Indonesian Journal of Cosmetic
E-ISSN: 3026-3352

Teratogenic Risks of Cosmetic Ingredients During Pregnancy: A Review

Tri Dewi Zakinah[1], Briliana Suryani Kusuma Kinasih[1], Nisa Raudotul Auli[1*], Jenifer Kolina[1]

1. Department of Cosmetic Engineering, Institut Teknologi Sumatera, Jl. Terusan Ryacudu, Way Huwi, Kec. Jati Agung, Kabupaten Lampung Selatan, Lampung 35365

***Corresponding Email: nisa.auli@kos.itera.ac.id**

ABSTRACT

Cosmetics are one of the necessities, especially for women to maintain healthy skin and appearance to become more confident. Cosmetics are products that are widely applied to the body, especially the skin, and their compositions come into contact with the skin for many years with the user. Therefore, the ingredients used in cosmetics must be safe and have concentrations that can be tolerated by the body, so as not to cause ongoing harmful effects. According to European law, all cosmetics approved for circulation in the European Union must be safe for users, and the responsibility for this lies with manufacturers, distributors, and importers. However, the use of cosmetics can have undesirable effects due to the presence of certain chemicals. often, these chemicals have harmful and long-lasting effects, especially for pregnant women as they can affect foetal growth and development. There are cosmetic ingredients that have been shown to be teratogenic and potentially harmful during and after pregnancy. This review explores the various teratogenic substances, their impact on pregnancy, and how to prevent the use of teratogenic cosmetic ingredients. It is acknowledged that exposure to mercury during pregnancy and childhood poses a serious risk to public health. To effectively guide future cosmetic recommendations, more studies especially examining mercury, hydroquinone, retinoic acid from cosmetics are necessary.

Key words: Hydroquinone, Mercury, Retinoic acid, Teratogenic, Pregnancy

INTRODUCTION

Cosmetic use has become an essential part of modern self-care routines, particularly among women of reproductive age. While cosmetics are generally regarded as safe for everyday use, growing evidence suggests that certain cosmetic ingredients may pose significant risks during pregnancy. These risks are particularly concerning when ingredients with potential teratogenic effects

are used, as they can interfere with fetal development during critical periods of organogenesis (Ananda et al., 2025; Subroto et al., 2025).
Teratogens are substances that can disturb the development of an embryo or fetus, leading to permanent structural, functional, or neurological abnormalities. Teratogenic exposure during the first trimester—when organ systems are forming—is especially harmful, often resulting in congenital malformations, growth restriction, or even fetal loss (Shepard, 1982; Giavini & Menegola, 2012). Common mechanisms by which teratogens exert their effects include oxidative stress, endocrine disruption, gene expression alterations, and toxic interference with morphogen signaling pathways, such as those involving retinoic acid.

In recent years, reports have emerged of adverse pregnancy outcomes linked to cosmetic product use. One such case reported by Counter & Buchanan (2004) documented neurological impairments in infants born to mothers who used unregulated skin-lightening creams during pregnancy. The children exhibited delayed speech and cognitive deficits, with toxic levels of heavy metals detected in their biological samples. These findings underscore the potential for transplacental transfer of harmful cosmetic ingredients and the resulting fetal toxicity.

In Indonesia, surveillance by the national regulatory agency (BPOM) continues to identify non-compliant cosmetic products, some of which contain substances known or suspected to be teratogenic (BPOM RI, 2023). Despite increasing awareness, the use of such products remains common among pregnant and breastfeeding women, often due to inadequate labeling or lack of consumer education.

Given the potential risks, it is essential to promote awareness of teratogenic hazards associated with certain cosmetic ingredients and advocate for stricter regulation, enhanced product labeling, and safer formulation practices to protect maternal and fetal health. This review highlights the potential teratogenic risks associated with certain active ingredients in cosmetics, notably mercury, hydroquinone, and retinoic acid, which may interfere with embryonic and fetal development when absorbed systemically.

