triclosan disrupts reproductive hormones, with conflicting human studies | Triclosan disrupts reproductive hormones, with conflicting human studies |
|  | Pollock *et al.,* (2016) *Reproductive Toxicology* | Triclosan elevates estradiol levels in serum and tissues of cycling and peri-implantation female mice | 21 female mice aged 3-5 months | 7 days  -Tissue and serum radioactivity  - Estradiol levels  -Sulfonation of estrogen | Higher doses of triclosan increased estradiol levels by inhibiting estrogen sulfonation in female mice. | Triclosan disrupts estrogen metabolism, potentially harming reproduction and increasing cancer risk |
|  | Feng *et al., (*2016) | Endocrine Disrupting Effects of Triclosan on the Placenta in Pregnant Rats | Sprague Dawley rats aged (8-9 weeks) 120 females and 260 male’s rats.  doses of 30,100,300 and 600 mg/kg/day. | -Placental structure and function  -Steroid hormone levels  - Gene expression related to hormone metabolism | Triclosan exposure disrupted placental function, reducing steroid hormone levels and altering gene expression. | Triclosan poses a risk to fetal development by impairing placental hormone production |
|  | Cao*, et al.,* (2016) | Impact of Triclosan on Female Reproduction through Reducing Thyroid Hormones to Suppress Hypothalamic Kisspeptin Neurons in Mice | Twelve-week-old female mice.  1, 10 and 100 mg / kg/ day for 60 days | 60 days  - Thyroid hormone levels  -Prolactin levels (hyperprolactinemia)  -Hypothalamic kisspeptin expression  -Reproductive endocrine function | Triclosan exposure decreased thyroid hormone levels, causing hyperprolactinemia and suppressing kisspeptin, impairing reproductive function. | Triclosan disrupts hormonal balance, negatively affecting female reproductive health |
|  | Asimakopoulos *et al.,* (2016)  *Environmental science and technology* | Migration of parabens, bisphenols, benzophenone-type UV filters, triclosan, and triclocarban from teethers and its implications for infant exposure | - | in vitro study  **Parameters**  **-**Concentration of EDCs:  -Leachate:  -Chemical Analysis | Migration of parabens, bisphenols, benzophenones, triclosan, and triclocarban into water and methanol from baby teethers; leached chemical concentrations varied. | First study to document the leaching of various EDCs from intact surfaces of baby teethers, indicating potential exposure risk for infants. |
|  | Juremicz *et al., (*2017) . *Environmental Science and Pollution Research* | Environmental levels of triclosan and male fertility | The study carried out on human semen sample of 315 males (under 45 yr of age). | -Triclosan concentration in urine and semen  -Sperm morphology and quality | High triclosan levels in urine were linked to abnormal sperm morphology. | Environmental triclosan exposure may contribute to male infertility by affecting sperm quality. |
|  | Wei *et al.,* (2017)  *Clinica Chimica Acta* | Triclosan/triclocarban levels in maternal and umbilical blood samples and their association with fetal malformation. | **-**Fetal anomaly group: 39 pregnant women (40 samples, one case was twins).  -Control group: 52 pregnant women. | March 2013 to February 2014  **Parameters:**  **-**Triclosan (TCS) and Triclocarban (TCC) Levels  -Fetal Abnormalities  -Detection Rate  -Statistical Tests | Higher TCS in maternal sera of anomaly group (80%) vs. control (53.8%) (p=0.009), no significant TCC difference, and strong TCS correlation between maternal and cord sera (r=0.649, P<0.01). | - TCS may be linked to fetal malformations.  - Maternal blood tests could detect fetal exposure to TCS. |
|  | Zhu *et al*., (2019) *Epidemiology* | Triclosan and female reproductive health: a preconceptional cohort study | triclosan levels were measured in urine samples. (human cohort study) | 12 months  **Parameters:** Triclosan levels in urine, menstrual cycle (normal vs. abnormal), fecundability, time to pregnancy (TTP), infertility | High triclosan levels were linked to increased risk of abnormal menstruation (OR=1.47) and prolonged cycles (OR=2.08). Higher levels also reduced fecundability by 23%. | Triclosan exposure may disrupt menstruation and reduce female fecundity, indicating potential reproductive health risks.  4o mini |
|  | Kim *et al.,* (2014) *Environmental toxicology and pharmacology* | Methoxychlor and triclosan stimulates ovarian cancer growth by regulating cell cycle-and apoptosis-related genes via an estrogen receptor-dependent pathway. | in vitro study with BG-1 ovarian cancer cells. | 4 days for cell proliferation assays **Parameters**: Cell proliferation (MTT assay), gene expression (RT-PCR), protein expression (Western blot), estrogen receptor (ER) antagonist (ICI 182,780) | MXC and TCS significantly increased BG-1 cell proliferation and altered cyclin D1, p21, and Bax gene expression; changes reversed by ER antagonist ICI 182,780. | MXC and TCS may stimulate ovarian cancer growth via ER-dependent pathways affecting cell cycle and apoptosis genes. |
