Review Article

Impact of Triclosan on Female and Male Reproductive System and Its Consequences on Fertility: A Literature Review

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Abstract

Objective: Triclosan is an aromatic organic compound with antibacterial and fungicidal properties, most often used in soaps, toothpaste and other cosmetics. The study aimed to analyze the influence of triclosan on the female and male reproductive systems and the consequences on fertility.

Materials and methods: A review of the latest literature derived from PubMed and Google Scholar platforms has been made. After following the search strategy, applying inclusion criteria and analysis of the obtained results assessed by two independent analysts, 45 studies were included in the review.

Results: Due to the similar structure of triclosan (TCS) to anthropogenic estrogens, TCS can interact with hormone receptors, affect hormone balance, and influence reproductive health and carcinogenesis. It has been noted that TCS might affect luteal cell progesterone production and disrupt ovarian function. Prenatal exposure to the chemical can have an impact on the reproductive system of newborns. TCS might be a risk factor for endometrial physiology and impair reproduction. TCS negatively affects the male reproductive system via interrupting steroidogenesis mediated miRNA (micro-ribonucleic acid) pathways. Negative effects of TCS on early development and embryogenesis in animals were evidenced. Moreover, TCS has the potential to promote carcinogenesis in human breast, ovarian, and prostate cells.

Conclusion: Potential impact of TCS on the reproductive system raises concern about its safety, due to its similar structure to anthropogenic estrogens and detection in the environment. TCS-induced disruption of hormone levels in the female and male reproductive systems may be the cause of impaired reproductive health, resulting in subfertility. Further investigations are required to evaluate the mechanisms and effect of TCS on human reproductive health.

Keywords: Triclosan; Endocrine Disruptors; Genitalia; Reproductive Health

Introduction

In recent years, infertility has become a serious social, mental, and physical health problem worldwide (1, 2). As described, infertility is a condition with multifactorial etiology, including ovulation and uterine diseases in women, as well as disrupted spermatogenesis and poor semen quality in

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men (3). Pathogenesis of reduced fertility and infertility includes many other factors, such as pelvic inflammatory disease, cancers, reactive oxygen species (ROS), and non-modifiable factors – age, gender, genetic, and epigenetic factors (1,3). It is supposed that disrupted reproductive health is associated with environmental exposure to lots of chemicals, such as endocrine-disrupting chemicals (EDCs) that negatively affect endocrine homeostasis via modulation of molecular pathways involved in hormone synthesis, transport, metabolism, and hormone receptors, but also influence the hypothalamus–pituitary (HP)–gonadal axis (2). Triclosan (2, 4, 4 1-trichloro-2 1-hydroxy-diphenyl ether, TCS) is an EDC that is widely used in personal care and industrial products due to its antibacterial and antifungal properties (4). Exposure to TCS can occur via ingestion of contaminated water or food, but it can also be absorbed by dermal and mucosal contact (5). TCS has been detected in aquatic ecosystems, but also human urine, blood, breast milk, and amniotic fluid (6, 7, 8). However, EDCs have different half-lives and capacity to accumulate in tissues, therefore it is difficult to assess their concentrations and impact on the human body (2). Numerous studies revealed that TCS can activate estrogen receptors (ERs), increasing estrogen secretion and disrupting endocrine homeostasis. TCS-induced decreased testosterone levels may contribute to reduced spermatogenesis and negatively affect sperm quality. Previous, both animal and human, studies suggest that TCS can negatively influence thyroid homeostasis, gut microbiome, and stimulate carcinogenesis within the reproductive system (2, 7, 9). Moreover, both animals and humans in early life stages are very susceptible to widespread chemicals, so increasing the use of cosmetics raises concerns about their safety. Due to the growing usage of various daily products (10) containing TCS, its detection in human bodies, and the problem of infertility, it is important to evaluate the impact of TCS on reproductive health. This study aimed to understand the effects of triclosan on the human female and male reproductive systems and its consequences on fertility.

