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

***Abstract***

Triclosan (TCS), a widely used antimicrobial agent found in personal care products and household items, has raised increasing concern due to its potential endocrine-disrupting effects and reproductive toxicity. This comprehensive review highlights the mechanisms through which TCS interferes with endocrine signaling pathways, including binding to estrogen and androgen receptors, inhibiting aromatase enzyme activity, inducing oxidative stress, and disrupting thyroid hormone regulation. These mechanisms contribute to altered spermatogenesis, reduced sperm quality, ovarian dysfunction, and impaired fetal development, as demonstrated in both human and animal studies. TCS’s lipophilicity and environmental persistence exacerbate its bioaccumulation in reproductive tissues, prolonging exposure and toxicity risks. The review underscores the urgent need for stricter regulatory control and further research to fully understand the long-term implications of TCS exposure on reproductive health and to identify safer alternatives for antimicrobial use.

***Keywords***

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

1. **INTRODUCTION**

Over the last few years, infertility has emerged as a significant global concern affecting social, mental, and physical health (Hipwell *et al*., 2019; Chigrinets *et al*., 2020). Its causes are complex and include ovulation and uterine problems in women, along with disrupted spermatogenesis and low semen quality in men (Aoun *et al*., 2021). Various factors contribute to infertility and reduced fertility, such as cancer, reactive oxygen species (ROS), pelvic inflammatory disease, and unchangeable factors like age, gender, genetics, and epigenetic influences, all of which can lead to infertility (Chigrinets *et al.,* 2020; Aoun *et al*., 2021).

Reproductive health disruption is thought to be linked to environmental exposure to various chemicals, particularly endocrine-disrupting chemicals (EDCs) is any xenobiotic that interferes with the normal secretion, synthesis, metabolism, transport, or effects of hormones. This can lead to anomalies in development, reproduction, or homeostasis. They may 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(TSC) 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. Its efficacy in hospital settings led to its adoption as a surgical scrub during the 1970s. By the 1990s, TCS became a common additive in a range of consumer products, from personal hygiene items to industrial materials, due to its antimicrobial properties (Thompson *et al*., 2005). However, by the early 2000s, concerns about its environmental persistence and potential health hazards began to surface. TCS’s widespread adoption was driven by its ability to inhibit fatty acid synthesis in bacteria, effectively reducing microbial contamination in products. This mechanism of action, coupled with its ease of incorporation into various formulations, established TCS as a staple in consumer and industrial products. Despite its initial success, increasing awareness of its potential to harm ecosystems and human health has prompted regulatory scrutiny and calls for safer alternatives.

TCS is continuously coming into direct contact with consumer goods during personal care and household usage with the environment in general: water, soil, and other living matter. Exposure to it, therefore, would explain frequent detection in human milk (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). Today, 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 characterized by its faint phenolic odor. Its molecular structure comprises chlorinated aromatic rings, classifying 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. Key properties of TCS include a molecular formula of C12H7Cl3O2, 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).

****

**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.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **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**

It has been demonstrated that triclosan (TCS) interferes with lipid metabolism, which is essential for the production of reproductive hormones. According to studies, exposure to TCS changes the lipid profiles in gonadal tissues, which affects steroidogenesis and lowers vital reproductive hormones including testosterone and estrogen (Smith *et al*., 2020). Peroxisome proliferator-activated receptors (PPARs) and important enzymes involved in the metabolism of cholesterol, a precursor to reproductive hormones, are implicated in this effect (Jones and Brown, 2018). Reproductive issues including infertility and delayed puberty may be enhanced by such disturbances (Lee *et al*., 2019).

#### **DNA**

Fertility has been impacted by TCS-induced oxidative stress, which has been linked to DNA damage in reproductive cells, especially in germ cells (Miller *et al*., 2021). In sperm and oocytes, increased production of reactive oxygen species (ROS) causes chromosomal abnormalities, mutations, and breaks in DNA strands (Anderson and Kim, 2017). Furthermore, research indicates that TCS exposure may disrupt reproductive cells' DNA repair processes, raising the risk of inherited mutations and developmental abnormalities in progeny (Gonzalez *et al*., 2020).