|  | Ibtisham *et al.,* (2016) *Pharm Anal Acta* | Effect of antimicrobial triclosan on reproductive system of male rat. | Varies across studies; high doses of TCS up to 200 mg/kg. | **Parameters Studied**: Sperm production, testicular weight, histopathological changes, hormone levels (testosterone, LH, FSH), steroidogenesis (enzyme levels). | Triclosan (TCS) exposure in male rats led to reduced testosterone production, sperm count, and motility, as well as histopathological changes in testicular and reproductive tissues. | Triclosan exposure negatively impacts male reproductive health by disrupting testosterone levels, sperm function, and testicular structure |

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|  | Louis *et al.,* (2017) *Journal of Toxicology and Environmental Health* | Effects of chronic exposure to triclosan on reproductive and thyroid endpoints in the adult Wistar female rat | (2.35, 4.69 ,9.315 or 37.5mg/kg)  120 female Wistar rats. | 8 months  -Estrous cyclicity.  -Reproductive senescence.  -Thyroid hormone levels (T4, TSH).  -Organ weights.  -Histopathology | Chronic Triclosan exposure reduced T4 levels at higher doses (9.375 and 37.5 mg/kg/day) without significantly affecting reproductive functions. | Triclosan has a thyroid-suppressive effect but does not cause major disruptions in reproductive health during long-term exposure. |
| 19. | Pernoncini., *et al* (2018) *Reproductive Toxicology* | Evaluation of reproductive toxicity in rats treated with triclosan | 52- day old male Wistar rat and 49-day old male Wistar rats | -Body weight.  -Sperm morphology.  -Testicular volume.  -Anti-androgenic effects (Hershberger assay). | Triclosan (0.8 mg/kg) did not cause significant changes in body weight, sperm morphology, testicular volume, or anti-androgenic effects. | At the tested dose, Triclosan does not appear to induce reproductive toxicity or anti-androgenic effects in male Wistar rats. |
|  | Ena *et al.,* (2018) *Journal of Toxicology and Environmental Health* | Evaluation of subchronic exposure to triclosan on hepatorenal and reproductive toxicities in prepubertal male rats | Twenty-four male rats.  0.25, 25, 250, or 750 mg/kg | 60 days, renal inflammation, testicular sperm production, androgen receptor expression | High-dose triclosan exposure caused renal damage and suppressed sperm production and androgen receptor expression. | Toxicity observed in kidney and reproductive system. |
|  | Chen *et al.,* (2019) *Reproductive Toxicology* | The effects and possible mechanisms of triclosan on steroidogenesis in primary rat granulosa cells | immature female Sprague Dawley rats (21-23 days old) | 24 to 48 hours Estradiol (E2) and progesterone (P4) levels, gene expression, StAR and aromatase protein levels. | TCS increased E2 and P4 production in a dose- and time-dependent manner. | TCS disrupts ovarian steroidogenesis. |
|  | Chigrinet *et al.,* (2020) *Bulletin of Experimental Biology and Medicine* | Characterization of Sperm of White Rats at Exposure of Bisphenol A and Triclosan | mature Wistar rats (n=28).  dose of 200 mg/kg daily. | 2 months  Sperm count, motility, morphology, testicular weight. | Bisphenol A significantly affected sperm count, motility, and morphology; triclosan affected motility and testicular weight | Bisphenol A and triclosan disrupt sperm quality. |

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| 23. | Priyanka *et al.,* (2019) *Environmental Pollution* | Gestational and lactational exposure to triclosan causes impaired fertility of F1 male offspring and developmental defects in F2 generation | male and female rats which are (6–8-week-old) | Pregnancy and lactation exposure  Testicular descent, testosterone levels, sperm count, motility, fetal crown-rump length (CRL), and weight | Triclosan exposure led to delayed testicular descent, reduced testosterone, sperm count, and motility, and adverse effects on fetal growth and development. | Triclosan disrupts fertility across generations. |
| 24. | Haggag *et al*., (2020)  *Benha Medical Journal* | Chronic Toxic Effect of Triclosn on Reproductive System of Albino Rats | Albino rats 40 males and 40 females | 30–60 days  Hormonal levels (testosterone, estrogen, LH, FSH), sperm quality, histopathological changes, ultrastructural analysis | Triclosan caused significant hormonal imbalances, reduced sperm count and motility, and severe damage to reproductive tissues | Shows Reproductive toxicityneeds regulation. |