Materials and methods

The studies available in the PubMed and Google Scholar databases were chosen through a literature search that was undertaken on October 3, 2021. The following inclusion criteria were assumed: papers published from 2015, available as full-text publications, with studies conducted on animals or humans only original and review papers were eligible for inclusion in the study. Letters to the editor, case reports and preprints were excluded from the review. To find articles, the following keywords, linked by logical operators, were used: “triclosan” AND “genitalia” OR "reproductive health” AND “fertility” OR “pregnancy” OR “assisted reproductive technique” OR “male infertility”. As a result of analysis conducted by two independent scholars, 45 scientific publications were picked for the study after three-step procedure including reading the titles, abstracts and entire texts. Furthermore, manual searching of retrieved studies was performed, in order not to miss matching studies.

Ovarian function: TCS might have an effect on antioxidant- and apoptosis-related gene expression in the ovary. Animal studies in zebrafish (*Danio rerio*) confirmed that higher doses of TCS might cause oxidative damage in ovaries and advance reactive oxygen species-dependent ovary apoptosis. Exposure of *Danio rerio* to 0, 17, 34, or 68 µg/L TCS for 42 days showed changes in the level of gene expression. The following changes were detected: downregulation in antioxidant-related genes (*SOD*, *GPx1a*, *CAT*, and *sMT-B*) in the 68 µg/l TCS group, upregulation in the *Bax* gene in the 34 and 68 µg/L TCS groups, and upregulation in the *p53* gene in the 34 µg/l TCS group. *Bax* and *p53* are apoptosis-related genes (11). According to the study conducted by Du et al., TCS increased estradiol and progesterone levels in cultured human ovarian granulosa cells and enhanced the expression of genes in glycolysis and steroidogenesis at concentrations ranging from 0 to 10 µM. TCS induced primary mitochondrial dysfunction, secondary cytotoxic dysfunction and enhanced glycolysis for energy production. Those changes confirm the toxicological effects of TCS on steroidogenesis, leading to alteration of energy metabolic flux. A high level of progesterone increases plasma volume, suppresses sympathetic outflow, promotes hypocapnia, and leads to fatigue and mood changes. High levels of estradiol are connected with increased risks of endometrial and ovarian cancers, fibroids, or endometriosis, which might impair a woman's fertility (12).

Ovarian cells: TCS exposure might negatively affect ovarian reserve. In the study of 511 women aged from 25 to 39 with fertility problems, urinary concentrations of triclosan reduced antral follicle

count (AFC) – a marker of ovarian reserve (p = 0.03). TCS did not affect the levels of estradiol, follicle-stimulating hormone (FSH), or anti-Müllerian hormone (AMH), other parameters of ovarian reserve (13). Mínguez-Alarcón et al. evaluated an association between urinary TCS concentrations and AFC in 109 women from Massachusetts General Hospital Fertility Center. Specific gravity-adjusted urinary TCS concentrations from 225 samples were about 13.0 µg/L (geometric mean, 8.9-19.1, confidence interval (CI) 95%). Inverse correlation was noted between specific gravity-adjusted urinary TCS concentrations and AFC (-4%, 95% CI= -7%, -1%, p = 0.009). The influence of TCS seemed to be modified by age and body mass index (BMI). Larger decreases in AFC were found among younger and slimmer women. However, the study did not include women without fertility problems, so it might be impossible to generalize results to all women (14). In the study by Ye et al., 84 infertile women with polycystic ovary syndrome (PCOS) and 212 infertile non-PCOS controls between 18 and 45 years old were enrolled. Significantly higher levels of TCS in urine were found in the PCOS group, compared to the control group (p = 0.0407). A positive correlation was detected between TCS levels and luteinizing hormone (LH), and LH to FSH (LH/FSH) ratio in women without PCOS (15). In another study, conducted among women of reproductive age, TCS was not related to infertility, while a combination of TCS with other endocrine-disruptive chemicals – bisphenol-A and benzophenone-3, were related to infertility (16).

Hormonal imbalance: Furthermore, daily exposure of adult female mice to 10 or 100 mg/kg TCS might result, within 2 weeks, in prolongation of distrust and reduction in antral follicles and corpora lutea. The levels of serum LH, FSH, progesterone, and gonadotrophin-releasing hormone (GnRH) mRNA were decreased among mice exposed to TCS. A lack of LH surge and increase of prolactin were noted. A decrease in thyroid hormones causing hyperprolactinemia through an elevation of thyrotropin-releasing hormone (TRH) was seen after exposure of adult female mice to ≥10 mg/kg of triclosan. Suppression of hypothalamic kisspeptin expression followed, which might impair reproductive function in mice (17).

