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Childhood and Adolescent Exposure to Chemicals Found in Personal Care Products

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Résumé

Contexte : Les produits de soins personnels contiennent plusieurs substances chimiques dont l'exposition est préoccupante pour les jeunes vu leur plus grande susceptibilité aux expositions chimiques. Aucune revue publiée n'a étudié l'exposition des jeunes aux substances chimiques dans ces produits.

Objectif : Cette revue de la portée vise à synthétiser des études de biosurveillance décrivant les concentrations de parabènes, phénols, phtalates et substances per- et polyfluoroalkylées (PFAS) après l'utilisation de produits de soins personnels chez les jeunes âgés de 5 à 19 ans.

Méthodes : La recherche a été effectuée dans MEDLINE, Embase et Global Health. L'éligibilité des articles a été évaluée. Les résultats des études éligibles ont été résumées et décrites.

Résultats : Trente-sept études ont été incluses, la première étant publiée en 2013. La majorité des études étaient transversales (n=35) et incluaient plus de 100 participants (n=27). Les substances chimiques les plus fréquemment étudiées étaient les phtalates (n=23), suivies des parabènes et des phénols (chacun n=18), puis des PFAS (n=1). La matrice biologique principalement utilisée était l'urine (n=36). Plusieurs études (n=31) ont rapporté au moins une association positive entre les produits de soins personnels et certaines classes chimiques, comme entre le maquillage et les parabènes; la lotion et les phénols; et le parfum et les phtalates.

Conclusion : Plus d'études sur ce sujet sont nécessaires pour documenter l'importance relative de l'utilisation des produits de soins personnels par rapport à l'exposition totale aux substances chimiques. L'uniformisation des questionnaires de collecte de données pourrait aider à réduire l'hétérogénéité des résultats.

Mots-clés : produits de soins personnels, parabènes, phénols, phtalates, substances perfluoroalkyles, substances polyfluoroalkyles, enfants, adolescents, exposition.

Abstract

Background: Personal care products (PCPs) contain a variety of chemicals including parabens, phenols, phthalates, and per- and polyfluoroalkyl substances (PFAS). Exposure to these chemicals is of concern for children and adolescents, as they are known possess an increased susceptibility to chemical exposures. To date, no published review has explored youth exposure to chemicals found in PCPs.

Objective: This scoping review aimed to provide an overview of biomonitoring studies that describe the concentrations of parabens, phenols, phthalates, and PFAS following PCP use among children and adolescents of any age from 5 to 19 years old.

Methods: The search was conducted in MEDLINE, Embase, and Global Health. Articles were screened and assessed for eligibility. From eligible studies, data were extracted to summarize and describe the findings.

Results: Thirty-seven studies were included, the first of which appeared in 2013. The majority of studies were cross-sectional (n=35) and included more than 100 participants (n=27). The most frequently studied chemicals were phthalates (n=23), followed by parabens and phenols (each n=18), and then PFAS (n=1). The biological matrix mainly used was urine (n=36). Thirty-one studies reported at least one positive association between personal care products and certain chemical classes, such as between makeup and parabens; lotion and phenols; and perfume and phthalates.

Conclusion: More rigorous studies on the exposure to chemicals found in PCPs among youth are needed to document the relative importance of PCP use with regard to total chemical exposure. Moreover, uniformity throughout data collection questionnaires may help to reduce heterogeneity between study findings.

Keywords : personal care products, parabens, phenols, phthalates, perfluoroalkyl substances, polyfluoroalkyl substances, children, adolescents, exposure

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17β-HSD1: 17β-hydroxysteroid dehydrogenase 1