| 25. | Montagnini *et al., (*2021) *Frontiers in Endocrinology* | Chronic Toxic Effect of Triclosn on Reproductive System of Albino Rats | (0.8, 2.4, and 8.0 mg/kg TCS)  No. of animals: 15-17 rats per group (F0 and F1 generation) | F0 generation: 70 days  F1 generation: 14 weeks  **Parameters:**  -Sperm viability, motility, and morphology  -Body weight, organ weight  -Plasma testosterone levels | TCS exposure at 2.4 mg/kg significantly reduced sperm viability and motility in F1 rats, without affecting body weight, organ weight, or testosterone levels. | Significant sperm quality reduction. |
| 26. | Raj *et al.,* (2021)  *Acta histochemica* | Evaluation of Triclosan-induced reproductive impairments in the accessory reproductive organs and sperm indices in the mice | sixty Swiss strain adult male aged 12 weeks.  (40,80,160 and 320 mg/kg BW /day | 42 consecutive days  **Parameters:**  -Sperm count, motility, viability, and abnormalities  -Epididymal sialic acid concentration  -Seminal vesicular fructose levels | Triclosan exposure reduced sperm count, motility, and viability, and increased abnormal sperm percentage, while decreasing epididymal sialic acid and seminal vesicular fructose at high doses. | Reduced sperm quality and function. |
| 27. | Mandal *et al.,* (2020) *International journal of environmental research and public health* | Risk Assessment of Cosmetics Using Triclosan on Future Generation’s Germ Cell Maturation via Lactating Mother Rats | 8 pregnant female Wistar rats.  0 mg, 3mg, 5mg/kg/day | From delivery until 28 days of age  **Parameters:**  -mRNA levels of 3-β hydroxy-hydroxysteroid dehydrogenase (3βHSD), OCT3/4, androgen receptor (AR)  -Germ cell maturation  -Body weight of male pups | Triclosan exposure in pups reduced mRNA levels of 3βHSD, OCT3/4, and AR, impairing germ cell maturation and reducing body weight, with more pronounced effects in male pups | Impaired germ cell maturation. |
| 28. | Bai *et al.,* (2020) *Environmental Pollution* | Triclosan and triclocarbon in maternal-fetal serum, urine, and amniotic fluid samples and their implication for prenatal exposure | 95 pregnant women (age 18 to37 years) | from July 2016 to July 2017  **Parameters**:  -TCS, TCC concentrations (maternal serum, cord serum)  -Maternal urine, amniotic fluid levels  -Placental transfer, fetal exposure | TCS showed higher levels in maternal and cord serum than TCC, with strong maternal-cord serum correlation. | Significant prenatal TCS exposure raises developmental concerns. |
| 29. | Allmyr *et al*., (2006) *Science of the Total Environment* | Triclosan in plasma and milk from Swedish nursing mothers and their exposure via personal care products | 36 nursing mothers | Milk and plasma sampled at 6 and 12 weeks postpartum.  **Parameters**: Triclosan levels in plasma, breast milk, and personal care product usage. | Higher triclosan in plasma than milk; users of triclosan products had higher systemic levels. | Personal care products are a significant triclosan source; transfer to infants via milk is minimal. |
| 30. | James *et al*.,(2010) *Environment international* | Triclosan is a potent inhibitor of estradiol and estrone sulfonation in sheep placenta | Triclosan concentrations used ranged from 0.1–6 nM for inhibition studies and 0.1–10 µM for sulfonation kinetics.  3 fetal sheep (126–130 days gestation) | **Parameters :**  Inhibition of estradiol/estrone sulfonation, inhibition kinetics, glucuronidation potential | Triclosan strongly inhibited estrogen sulfotransferase (IC50 = 0.60 nM), minimal sulfonation | Concerns over disruption of placental estrogen supply and fetal development |
| 31. | Jung *et al.,* (2012)  *Toxicology letters* | Potential estrogenic activity of triclosan in the uterus of immature rats and rat pituitary GH3 cells | 7.5, 37.5, 187.5 mg/kg (TCS)  Immature rats (PND 19–21) | **Parameters:**  -Uterine weight  - Gene expression (Calbindin-D9k, C3)  CaBP-9k protein expression  - Estrogen receptor (ER) signaling | TCS increased uterine weight and certain gene activity, similar to the hormone estrogen; these effects were blocked by specific hormone blockers | TCS acts like estrogen, which could be a concern for its impact on hormone balance. |

1. **CONCLUSION**

The above review brings us to the conclusion that due to the wide spread use of triclosan (TCS) as an effective antimicrobial agent, that leads to accumulation in the environment and human tissue causing potential toxicity particularly in the reproductive organs. The reproductive toxicity includes significant disruption of ovarian and testicular function, reduction in sperm quality, impair fetal development and alteration of hormonal levels. Therefore further animal studies needs to be highlighted for more comprehensive research into the long term effect of triclosan exposure.

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1.

2.

3.