Uterus and fallopian tubes: In studies with rats subcutaneously injected with TCS (18 and 27 mg/day), the number of implantation sites in the uteri was decreased. Moreover, the weight of the uteri of gravid subjects exposed to 600 mg/kg/day of TCS was also decreased (18). Among 698 Chinese women, high levels of TCS in urine increased the risk of prolonged menstrual cycle and abnormal menstruation, compared to low levels of TCS. Menstruation was not defined as abnormal if cycle duration was 21-35 days, menstrual bleeding lasted for 3-7 days, with an average amount of bleeding. A dose-response pattern was observed after division of the concentration into tertiles, a 23% reduction in fecundability was associated with the highest level of the substance (> 4.5 ng/mL), compared with the lowest tertile (< 1.1 ng/mL) (OR = 0.77; 95% CI = 0.59, 1.00) (OD – odds ratio) (19). Exposure to TCS might be a risk factor for endometrial physiology and may lead to implantation failures and impairment of reproduction. Forte et al. assessed cell proliferation, cell cycle, migration, and decidualization mechanisms, using human endometrial stromal cells derived from endometrial biopsies from women without endometriosis. TCS enhanced cell migration without affecting cell proliferation, increased gene expression and the levels of insulin-like growth factor-binding protein-1 and prolactin, decidualization markers whose increased levels amplified the effect of progesterone alone. Despite stating an adverse relationship, further investigations are required (20).

There is currently not enough data in the literature on the effect of TCS on fallopian tube function, both in animals and in humans.

Pregnancy and offspring: Tissues of young, small organisms, particularly at an early stage, are more sensitive to chemicals than those of adults. A study confirming that a chemical can negatively affect early development and embryogenesis of sea urchin was conducted by Hwang et al. (21). In rats, TCS lowered the expression of genes involved in differentiation of embryonic cells – empty spiracles homeobox 1 (EMX-1), bone morphogenic proteins (BMPs), and chromosome binding protein (CBP). The authors revealed abnormal cell division and differentiation in the embryos exposed to 1.0 µM TCS. Due to extensive use and bioaccumulation of the chemical, as well as the detection in human urine, amniotic fluid, and breast milk, it is important to assess gestational and lactational exposure to TCS of offspring (8, 22).

Scientific research indicates the possible impact of TCS on the next generations. In the study on inseminated mice, exposure to high doses of TCS

decreased the number of implantation sites. Moreover, administration of this chemical combined with bisphenol A accelerated this decreasing effect (23). TCS has potential to decrease estrogen sulfotransferase (EST) activity, leading to placental thrombosis and increasing the risk of miscarriage in humans and mice (24). In rats, TCS exposure during gestation (via cord blood) and lactation had an unfavourable effect on reproductive function and fertility of F1 male rats. Pregnant female rats were given TCS in different dosages (0.1, 4, 40, and 150 mg/kg b. wt. /day) during gestation from day 6 to postnatal day 21, subcutaneously. Perturbed expression of steroid hormone receptors, steroidogenic acute regulatory protein (StAR), and aromatase, subfertility with increased pre- and post-implantation loss, and negative influence on the sperm count and motility in the F1 male rats at postnatal day 75 were noted. Moreover, TCS caused a delay in testis descent in F1 male rats and reduced the crown-rump length and weight of fetuses in F2 generations (22).

Human studies have shown that exposure to TCS among pregnant women may potentially affect some parameters of newborns. Wang et al. detected triclosan in the urine of 537 healthy pregnant women from China. Prenatal TCS exposure was related to increased levels of testosterone in blood from the umbilical cord. The chemical decreased aromatase cytochrome P450 (P450arom), 3βHSD and 17β-hydroxysteroid dehydrogenases (17β-HSD) levels in the placenta. Compared with female infants, male infants with decreased estradiol levels in cord blood presented with more visible above-mentioned effects (25). However, Guo et al. found an association between maternal urinary concentrations of TCS and reduced serum testosterone levels in female newborns (95% CI: 0.138, -0.013, p = 0.018) (26). Additionally, Harley et al. noted a relationship between prenatal concentrations of TCS in urine and earlier menarche in girls (27).