METHODOLOGY

In conducting this study, the researcher chose a qualitative method as the basis for the literature review approach. In collecting data, the researcher focused on studying the potential of teratogenic ingredients for pregnant

women. The literature review study method is very efficient to use in the preparation of related studies that are in accordance with current developments. The use of this method is about existing knowledge, finds gaps in knowledge, and forms a theoretical basis for subsequent research. In conducting the literature review, the researcher focused on leading journals relevant to the research title for the past 10 years, with the aim of collecting high-quality scientific information that supports the theoretical basis of the research. Article searches were conducted using academic databases such as Google Scholar, ScienceDirect, ResearchGate, Pubmed and others using keywords such as cosmetic ingredients, teratogenic, and pregnancy.

RESULT AND DISCUSSION

Environmental substances known as teratogens include medications, infections, malnutrition, and physical or chemical components while contact with an embryo or fetus, can result in congenital abnormalities and cause the infant to change permanently in terms of function or appearance (Shepard, 1982). According to Giavini and Menegola (2012), teratogens most frequently act through the following mechanisms: retinoic acid imbalance, endocrine disruption, vascular disruption, oxidative stress, hyperacetylation, cholesterol imbalance, and changes in folate metabolism and folate antagonism. There are many types of teratogens, but this review discusses a few that are widely used in cosmetics and have the most negative impact on pregnancy and lactation globally.

Mercury

Inorganic salts such as mercuric chloride and mercuric oxide are usually the source of mercury in cosmetic products. Mercury compounds in cosmetic creams make the skin look fair by inhibiting melanin production (Al-Saleh et al., 2004). Mercury contained in cosmetic creams is absorbed by the skin through transepidermal and transappendageal pathways (Figure 1), with the latter involving transfer through sebaceous glands, sweat glands, and hair follicles, leading to the accumulation of mercury in the hair on the scalp (Chan, 2011). inorganic: Mercury can cause allergic contact dermatitis, skin redness, erythroderma, nail discolouration, purpura, and greyish skin tone. Once absorbed, inorganic mercury spreads to all tissues. It can cause toxicity to the kidneys and other organs such as the brain and the nervous system. Tremor, muscle weakness, peripheral neuropathy, depression, psychosis, anxiety, dizziness, headaches, and vision loss are the most common ailments. During pregnancy, mercury exposure can negatively affect fetal

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development, especially the central nervous system. Factors such as mercury concentration, frequency of product application, skin integrity, lipophilicity of carriers in cosmetic products, and hydration of the stratum corneum affect skin absorption. Mercury exposure may occur after hand-to-mouth contact or topical application around the mouth (BPOM RI, 2023).

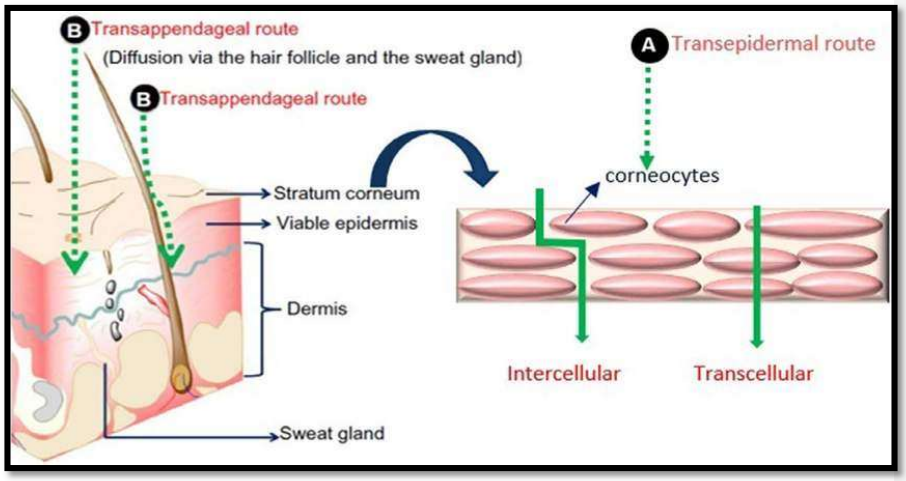


Figure 1. Schematic of skin penetration routes (Razafi et al., 2017)

In the health sector, mercury is used to make dental amalgam and thermometers, which are thermometers made of mercury. Mercury, which is commonly used as bleach, has the potential to teratogenically affect foetal development. In nursing mothers, mercury can accumulate in breast milk, increasing the risk to the baby. Studies show effects such as delayed motor and cognitive development (Supriningrum & Jubaidah, 2019).