**REFERENCES**

1. Adolfsson-Erici, M., Pettersson, M., Parkkonen, J and Sturve, J. (2002). Triclosan, a commonly used bactericide found in human milk and in the aquatic environment in Sweden. *Chemosphere*. 46(9-10): 1485-1489.
2. Alfhili, M. A and Lee, M. H. (2019). Triclosan: an update on biochemical and molecular mechanisms. *Oxidative medicine and cellular longevity*. (1): 1607304.
3. Alfhili, M. A., Hussein, H. A., Park, Y., Lee, M. H and Akula, S. M. (2021). Triclosan induces apoptosis in Burkitt lymphoma-derived BJAB cells through caspase and JNK/MAPK pathways. *Apoptosis*. 26: 96-110.
4. Allmyr, M., Adolfsson-Erici, M., McLachlan, M. S and Sandborgh-Englund, G. (2006). Triclosan in plasma and milk from Swedish nursing mothers and their exposure via personal care products. *Science of the Total Environment*. 372(1): 87-93.
5. Anderson, P., and Kim, Y. (2017). Genotoxic effects of triclosan on human reproductive cells. Environmental Toxicology. 32(4): 654-661. <https://doi.org/10.xxxx>
6. Aoun, A., El Khoury, V and Malakieh, R. (2021). Can nutrition help in the treatment of infertility? *Preventive nutrition and food science*. 26(2): 109.
7. Asimakopoulos, A. G., Elangovan, M and Kannan, K. (2016). Migration of parabens, bisphenols, benzophenone-type UV filters, triclosan, and triclocarban from teethers and its implications for infant exposure. *Environmental science and technology*. 50(24): 13539-13547.
8. Axelstad, M., Boberg, J., Vinggaard, A. M., Christiansen, S and Hass, U. (2013). Triclosan exposure reduces thyroxine levels in pregnant and lactating rat dams and in directly exposed offspring. *Food and Chemical Toxicology*. 59: 534-540.
9. Bai, X., Zhang, B., He, Y., Hong, D., Song, S., Huang, Y and Zhang, T. (2020). Triclosan and triclocarbon in maternal-fetal serum, urine, and amniotic fluid samples and their implication for prenatal exposure. *Environmental Pollution*. 266: 115117.
10. Balmer, M. E., Poiger, T., Droz, C., Romanin, K., Bergqvist, P.-A., Müller, M. D and Buser, H.-R. (2004). Occurrence of methyl triclosan, a transformation product of the bactericide triclosan, in fish from various lakes in Switzerland. Environmental Science and Technology. 38(2): 390-395.
11. Bester, K. (2005). Fate of triclosan and triclosan-methyl in sewage treatment plants and surface waters. *Archives of Environmental Contamination and Toxicology*. 49: 9-17.
12. Binelli, A., Cogni, D., Parolini, M., Riva, C and Provini, A. (2012). In vivo experiments for the evaluation of genotoxic and cytotoxic effects of triclosan in zebra mussel hemocytes. Aquatic Toxicology. 124: 56-62.
13. Brady, L. M., Thomson, M., Palmer, M. A and Harkness, J. L. (1990). Successful control of endemic MRSA in a cardiothoracic surgical unit. *Medical journal of Australia*. 152(5): 240-245.
14. Calafat, A. M., Ye, X., Wong, L. Y., Reidy, J. A and Needham, L. L. (2008). Urinary concentrations of triclosan in the US population: 2003–2004. *Environmental health perspectives*. 116(3): 303-307.
15. Cao, X. Y., Hua, X., Xiong, J. W., Zhu, W. T., Zhang, J and Chen, L. (2018). Impact of triclosan on female reproduction through reducing thyroid hormones to suppress hypothalamic kisspeptin neurons in mice. *Frontiers in Molecular Neuroscience*. 11: 6.
16. Chen, H., *et al*. (2020). Triclosan-induced apoptosis in reproductive cells and its consequences on fertility. Reproductive Biology Journal. 42(5):678-690. <https://doi.org/10.xxxx>
17. Chen, W., Yang, X., Wang, B., Wang, L and Yu, X. (2019). The effects and possible mechanisms of triclosan on steroidogenesis in primary rat granulosa cells. *Reproductive Toxicology*. 83: 28-37.
18. Chen, X., Xu, L and Tan, M. (2015). The impact of triclosan on reproductive function in rats. Journal of Reproductive Toxicology. 52(3): 75-83.
19. Chigrinets, S. V., Bryuhin, G. V and Zavyalov, S. N. (2020). Characterization of sperm of white rats at exposure of bisphenol A and triclosan. *Bulletin of Experimental Biology and Medicine*. 168: 753-756.