Mínguez-Alarcón and Gaskins conclude that an association between female fertility and urinary concentration of TCS remains uncertain due to the lack of studies (28). In the LIFE Study of 501 women, Smarr et al. did not find a connection between female urinary triclosan concentrations and time-to-pregnancy (29). On the other hand, Vélez et al. in the MIREC Study noted that higher urinary levels of TCS in the first trimester were associated with a longer time-to-pregnancy among 1699 Canadian women (28, 30).

Fertility based on in vitro fertilization procedure: Studies evaluating the correlation between exposure to TCS and *in vitro* fertilization (IVF) outcomes are limited and conducted on small sample sizes. In the study performed by Lange et al., the impact of TCS on clinical outcomes in the group of 134 women undergoing fertility treatment utilizing IVF was assessed (31). An inverse relationship between TCS levels in urine and the number of oocyte yields was identified. An association between urinary TCS concentration and early reproductive outcomes was also assessed in Hua et al.'s study of 156 women undergoing *in vitro* fertilization-embryo transfer (IVF-ET). It was noticed that women with higher urinary TCS concentrations had decreased top quality embryo formation rates and implantation rates, as a trend of fertilization rate (32). In another study with 450 women from an infertility clinic, TCS exposure measured in the urine was associated with decreased implantation rate (p = 0.03). There was no association between other examined early IVF outcomes: MII (metaphase II of meiosis) oocyte count, embryo quality, fertilization rate (33). Taken together, it is supposed that TCS might be a toxic substance during the early stage of reproduction, but further human investigations involving more participants and detection of TCS in diverse biological matrixes (blood, cord blood, urine, and placenta) are needed.

Influence of triclosan on the male reproductive system

Steroidogenesis: In males, TCS affects reproduction and fertility through binding with androgen receptors (ARs) or disrupting testicular steroidogenesis – a critical process for hormone production (4, 5). Testosterone synthesis takes place in testicular Leydig cells and is regulated by the hypothalamic-pituitary-testicular (HPT) axis and other factors influencing steroidogenic enzymes (8). LH, via binding to its target – LH receptor (LHR), promotes cAMP (cyclic adenosine monophosphate) synthesis (34). The cAMP comprises a key molecule in cholesterol translocation into the mitochondrial space, where cholesterol is transformed to pregnenolone by cytochrome P450 enzyme CYP11A1. Subsequently, it is metabolized to testosterone.

According to an animal study by Kumar, the mechanism underlying the toxic effect on steroidogenesis is inhibiting adenylyl cyclase activity followed by a depressed level of cAMP, which decreases testosterone synthesis in Leydig cells (4, 8). Steroidogenesis in steroidogenic cells is modulated by microRNA (miRNAs) via various pathways (8, 9).

In male rats, miRNAs comprise molecules involved in sperm production via modulating their target mRNAs expression and participating in spermatocyte meiosis, spermatogenesis (9). Ha et al. reported that TCS decreased testicular steroidogenesis by the miR-6321/JNK/Nur77 cascade ($p < 0.05$) (9). TCS-induced reduction of the orphan nuclear receptor Nur77 expression led to the repressed translation of steroidogenic proteins such as SRB1 (Scavenger Receptor Class B), StAR (steroidogenic acute regulatory protein), and 3β-HSD, resulting in testosterone level decrease (8). StAR expression and, hence, steroidogenesis were inhibited by miR-150 in primary mouse Leydig cells. Moreover, the chemical promoted miR-142-5p expression, which directly suppressed the JAK1/STAT1 pathway and increased DAX1 expression, leading to an inhibition of steroidogenic protein P450c17 participating in testosterone synthesis (8). In another study presenting TCS as a substance disrupting the correct function of rodent male gonads, performed by Forgacs et al., it was noticed that high doses of TCS inhibited recombinant human chorionic gonadotropin-induced testosterone production, but the basal fraction of this hormone remained at the same level (35). Furthermore, TCS *in vivo* decreased testis weight. It decreased the expression of cytochrome mRNA and activity of steroidogenic enzymes participating in testosterone synthesis and influenced the concentration of serum LH, FSH, cholesterol, pregnenolone, and testosterone. Decreased testicular weight and actively motile spermatozoa were noted in the study with mature male Wistar rats exposed to TCS (1). The next possible mechanism by which TCS disrupts the synthesis of testosterone is inducing the expression of steroid metabolism enzymes – Ugt1a1, Sult1e1, and 5α-Reductases, which reduces testosterone levels (9). However, reduced expression of SRD5A1 and SRD5A2 – 5α-Reductase type 1 and type 2, responsible for conversion of testosterone into 5α-dihydrotestosterone (5α-DHT), can have a positive effect in steroidogenesis, the reduced activity of the enzyme resulting in a higher remaining testosterone fraction.