A person can absorb Mercury quickly through three ways: inhalation (inhaled through the nose), ingestion, and absorption through the skin. If you put mercury in cosmetics, such as face creams, for a long time, the mercury will be absorbed through the skin and then accumulate in the body. This can cause allergies, irritation, dark spots, and even potentially fatal diseases as it harms the kidneys and brain. Exposure to mercury in pregnant women can cause toxicity effects on the kidneys and central nervous system, interfere with fetal development, even damage it, and stunt the growth of the baby. Mercury can also cause female infertility and unviable foetal abnormalities. Babies born to mothers exposed to mercury toxins may experience brain

damage, mental retardation, blindness, and decreased abilities (Susanti, 2013).

Environmental exposure to mercury (Hg) may play a role in the elevated rates of adverse birth outcomes (Murcia *et al*., 2016). Hg is recognized as an endocrine-disrupting heavy metal (Liu *et al*., 2023) and is classified as a common endocrine-disrupting chemical (EDC). EDCs consist of external mixtures of chemicals that can disrupt any facet of hormone function (Zoeller *et al*., 2012).

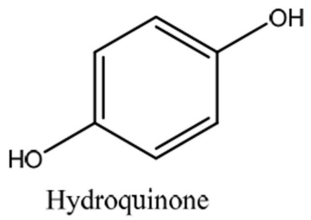
The findings indicated a positive correlation between maternal Hg exposure (MHE) and low birth weight. MHE is identified as a risk factor for low birth weight and is linked to atypical anthropometric measurements at birth. Nevertheless, there is a lack of sufficient evidence connecting Hg exposure to small-for-gestational-age and preterm birth (Pan *et al*., 2024).

During pregnancy, elevated levels of Hg may correlate with an increased risk of birth defects, preterm birth, ADHD, ASD, as well as low birth weight, length, and head circumference. Greater total Hg exposure during pregnancy was associated with a heightened risk of various adverse outcomes in the child. However, the relationships between Hg exposure during pregnancy and neurodevelopment in the child remain inconclusive (Dack *et al*., 2021). Infants exposed in utero to mercury through maternal use of mercury-containing skin-lightening products showed neurological impairments, including delayed speech and cognitive function (Counter & Buchanan, 2004). Mercury (Hg) levels in blood, urine, fingernails, and hair were found to be elevated in children diagnosed with autism spectrum disorder when compared to those without the disorder (Ding *et al*., 2023; Stojsavljevic *et al*., 2023; Sulaiman *et al*., 2020; Zhang *et al*., 2021; Ramazani *et al*., 2024).

Hydroquinone

Hydroquinone (benzene 1,4-diol or quinol) is a melanin synthesis inhibitor and antioxidant that has been an important part of skin lightening creams for almost fifty years. Hydroquinone, a type of phenol with the chemical formula $C_6H_6O_2$, is one of the organic aromatic compounds called hydroquinone. Hydroquinone is an ingredient used in whitening creams by irresponsible people. Exogenous ochronosis, or permanent hyperpigmentation, is most common in women who use whitening cosmetics containing hydroquinone

(Pisacha *et al*., 2023). Exogenous ochronosis is localized hyperpigmentation of the skin that is blue-black or gray-brown without systemic symptoms or symptoms (BPOM RI, 2023).



Picture 1. Chemical structure of hydroquinone (Andersen *et al*., 2013)

Hydroquinone is one of the cosmetic chemicals that can cause skin peeling when applied to human skin. It makes the skin appear brighter as it inhibits the natural melanin formation of human skin. However, if used for a long period of time it can cause ochronosis, which consists of bluish-brown pustules, itching, and burning of the skin (Suyudi *et al*., 2022). The mechanism of hydroquinone whitening the skin is by stopping the tyrosinase enzyme, which inhibits the conversion of L-3,4 dihydroxyphenylalanine (L-DOPA) into melanin (Sofen *et al*., 2016).