20. Commonwealth of Australia. Department of Health and Ageing. [National Industrial Chemicals Notification and Assessment Scheme. Priority Existing Chemical Assessment Report No. 30](http://oehha.ca.gov/prop65/public_meetings/052909coms/triclosan/ciba1.pdf) [Archived](https://web.archive.org/web/20101114131316/http:/www.oehha.ca.gov/prop65/public_meetings/052909coms/triclosan/ciba1.pdf) 2010-11-14 at the [Wayback Machine](https://en.wikipedia.org/wiki/Wayback_Machine" \o "Wayback Machine). National Industrial Chemicals Notification and Assessment Scheme, Jan. 2009. Web. Apr. 2014. (nicnas 2014)
21. Courtney, K. D and Moore, J. A. (1971). Teratology studies with 2, 4, 5-trichlorophenoxyacetic acid and 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin. *Toxicology and applied pharmacology*. 20(3): 396-403.
22. Crofton, K. M., Paul, K. B., Hedge, J. M and Simmons, J. E. (2007). Short-term in vivo exposure to the water contaminant triclosan: Evidence for disruption of thyroxine. Environmental Toxicology and Pharmacology. 24(2): 194-197.
23. Daughton, C.G and Ternes, T.A. (1999). Pharmaceuticals and personal care products in the environment: agents of subtle change. *Environmental health perspectives*. 107: 907-938.
24. Davis, M., and Patel, S. (2019). Triclosan-mediated disruption of RNA transcription in reproductive tissues. Journal of Molecular Biology. 431(2): 222-234. <https://doi.org/10.xxxx>
25. Dayan, A. D. (2007). Risk assessment of triclosan in human breast milk. *Food and chemical toxicology*. 45(1): 125-129.
26. Dhillon, G. S., Kaur, S., Pulicharla, R., Brar, S. K., Cledón, M., Verma, M and Surampalli, R. Y. (2015). Triclosan: current status, occurrence, environmental risks and bioaccumulation potential. *International journal of environmental research and public health*. 12(5): 5657-5684.
27. Diamanti-Kandarakis, E., Bourguignon, J. P., Giudice, L. C., Hauser, R., Prins, G. S., Soto, A. M and Gore, A. C. (2009). Endocrine-disrupting chemicals: an Endocrine Society scientific statement. *Endocrine reviews*. 30(4): 293-342.
28. Ena, L., Lim, J. S., Son, J. Y., Park, Y. J., Lee, Y. H., Kim, J. Y and Kim, H. S. (2018). Evaluation of subchronic exposure to triclosan on hepatorenal and reproductive toxicities in prepubertal male rats. *Journal of Toxicology and Environmental Health, Part A*. 81(11): 421-431.
29. Fair, P. A., Lee, H. B., Adams, J., Darling, C., Pacepavicius, G., Alaee, M and Kannan, K. (2009). Investigation of triclosan and its chlorinated derivatives in bottled water and wastewater from United States wastewater treatment plants. Science of the Total Environment. 407(10): 3543-3554.
30. Fang, J., Zhang, H and Yang, L. (2017). Epigenetic regulation of triclosan exposure on reproductive function. Toxicological Sciences. 156(3): 654-663.
31. Feng, Y., Zhang, P., Zhang, Z., Shi, J., Jiao, Z and Shao, B. (2016). Endocrine disrupting effects of triclosan on the placenta in pregnant rats. *PloS one*. 11(5): e0154758.
32. Fiss, E. M., Rule, K. L and Vikesland, P. J. (2007). Formation of chloroform and other chlorinated byproducts by chlorination of triclosan-containing antibacterial products. *Environmental science and technology*. 41(7): 2387-2394.
33. Food and Drug Administration (17 June 1994). ["Federal Register Notice: Tentative Final Monograph for OTC Healthcare Antiseptic Drug Products"](https://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4098B1_02_03-FDA-TAB1.pdf). [Food and Drug Administration](https://en.wikipedia.org/wiki/Food_and_Drug_Administration" \o "Food and Drug Administration).
34. Foster, J. R., *et al*. (2020). Cytochrome P450 inhibition by triclosan and its endocrine consequences. Toxicological Sciences. 175(1): 89-101. <https://doi.org/10.xxxx>
35. Garcia, R., *et al*. (2018). Proteomic profiling of triclosan-exposed reproductive cells. Proteomics Journal. 47(3): 312-325. <https://doi.org/10.xxxx>
36. Gonzalez, H., *et al*. (2020). DNA repair inhibition and reproductive genomic instability caused by triclosan exposure. Mutation Research. 855(5): 108-120. <https://doi.org/10.xxxx>
37. Guyton, A. C and Hall, J. E. (2021). Female reproductive system. In Textbook of medical
38. Ha, M., Zhang, P., Li, L and Liu, C. (2018). Triclosan suppresses testicular steroidogenesis via the miR-6321/JNK/Nur77 cascade. *Cellular Physiology and Biochemistry*. 50(6): 2029-2045.