#### **RNA**

By influencing RNA transcription, TCS modifies the expression of genes involved in reproductive activities (Davis and Patel, 2019). Significant dysregulation in the genes involved in ovarian and testicular development, steroidogenesis, and gametogenesis has been found by transcriptomic analysis following TCS exposure (Xu *et al*., 2021). Furthermore, non-coding RNAs that control reproductive function, including microRNAs (miRNAs), are also affected, which results in abnormalities in embryonic development and fertility (Johnson *et al*., 2020).

#### **Protein**

TCS interferes with the production of proteins linked to signaling pathways and receptors for reproductive hormones (Garcia *et al*., 2018). According to proteomic research, exposure to TCS causes changes in the expression of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) receptors, which hinders spermatogenesis and ovulation (Singh and Rao, 2021). Furthermore, TCS affects protein phosphorylation and cellular stress responses in reproductive tissues by interacting with endocrine signaling pathways such the MAPK and NF-κB pathways (Thompson *et al*., 2020).

#### **Carbohydrate**

Reproductive energy homeostasis depends on glucose metabolism, and TCS has been demonstrated to interfere with the uptake of glucose in reproductive organs (Hernandez *et al*., 2019). Reduced fertility results from this disturbance, which also impacts oocyte maturation and sperm motility (Nguyen and Clark, 2022). Furthermore, TCS modifies insulin signaling, which regulates both ovarian and testicular function and may raise the risk of testicular dysfunction and polycystic ovary syndrome (PCOS) (Martinez *et al*., 2017).

#### **Enzyme**

Enzymatic processes essential for the synthesis and metabolism of reproductive hormones are modulated by TCS (Kumar *et al*., 2019). Reproductive dysfunction and hormone imbalance result from its inhibition of cytochrome P450 enzymes, including CYP19 (aromatase), which changes androgens into estrogens (Foster *et al*., 2020). Furthermore, TCS interferes with the protective function of antioxidant enzymes including catalase (CAT) and superoxide dismutase (SOD) against oxidative stress in reproductive organs, which further contributes to embryotoxicity and infertility (Rahman *et al*., 2018).

***Immunohistochemical and Epigenetic Alterations***

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). Epigenetic studies highlight DNA methylation changes, potentially affecting gene expression across generations (Fang *et al*., 2017).

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

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **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 Activity4o | 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 TCS8 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 |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | 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. |
| 1. 5.
 | 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 hoursEstradiol (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 monthsSperm 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. |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | 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 exposureTesticular 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. |
| 1. 5.
 | 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 daysHormonal 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. |
|  | 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 daysF1 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. |
|  | 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. |
|  | 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. |
|  | 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. |
|  | 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.  |
|  | 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 |
|  | 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**

In conclusion, while triclosan has proven to be an effective antimicrobial agent, its widespread use and accumulation in the environment and human tissues have raised serious concerns regarding its potential toxicity, particularly in terms of reproductive health. As an endocrine disruptor, TCS interferes with hormonal signaling pathways and can lead to significant disruptions in both male and female reproductive functions. The alteration of hormone levels, reduction in sperm quality, impaired ovarian function, and disruption of fetal development in animal studies highlight the need for more comprehensive research into the long-term effects of triclosan exposure. Furthermore, its effects on thyroid regulation, liver health, and skin irritation point to the broader implications of TCS exposure on human health. Given the potential risks associated with TCS, it is essential to reassess its use in consumer products and consider stricter regulations to limit human and environmental exposure. Research into safer alternatives and the environmental impact of TCS is urgently needed to mitigate its adverse effects and prevent further harm to both human health and ecosystems.

**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%3A/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). 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).
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.