Based on the Head of BPOM Regulation number KH.03.1.23.08.11.07517 of 2011 concerning Technical requirements for cosmetic ingredients, hydroquinone has been banned from use as a bleach in cosmetics. Hydroquinone is only used for artificial nails at 0.02% (BPOM RI, 2022). Hydroquinone >2% belongs to the class of hard drugs and is used for hyperpigmentation diseases, chloasma, freckles, melasma, and post inflammatory hyperpigmentation and is only given by prescription. The side effects of high-dose and long-term use of hydroquinone are exogenous ochronosis, cataracts, colloidal pigment milia, sclera, nail pigmentation, loss of skin elasticity, and impaired wound healing. Cosmetics containing hydroquinone can increase the risk of dermatitis and hormonal disorders in pregnant women (Subroto *et al*., 2025).

Although there is a dearth of data investigating the teratogenicity of hydroquinone, in vitro studies have shown that hydroquinone can cause chromosomal abnormalities in eukaryotic cells (Devillers *et al*., 1990). In the previous category labeling system, hydroquinone was labeled as a Category C drug by the FDA. The Category C drug description states that animal reproduction studies have shown adverse effects on the fetus without

adequate and well-controlled studies in humans, but the potential benefits may warrant use of the drug in pregnant women despite the potential risks (Drugs.com, 2025). Despite being categorized as a Category C drug, most over-the-counter (OTC) topical hydroquinone preparations do not carry this important warning (Bio & Cies, 2017).

In a study conducted by Rubiyati & Setiawan (2016), it was shown that hydroquinone administration to pregnant rats can reduce the average number of fetuses, fetal weight, and implantation. Congenital malformations caused by hydroquinone administration were neural tube defect, anotia, microtia, Intra Uterine Fetal Defect, limb defect, tail defect. It was concluded that hydroquinone administration to pregnant rats inhibited fetal growth, decreased the number of fetuses, and increased fetal malformations.

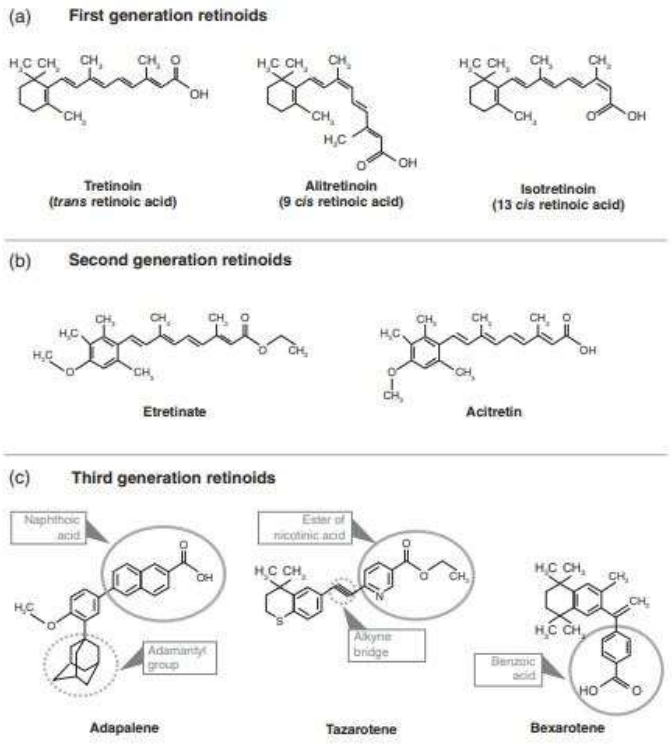
Retinoic Acid

Retinoic acid, an active form of vitamin A and common ingredient in skincare which is widely utilized in the treatment of acne, particularly for improving the appearance of post-inflammatory lesions and reducing the visibility of enlarged pores. Due to its potent pharmacological activity, retinoic acid should be administered strictly under medical supervision and for a limited duration of use. Prolonged unsupervised use of retinoic acid in facial creams may lead to adverse dermatologic effects, including skin irritation and burning sensations. Moreover, systemic exposure to retinoic acid during pregnancy carries a significant risk of teratogenicity, potentially resulting in fetal malformations (Sari *et al.*, 2024).