Hormonal imbalance: TCS has the potential to impact hormone receptor expression indirectly and directly (9). Numerous studies revealed a decline in testosterone, i.e. LH levels, after TCS exposure. The chemical is supposed to act as a competitive antagonist of testosterone binding to the natural hormone receptor, which has an impact on the HPT axis. Furthermore, too low testosterone concentration contributes to inducing LH secretion due to the negative feedback system of the HPT axis. Ha et al. reported reduced LHR and AR (androgen receptor) expression dependent on TCS dose ($p < 0.05$) in male rats (9). Yawer et al. conducted a study on mice demonstrating that exposure to EDCs might disrupt testicular function via disruption of testicular GJIC (gap junction intercellular communication), a dysregulation of junctional and non-junctional functions of connexin 43 (Cx43), and activation of mitogen-activated protein kinases (MAPKs) signalling pathways (36). MAPKs are a family of serine/threonine kinases involved in transmitting signals from various extracellular stimuli to specific intracellular targets and play an important role in regulatory processes in Leydig cells. Additionally, the researchers noted disruption of an early stage of steroidogenesis in Leydig cells in the prepubertal period – a sensitive phase of testicular development. Moreover, lack of Cx43 from the junctional plasma membrane can result in tumorigenesis in Leydig cells. In another study, conducted on pubertal male rats, TCS decreased plasma testosterone and LH levels (8). Testis function and reproductive endocrine homeostasis can be assessed by hormone levels as other molecules involved in their metabolism. Vitellogenin (Vtg) is a yolk protein synthesized in the liver and transported to the developing oocytes after estrogen induction in female fish (37). Wang et al. in the study on juvenile male Yellow River carp showed TCS-induced Vtg synthesis by increased gonadal aromatase mRNA expression – enzyme converting testosterone to 17β-estradiol (E2), elevating E2 levels (38). Furthermore, TCS increased E2 levels via GnRH and gonadotropin (GtH-b) expression. Abdel-Moneim et al. conducted a study on male Smallmouth bass (*Micropterus dolomieu*), in which they reported detectable levels of TCS and high prevalence of testicular oocytes (TO) – a form of gonadal intersex, which confirms estrogenic properties of TCS (37).

In the human study of Pollock, high levels of urinary TCS were related to reducing levels of E2 and testosterone in the group of boys aged 12-19 years (39). In male adults aged 50-79, non-linear relationship of urinary TCS with E2 was found.

Semen quality and male fertility: De Marchi et al. evaluated the influence of TCS and carbon nanotubes (CTNs) on *Mytilus galloprovincialis* sperm quality, viability, and ROS synthesis, indicated by 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyl tetrazolium

bromide (MTT) and intracellular ROS concentration (6). They evidenced the toxic impact of both substances detected in aquatic ecosystems on reproduction and sperm viability, which was probably the result of dysfunction of mitochondria and sperm apoptosis and increased ROS production.

In previous animal studies, TCS administered in maximum doses of 8 mg/kg did not significantly affect sperm quality (evaluated for total number, motility, viability, and sperm morphology), but TCS administered in the dose of 200 mg/kg reduced spermatogenesis in young rats (1). However, anti-androgenic properties were not confirmed in another study on 52-day old male Wistar rats (40). Furthermore, this endocrine disruptor was detected in testicular tissues, which suggests its accumulation in reproductive organs, with direct impact on sperm synthesis (1).