17β-HSD2: 17β-hydroxysteroid dehydrogenase 2

BPA: Bisphenol A

BPF: Bisphenol F

BPS: Bisphenol S

CNS: Central nervous system

DNA: Deoxyribonucleic acid

EDC: Endocrine-disrupting chemical

EGF: Epidermal growth factor

ERα: Estrogen receptor alpha

ERβ: Estrogen receptor beta

FSH: Follicle stimulating hormone

GnRH: Gonadotrophin hormone

IGF-1: Insulin-like growth factor-1

LH: Luteinizing hormone

PCP: Personal care product

PFAS: Per- and polyfluoroalkyl substances

PFOA: Perfluorooctanoate

PFOS: Perfluorooctane sulfonate

T3: Triiodothyronine

T4: Thyroxine

TSH: Thyroid-stimulating hormone

To Aurko, in loving memory

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I
Introduction

1.1 Context

The creation and application of chemicals has increased in exponential manner since the Industrial Revolution. As of 2019, it was estimated that 28,000 chemical substances were listed in the Canadian Domestic Substances List and that a total of 85,000 chemicals were available for sale in the United States (United Nations Environment Programme (UNEP), 2019). Thus, in our modern lifestyle, the use of chemical-based products on a daily basis is far from uncommon. Indeed, both occupational and non-occupational environments possess numerous sources of chemical exposure, among which many are of domestic origin such as furniture, electronic products, pesticides, household cleaning products, and personal care products (PCPs) (Rudel & Perovich, 2009; Zota et al., 2017). Lately, the PCPs market has been growing and trending more strongly with a rise in popularity of skincare, self-care and beauty products, through social media content creators (*i.e.,* influencers) is noticeable in all regions across the globe (Garcia, 2019; Hadero & D'innocenzio, 2022; Mohatarem, 2021; Wang & Lee, 2021).

PCPs contain a broad-spectrum of chemicals that humans are exposed to during use. While chemicals provide several advantages, they are often the culprits behind adverse effects on human health. An important group of frequent PCPs users are children and adolescents. In 2016, 80% of the population aged 9 to 11 years were reported to use beauty products and PCPs in the United States (Mintel Press Office, 2016). In total, 90% of American girls aged 9 to 17 years used beauty products (Mintel Press Office, 2016). In boys, the percentage for beauty product use was of 69% (Mintel Press Office, 2016). Therefore, exposure to chemicals within this population group is evident. At present, such data is not available for the Canadian population.

The transition from childhood to adulthood is one characterized by adolescence, which is a phase distinguished by various behavioural and physiological changes in development (Alberga et al., 2012). Moreover, the phenomenon of puberty takes place during adolescence, initiating a myriad of developmental processes that occur throughout several years (Lucaccioni et al., 2020). Due to these facts, the period of adolescence could be a critical window of exposure and vulnerability. Recent studies have reported the presence of chemicals in PCPs (Martín-Pozo et al., 2021; Vindenes et al., 2021; Whitehead et al., 2021) and others have also proposed the period of adolescence as a period of vulnerability to environmental exposures (Shoaff et al., 2020).

To our knowledge, there is a lack of existing review highlighting the exposure to chemicals found in PCPs among youth. Knowing that PCP use is common among children and adolescents, and that this population group may be more at risk to potential toxic effects of chemicals, it is imperative to understand their exposure to chemicals through the use of PCPs. For this reason, in the present thesis we will conduct a scoping review compiling published studies that have aimed to investigate childhood and adolescent exposure to chemicals belonging to four primary families through PCP use: parabens, phenols, phthalates, and per- and polyfluoroalkyl substances (PFAS). By doing so, this thesis will contribute to knowledge on exposure to chemicals through PCP use in children and youth.

1.2 Thesis Structure

Following this first chapter, this thesis will begin with a literature review on PCPs and their definition; the description of the chemical families of parabens, phenols, phthalates, and PFAS; the concept of developmental windows of vulnerability; a brief overview of children and adolescents' PCP use patterns; the existing regulations related to the studied chemicals; and the relevance of redacting a scoping review on childhood and adolescent exposure (Chapter 2). Next, the objective (Chapter 3) and the methodology followed (Chapter 4) to draft the scoping review will be explained. To continue, research results will be presented in the form of a scoping review (Chapter 5), followed by a general discussion of the results, the strengths and limitations of the research conducted, the implications for future research (Chapter 6), and a conclusion (Chapter 7).

II
Literature Review

2.1 Personal Care Products

PCPs are known to be domiciliary products used for beautifying, grooming, cleaning, and maintenance of personal hygiene (Lang et al., 2016; Montes-Grajales et al., 2017). This category of products includes soaps, shampoo, cosmetics, fragrances, lotions, toothpaste, hair dyes, deodorants, and an array of other skin care products (*e.g.,* sunscreens, face cleansers, and more) (Harikishore Kumar Reddy, 2017; Khalid & Abdollahi, 2021; Lang et al., 2016). In Canada, PCPs are categorized into three groupings for regulation purposes: drugs, cosmetics, and natural health products (Lang et al., 2016). Different categories of PCPs, their description, examples of products, and regulations are summarized in Table I below.