The earliest retinoids, retinoic acid derivatives, were strictly regulated by the U.S. Food and Drug Administration due to their teratogenic effects when used during pregnancy. Williams *et al*. (2020) classified retinoids into three generations based on their chemical structures (Picture 1). Isotretinoin, first-generation retinoid, exerts teratogenic effects through the induction of hypervitaminosis A. Retinoids play a critical role in embryonic development, particularly through their regulation of the HOX gene signaling pathways, which are essential for the patterning of the branchial (pharyngeal) arches during the fourth week of embryonic development. As a result, structures derived from the pharyngeal arches are especially vulnerable to isotretinoin exposure during early pregnancy. The most commonly observed congenital malformations include craniofacial, central nervous system, cardiovascular and thymic abnormalities (Table 1).

Table 1. Malformations associated with isotretinoin use (Browne *et al*., 2014)

Craniofacial defects	Ear defects, eye defects, cleft palate, micrognathia (small jaw), depressed nasal bridge, dysmorphism, ocular hypertelorism (widely spaced eyes)
Central nervous system defects	Microencephaly, facial nerve palsy, hydrocephalus, cortical and cerebellar defects
Cardiovascular defects	Fallot's tetralogy, septal defects, transposition of the great vessels and aortic arch hypoplasia
Thymic abnormalities	Hypoplasia, aplasia, and ectopia



Picture 1. First, second, and third-generation retinoids (Williams *et al*., 2020)

The first- and second-generation retinoids developed for oral application which leads to severe toxicity. Some early retinoids have been subsequently reformulated for topical application, thereby significantly reducing their potential for systemic absorption and toxicity. Furthermore, the third-generation of retinoids, such as adapalene, tazarotene, and bexarotene, provide more rigid structures than the former generations which result in enhancing retinoic acid receptor selectivity, thus reduce their toxicities. Consequently, the latest generation of retinoids that are reformulated for topical use exhibit a lower teratogenic potential in animal studies (Williams *et al*., 2020).

The study by Lee *et al.* (2012) reveals a paradoxical teratogenic mechanism of retinoic acid. An overdose of retinoic acid during early pregnancy can paradoxically cause long-term retinoic acid deficiency in the embryo. This occurs because excessive retinoic acid temporarily suppresses the genes responsible for retinoic acid synthesis (RALDH1, RALDH2, RALDH3) while upregulating other genes that are involved in retinoic acid catabolism (CYP26A1, CYP26B1). As a result, the retinoic acid levels drop below normal at critical stages of organ development, leading to defects such as kidney agenesis, apoptosis in fetal tissues, and other malformations. Remarkably, these abnormalities can be prevented by applying low doses of retinoic acid to maintain the retinoic acid balance during pregnancy, since this substance is essential during early embryogenesis.

CONCLUSION

This review underscores the considerable teratogenic risks associated with certain active cosmetic ingredients, specifically mercury, hydroquinone, and retinoic acid, when used during pregnancy. These substances, frequently present in skin-lightening products and anti-acne formulations, have been implicated in a range of serious congenital anomalies, including craniofacial malformations, central nervous system defects, cardiovascular abnormalities, and thymic dysgenesis. Mercury exposure has been linked to neurodevelopmental delays and systemic toxicity, while hydroquinone has demonstrated adverse effects on fetal growth and has been associated with genotoxicity and chromosomal aberrations. Retinoic acid, despite its therapeutic utility, carries a well-documented risk of embryopathy due to its disruption of HOX gene signaling pathways and its dysregulation of endogenous retinoid metabolism during critical stages of embryogenesis.

Based on the findings of this review, it is strongly recommended that pregnant women avoid the use of cosmetic products containing these substances. Indonesian Food and Drug Authority (BPOM) have issued specific

bans or restrictions on the use of mercury, hydroquinone, and retinoic acid in cosmetic products, especially non-prescription cosmetic products. Public education initiatives should be intensified to raise awareness of the risks associated with teratogenic ingredients in cosmetics. Furthermore, healthcare professionals should actively counsel patients on the safe use of skincare during pregnancy, while the cosmetic industry is urged to develop and promote formulations that utilize non-teratogenic, pregnancy-safe alternatives.

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