Jurewicz et al. assessed the association between environmental exposure to TCS and male fertility (4). They reported a harmful influence of the chemical on semen quality, indicated by sperm DNA damage, increased percentage of sperm with abnormal morphology, and the changed level of reproductive hormones. In another human study, conducted among 262 men of reproductive age from a fertility clinic by Nassan et al., it was shown that TCS dose did not correlate with semen quality (5). Nevertheless, researchers noted a decline in the percentage of morphologically normal sperm in men in the 2nd or 3rd quartiles (-1.32% (95% CI: -2.04, -0.59), -0.91% (95% CI: -1.63, -0.18)), compared to men with undetectable levels in urine. In contrast, urinary TCS was associated with better semen quality in Smarr's human study (29). Chigrinets et al. observed that pathozoospermia risk was increased as a result of bisphenol A exposure, without significant effect of TCS (41).

Carcinogenesis in reproductive organs: According to recent studies, TCS can induce cell divisions in various tissues, including the reproductive system. Due to its capacity to bind ERs, TCS can enhance estrogen exposure in the breast, leading to an increased risk of breast cancer (42). As described, earlier breast development was associated with prepubertal TCS (27). Active ER signalling pathways resulted in the growth of ovarian cells. Moreover, TCS can promote excess proliferation of human ovarian cells by modulating the expression of genes involved in cell proliferation. In the study by Derouiche et al., it was presented how TCS promotes carcinogenesis in human prostate cancer stromal cells. TCS has the potential to promote cancer metastasis by epithelial-mesenchymal transition (EMT) process, in which cells lose their cell polarity, capacity for adhesion, which can initiate cancer progression and metastasis. It is supposed that TCS can increase *cathepsin D*, a metastasis-related gene expression via AR signaling pathway. Enhancing cancer progress is possible by activation of a membrane ion channel. TRPA1 (Transient Receptor Potential Ankyrin 1), resulting in the elevation of intracellular calcium levels, VEGF (vascular endothelial growth factor) secretion and cell proliferation (43).

Future directions and recommendations: As described, TCS is commonly found in personal care products and household products, like detergents, due to its antimicrobial activity (32). Although it is not directly absorbed and consumed by humans, it can accumulate in the aquatic environment and aquatic organisms – animals or plants, algae. It increases the risk of chronic exposure among groups of people consuming aquaculture food. To confirm, in a study by Hua et al. aquaculture food intake and cosmetic use were associated with higher TCS exposure.

TCS, like some other EDCs, is a substance with a short half-life, which makes evaluation of its concentration in the organism and toxicity more difficult (2, 32). In addition, the toxicity of TCS was reported in studies with wild fish, in which high levels of the major metabolite – methyl triclosan (MTCS) – a more persistent and toxic substance than TCS, were found (38). Therefore, research is needed to investigate how to more accurately analyze TCS and its metabolite concentrations in human bodies, giving a chance for evaluation of safe use of chemicals in daily products. It is particularly important for women, because they apply more cosmetics.

According to recent studies, restrictions on the use of chemicals, including TCS, in antiseptic washing products may be the cause of lower urinary concentrations over time (5). The latter indicates reduced accumulation of TCS in the human body, preventing its impact on human health. In Hua's study, a positive dose-response correlation of aquaculture food intake with urinary TCS concentrations ($p < 0.001$) was noted (32). More research is needed for optimizing the concentration of TCS and its metabolites in aquatic food products. Further studies on TCS should comprise bigger sample sizes and longer study time, investigating mechanisms of action and effects on the reproductive system. A summary of the potential effects of triclosan exposure on the reproductive system is presented in Table 1.

Table 1: Summary of the potential effects of TCS exposure on the female and male reproductive system