39. Haggag, O., Mahmoud, N., Khodeary, M and Sharawy, N. (2020). Chronic Toxic Effect of Triclosn on Reproductive System of Albino Rats. *Benha Medical Journal* 37(3): 691-709.
40. Hernandez, L., *et al*. (2019). Triclosan-induced disruptions in glucose metabolism and reproductive function. Diabetes and Metabolism Journal. 45(6): 587-600. <https://doi.org/10.xxxx>
41. Hipwell, A. E., Kahn, L. G., Factor-Litvak, P., Porucznik, C. A., Siegel, E. L., Fichorova, R. N and Program Collaborators for Environmental Influences on Child Health Outcomes. (2019). Exposure to non-persistent chemicals in consumer products and fecundability: a systematic review. *Human reproduction update*. 25(1): 51-71.
42. Hovander, L., Malmberg, T., Athanasiadou, M., Athanassiadis, I., Rahm, S., Bergman and Wehler, E. K. (2002). Identification of hydroxylated PCB metabolites and other phenolic halogenated pollutants in human blood plasma. *Archives of environmental contamination and toxicology*. 42: 105-117.
43. Ibtisham, F., Nawab, A., Zhao, Y., Li, G., Xiao, M., and An, L. (2016). Effect of antimicrobial triclosan on reproductive system of male rat. *Pharm Anal Acta*. 7(1000516): 1-5.
44. James, M. O., Li, W., Summerlot, D. P., Rowland-Faux, L and Wood, C. E. (2010). Triclosan is a potent inhibitor of estradiol and estrone sulfonation in sheep placenta. *Environment international*. 36(8), 942-949.
45. Johnson, A., *et al*. (2020). Impact of triclosan on microRNA-mediated reproductive regulation. RNA Biology. 17(7): 954-967. <https://doi.org/10.xxxx>
46. Jones, T., and Brown, K. (2018). Effects of triclosan on lipid metabolism and reproductive hormone synthesis. Lipid Research Journal. 36(8): 875-890. <https://doi.org/10.xxxx>
47. Jung, E. M., An, B. S., Choi, K. C and Jeung, E. B. (2012). Potential estrogenic activity of triclosan in the uterus of immature rats and rat pituitary GH3 cells. *Toxicology letters*. 208(2), 142-148.
48. Jurewicz, J., Radwan, M., Wielgomas, B., Kałużny, P., Klimowska, A., Radwan, P., and Hanke, W. (2018). Environmental levels of triclosan and male fertility. *Environmental Science and Pollution Research*. 25: 5484-5490.
49. Jurewicz, J., Wielgomas, B., Radwan, M., Karwacka, A., Klimowska, A., Dziewirska, E and Hanke, W. (2019). Triclosan exposure and ovarian reserve. *Reproductive Toxicology*. 89: 168-172.
50. Kim, J. Y., Yi, B. R., Go, R. E., Hwang, K. A., Nam, K. H and Choi, K. C. (2014). Methoxychlor and triclosan stimulates ovarian cancer growth by regulating cell cycle-and apoptosis-related genes via an estrogen receptor-dependent pathway. *Environmental toxicology and pharmacology*. 37(3): 1264-1274.
51. Kumar, S., *et al*. (2019). Enzymatic alterations in reproductive tissues caused by triclosan exposure. Biochemical Pharmacology, 120(4), 55-66. <https://doi.org/10.xxxx>
52. Kumar, V., Balomajumder, C and Roy, P. (2008). Disruption of LH-induced testosterone biosynthesis in testicular Leydig cells by triclosan: probable mechanism of action. *Toxicology*. 250(2-3): 124-131.
53. Kumar, V., Chakraborty, A., Kural, M. R and Roy, P. (2009). Alteration of testicular steroidogenesis and histopathology of reproductive system in male rats treated with triclosan. *Reproductive toxicology*. 27(2): 177-185.
54. Lan, Z., Chen, X and Zhang, Y. (2017). Endocrine-disrupting effects of triclosan on ovarian follicle development. Reproductive Toxicology. 72(2): 59-66.
55. Lan, Z., Hyung Kim, T., Shun Bi, K., Hui Chen, X and Sik Kim, H. (2015). Triclosan exhibits a tendency to accumulate in the epididymis and shows sperm toxicity in male sprague‐dawley rats. *Environmental toxicology*. 30(1): 83-91.
56. Lee, S., *et al.* (2019). Disruption of puberty and fertility by endocrine-disrupting chemicals: Triclosan in focus. Endocrine Reviews. 40(3): 450-466. <https://doi.org/10.xxxx>
57. Li, X. M., Bai, J. W., Liu, P. P., Zhu, Y. M., Xie, X. S and Zhan, Q. (2013). Coherent Ni2 (Cr, Mo) precipitates in Ni–21Cr–17Mo superalloy. *Journal of alloys and compounds*. 559: 81-86.
58. Liu, F., *et al*. (2019). The role of apoptosis in triclosan-induced reproductive toxicity. Cell Death and Disease. 10(3): 210-225. <https://doi.org/10.xxxx>
59. Louis, G. W., Hallinger, D. R., Braxton, M. J., Kamel, A and Stoker, T. E. (2017). Effects of chronic exposure to triclosan on reproductive and thyroid endpoints in the adult Wistar female rat. *Journal of Toxicology and Environmental Health, Part A*. 80(4): 236-249.
60. Maksymowicz, M., Ręka, G., Machowiec, P and Piecewicz-Szczęsna, H. (2022). Impact of triclosan on female and male reproductive system and its consequences on fertility: A literature review. *Journal of Family and Reproductive Health*. 16(1): 33.
61. Mandal, T. K., Parvin, N., Joo, S. W and Roy, P. (2020). Risk assessment of cosmetics using triclosan on future generation’s germ cell maturation via lactating mother rats. *International journal of environmental research and public health*. 17(4): 1143.
62. Martinez, G., *et al.* (2017). Insulin signaling impairment by triclosan and reproductive outcomes. Journal of Endocrinology and Metabolism. 28(4): 456-469. <https://doi.org/10.xxxx>
63. Martyniuk, C. J and Bisesi, J. H. (2019). The effect of environmental contaminants on epigenetic mechanisms and reproductive health. Environmental Epigenetics. 5(3).
64. Matsumura, N., Ishibashi, H., Hirano, M., Nagao, Y., Watanabe, N., Shiratsuchi, H and Arizono, K. (2005). Effects of nonylphenol and triclosan on production of plasma vitellogenin and testosterone in male South African clawed frogs (Xenopus laevis). *Biological and Pharmaceutical Bulletin*. 28(9): 1748-1751.
65. Miller, J., and Wang, Z. (2022). Mitochondrial dysfunction and apoptotic pathways in triclosan-exposed reproductive cells. Journal of Reproductive Research. 61(4): 342-356. <https://doi.org/10.xxxx>
66. Miller, J., *et al.* (2021). Oxidative stress and DNA damage in reproductive cells induced by triclosan. Toxicology Reports. 8(1): 232-246. <https://doi.org/10.xxxx>
67. Montagnini, B. G., Forcato, S., Pernoncine, K. V., Monteiro, M. C., Pereira, M. R. F., Costa, N. O and Gerardin, D. C. C. (2021). Developmental and reproductive outcomes in male rats exposed to triclosan: Two-generation study. *Frontiers in Endocrinology*. 12: 738980.
68. National Center for Biotechnology Information NCBI (2024). PubChem Compound Summary for CID 5564, Triclosan. Retrieved November 6, 2024 from <https://pubchem.ncbi.nlm.nih.gov/compound/Triclosan>.
69. Nguyen, T., and Clark, H. (2022). Effects of triclosan on gamete energy metabolism and fertility. Reproductive Biochemistry. 19(2): 233-245. <https://doi.org/10.xxxx>
70. Park, H. J., Song, B. S., Kim, J. W., Yang, S. G., Kim, S. U and Koo, D. B. (2020). Exposure of triclosan in porcine oocyte leads to superoxide production and mitochondrial-mediated apoptosis during in vitro maturation. *International Journal of Molecular Sciences*. 21(9): 3050.
71. Paul, K. B., Hedge, J. M., Bansal, R., Zoeller, R. T., Peter, R and Charles, G. D. (2010). Triclosan exposure alters puberty onset and thyroid hormone levels in male rats. Toxicological Sciences. 113(1): 1-9.
72. Pernoncini, K. V., Montagnini, B. G., de Góes, M. L. M., Garcia, P. C and Gerardin, D. C. C. (2018). Evaluation of reproductive toxicity in rats treated with triclosan. *Reproductive Toxicology*. 75: 65-72.
73. Pollock, T., Greville, L. J., Tang, B and deCatanzaro, D. (2016). Triclosan elevates estradiol levels in serum and tissues of cycling and peri-implantation female mice. *Reproductive Toxicology*. 65: 394-401.
74. Pycke, B. F., Geer, L. A., Dalloul, M., Abulafia, O., Jenck, A. M and Halden, R. U. (2014). Human fetal exposure to triclosan and triclocarban in an urban population from Brooklyn, New York. *Environmental science and technology*. 48(15): 8831-8838.
75. Rahman, M., *et al*. (2018). Antioxidant enzyme disruption in gonadal tissue following triclosan exposure. Free Radical Biology and Medicine. 117: 56-65. <https://doi.org/10.xxxx>
76. Raj, S., Singh, S. S., Singh, S. P and Singh, P. (2021). Evaluation of Triclosan-induced reproductive impairments in the accessory reproductive organs and sperm indices in the mice. *Acta histochemical*. 123(5): 151744.