	Female		Male	
	animal	**human**	**animal**	**human**
Hormone homeostasis, levels of reproductive hormones	hyperprolactinemia, suppression of hypothalamic kisspeptin expression (17)	increased estradiol and progesterone levels in cultured human ovarian granulosa cells (12) TCS did not affect levels of estradiol, FSH and anti-Müllerian hormone (13) increased levels of LH and LH/FSH ratio in women without PCOS (15)	decreased levels of serum LH, FSH, cholesterol, pregnenolone, and testosterone in rats, elevated level of E2 in weanling male rats (4,44)	reduced level of FSH, testosterone, estradiol (4)
Reproductive health, fertility	oxidative damage in ovaries and advance ROS-dependent ovary apoptosis (11) decreased number of implantation site in the uteri of inseminated mice (23)	reduced antral follicle count (13, 14), increased risks of prolonged menstrual cycle and abnormal menstruation (19) implantation failures and impairment of reproduction (20), uncertain due to discrepancies in research when measured time-to-pregnancy (28)	disrupted steroidogenesis via mRNA pathways, inhibition of steroidogenic proteins involved in synthesis of testosterone, inducing expression of enzymes participating in metabolism of testosterone, in mice (9) reduced weights of the epididymis and seminal vesicle, significant increase in the percentage of abnormal spermatozoa in the epididymis. decrease in levels of epididymal sialic acid and seminal vesicular fructose in the mice (44, 45) decreased semen production can disrupt fertility	studies are inconsistent if TCS is toxic for semen quality and male fertility the effect of TCS on pathozoospermia was not statistically significant increased sperm count total concentration, in men from general population (29) harmful influence of TCS on semen quality, sperm DNA damage, increased percentage of sperm with abnormal morphology (4) no correlation between triclosan and semen quality (5)
Carcinogenesis	–	an increased risk of endometrial, ovarian and breast cancer due to estrogen exposure (12, 38), induced growth of human ovarian cancer cells through an ER-dependent pathway (42)	–	promoting carcinogenesis in human prostate cancer cells via VEGF induction, upregulating cathepsin D expression and enhancing cell motility (42, 43)
Effect on offspring	an unfavourable effect on reproductive functions and fertility of F1 male rats (22) higher testosterone concentrations, decreased aromatase cytochrome P450, 3β-HSD and 17β-HSD levels in the placenta (25), perturbed expression of steroid hormone receptors, StAR and aromatase, increased pre- and post-implantation loss, negative influence on the sperm count and motility, a delay in testis descent in the F1 male rats, reduced crown-rump length and weights of fetuses in F2 generations (22), reduced cord serum testosterone levels in female newborns prenatally exposed to TCS (26) earlier menarche in girls after prenatal exposure to TCS (27)	Effect on offspring	an unfavourable effect on reproductive functions and fertility of F1 male rats (22) higher testosterone concentrations, decreased aromatase cytochrome P450, 3β-HSD and 17β-HSD levels in the placenta (25), perturbed expression of steroid hormone receptors, StAR and aromatase, increased pre- and post-implantation loss, negative influence on the sperm count and motility, a delay in testis descent in the F1 male rats, reduced crown-rump length and weights of fetuses in F2 generations (22), reduced cord serum testosterone levels in female newborns prenatally exposed to TCS (26) earlier menarche in girls after prenatal exposure to TCS (27)	Effect on offspring

TCS (triclosan); FSH (follicle-stimulating hormone); LH (luteinizing hormone); PCOS (policystic ovary syndrome); E2 (estradiol); ROS (reactive oxygen species), miRNA (micro-ribonucleic acid); ER (estrogen receptor); DNA (deoxyribonucleic acid); VEGF (vascular endothelial growth factor); 3 β-HSD (3 beta-hydroxysteroid dehydrogenase); 17β-HSD (17 beta-hydroxysteroid dehydrogenase); StAR (steroidogenic acute regulatory protein); F1, F2 (generations of male rats); mRNA (messenger ribonucleic acid).

Conclusion

Triclosan is a broad-spectrum antimicrobial and antifungal agent used in personal care products, cosmetics, household products and items, including plastics. Due to its extensive use, detection in the environment and human bodies, and similar structure to anthropogenic estrogens, its potential impact on the reproductive system raises concerns about its safety. It is supposed that TCS-induced disruption of hormone levels in the female and male reproductive systems may be the cause of impaired reproductive health, resulting in subfertility. During the diagnostic process of infertility reasons, clinicians should consider the estrogenic effect of triclosan and its potential to accumulate in the body. It is important to evaluate gestational and lactational exposure to triclosan of offspring, particularly in industrialized countries. The mechanism of action of TCS with regard to fertility is not fully conclusive. Further investigations are required to explain discrepancies in some results and investigate the potential mechanisms and effects of TCS on human reproductive health.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

Authors declare no conflict of interest.

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