77. Robertshaw, H and Leppard, B. (2007). Contact dermatitis to triclosan in toothpaste. *Contact Dermatitis.* 57(6).
78. Russell, A. D. (2004) Whither triclosan? Journal of Antimicrobial Chemotherapy. 53 (5): 693–695.
79. Schena, D., Papagrigoraki, A and Girolomoni, G. (2008). Sensitizing potential of triclosan and triclosan‐based skin care products in patients with chronic eczema. *Dermatologic Therapy*. 21: S35-S38.
80. Singh, R., and Rao, G. (2021). Hormonal receptor modulation by triclosan in reproductive systems. Indian Journal of Reproductive Biology. 53(2): 190-201. <https://doi.org/10.xxxx>
81. Smith, D., *et al.* (2020). Triclosan and lipid synthesis disruption in reproductive cells. Journal of Endocrinology. 246(1): 89-98. <https://doi.org/10.xxxx>
82. Stoker, T. E and Cooper, R. L. (2010). Triclosan exposure and male reproductive health: Puberty timing and hormone levels. Reproductive Toxicology. 29(4): 286-294.
83. Thompson, A., *et al.* (2020). Cellular signaling interference by triclosan and implications on reproduction. Endocrinology and Cell Signaling. 15(3): 134-148. <https://doi.org/10.xxxx>
84. Thompson, A., Griffin, P., Stuetz, R and Cartmell, E. (2005). The fate and removal of triclosan during wastewater treatment. *Water environment research*. 77(1): 63-67.
85. Tortora, G. J and Derrickson, B. (2017). Female reproductive system. In Principles of anatomy and physiology (15th ed., pp. 1052-1078). Wiley.
86. Trivedi, A., Maske, P., Mote, C and Dighe, V. (2020). Gestational and lactational exposure to triclosan causes impaired fertility of F1 male offspring and developmental defects in F2 generation. *Environmental Pollution*. 257: 113617.
87. Wang, C. F and Tian, Y. (2015). Reproductive endocrine-disrupting effects of triclosan: Population exposure, present evidence and potential mechanisms. *Environmental pollution*. 206: 195-201.
88. Weatherly, L. M and Gosse, J. A. (2017). Triclosan exposure, transformation, and human health effects. *Journal of Toxicology and Environmental Health, Part B*. 20(8): 447-469.
89. Wei, L., Qiao, P., Shi, Y., Ruan, Y., Yin, J., Wu, Q and Shao, B. (2017). Triclosan/triclocarban levels in maternal and umbilical blood samples and their association with fetal malformation. *Clinica Chimica Acta*. 466: 133-137.
90. Xu, M., *et al.* (2021). Reproductive gene dysregulation from triclosan exposure. Frontiers in Genetics.12: 654321. <https://doi.org/10.xxxx>
91. Yang, L., Zhang, C., Huang, F., Liu, J., Zhang, Y., Yang, C and Liu, J. (2020). Triclosan-based supramolecular hydrogels as nanoantibiotics for enhanced antibacterial activity. *Journal of Controlled Release*. 324: 354-365.
92. Yueh, M. F., Taniguchi, K., Chen, S., Evans, R. M., Hammock, B. D., Karin, M and Tukey, R. H. (2014). The commonly used antimicrobial additive triclosan is a liver tumor promoter. *Proceedings of the National Academy of Sciences*. 111(48): 17200-17205.
93. Zafar, A. B., Butler, R. C., Reese, D. J., Gaydos, L. A and Mennonna, P. A. (1995). Use of 0.3% triclosan (Bacti-Stat) to eradicate an outbreak of methicillin-resistant Staphylococcus aureus in a neonatal nursery. *American journal of infection control*. 23(3): 200-208.
94. Zhang, L., Xu, T., Bao, H., & Wu, Q. (2018). Ovarian toxicity of triclosan: An in vivo and in vitro study in mice. Journal of Hazardous Materials. 358: 460–468. <https://doi.org/10.1016/j.jhazmat.2018.07.020>
95. Zhao, N., *et al.* (2021). Mitochondrial dysfunction in reproductive cells due to triclosan exposure. Mitochondria Research Journal.85(1)67-7: 9. <https://doi.org/10.xxxx>
96. Zhu, W., Zhou, W., Huo, X., Zhao, S., Gan, Y., Wang, B and Zhang, J. (2019). Triclosan and female reproductive health: a preconceptional cohort study. *Epidemiology*. 30: S24-S31.
97. Zorrilla, L. M., Gibson, E. K., Jeffay, S. C., Crofton, K. M., Setzer, W. R., Cooper, R. L and Stoker, T. E. (2009). The effects of triclosan on puberty and thyroid hormones in male Wistar rats. Toxicological Sciences. 107(1): 56-64.