A vast majority of the chemicals in PCPs are known to possess the potential to perturb the human endocrine system, thus naming them as endocrine-disrupting chemicals (EDCs). As per the U.S. Environmental Protection Agency, EDCs are exogenous chemical compounds (or chemical mixtures) that can disrupt the production, elimination, release, transport, metabolism, or receptor binding action of the human body's natural hormones known to participate in upholding homoeostasis and in important developmental and behavioural processes (Kabir et al., 2015; Lauretta et al., 2019). Exposure to EDCs are possibly associated with increased risk of asthma, allergies (Raley et al., 2021), cancer, diabetes, obesity, reproductive issues (De Coster & van Larebeke, 2012; Rachoń, 2015), and adverse behavioural and cognitive outcomes (Engel et al., 2010; Miodovnik et al., 2011). In addition, EDCs have the potential to negatively impact stages of development in exposed individuals (Predieri et al., 2022). Knowing that the chemicals contained in PCPs are absorbed by the body following use, despite the products being designed to be used externally (Harikishore Kumar Reddy, 2017), exposure to chemicals through the use of PCPs can lead to significant risks for the human health and contribute to the development of diseases.

2.1.1 Existing Regulations in Canada

As stated previously, for regulation related purposes, PCPs are categorized as either drugs, cosmetics, or natural health products in Canada (Lang et al., 2016). The Food and Drugs Act is categorized into three types of regulations which apply to PCPs: the Cosmetics Regulations, the Natural Health Products Regulations, the Food and Drug Regulations (Government of Canada, 2020). Cosmetics are defined as "any substance or mixture of substances, manufactured, sold or represented for use in cleansing, improving or altering the complexion, skin, hair or teeth and includes deodorants and perfumes." according to the Food and Drugs Act and are required to comply with the criteria in the Food and Drugs Act and the Cosmetic Regulations (Government of Canada, 2021). Drugs are defined as:

> … Any substance or mixture of substances manufactured, sold or represented for use in (a) the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state, or its symptoms, in human beings or animals, (b) restoring, correcting or modifying organic functions in human beings or animals, or (c) disinfection in premises in which food is manufactured, prepared or kept; (Health Canada, 2008, p. 2)

This category of products comprises non-prescription and prescription pharmaceuticals (Government of Canada, 2022b). Natural health products are "a subset of drugs pertaining to medicinal ingredients of natural origin … " as defined by Health Canada (2008). Products such as creams, ointments, herbal remedies, homeopathic medicines, and vitamins and minerals can be categorised as natural health products (Government of Canada, 2016). Other PCPs such as antiperspirants, facial products, mouthwashes, shampoos, and toothpastes may also be natural health products (Government of Canada, 2016).

Cosmetics and cosmetic ingredients are covered by the Cosmetic Regulations (Government of Canada, 2021). Along with the Food and Drugs Act, this regulation demands that the production, preparation, and storage of cosmetic products for sale are fulfilled in a sanitary setting (Government of Canada, 2021). Moreover, this regulation demands that the ingredients found in a cosmetic product be registered in a list by the manufacturer or importer (Government of Canada, 2021). Manufacturers must also inform Health Canada of the cosmetics products they are selling (Government of Canada, 2021). According to Health Canada, other regulations may concern cosmetics such as the Consumer Packaging and Labelling Act and the Canadian Environmental Protection Act (Government of Canada, 2021). In addition to this, cosmetic ingredients that are banned or restricted are registered in the Cosmetic Ingredient Hotlist which is used by Health Canada (Government of Canada, 2022a). In summary, cosmetics are covered by different overlapping regulations.

Although regulation categories exist in Canada, a specific PCP may be regulated differently depending on its ingredients, purpose, and use (Government of Canada, 2022d). For example, a sunscreen may be considered as either a cosmetic, a natural health product, or even a non-prescription medication depending on its description (Government of Canada, 2022d). In the event that a PCP cannot be classified as only a cosmetic or a drug, it is considered as a product at the cosmetic-drug interface (Government of Canada, 2022c). To categorize such products, Health Canada uses a guidance document for purpose to aid regulators in their decision-making, along with other existing regulatory references (Government of Canada, 2022c).

Table I. Personal care product categories with their description, product examples, and regulation

Category	Description	Product Examples	Regulation
Bath, Shower, Hair and Soap Products	Includes products used for bathing or showering, handwashing, grooming, hair styling, hair caring, and hygienic purposes.	After-shave Bar soap Body wash Cleansing gel or cream Conditioner Face gel Face wash Hair balm Hair bleach Hair dye Hair gel Hair serum Hair spray Hand sanitizer Hand wash Liquid soap Mouthwash Shampoo Shaving cream Shower gel	The Food and Drugs Act, which includes (Government of Canada, 2020) : - The Cosmetics Regulations - The Natural Health Products Regulations - The Food and Drug Regulations A PCP may be regulated differently depending on its ingredients, purpose, and use (Government of Canada, 2022d).
Fragrances, Perfumes, and Deodorant	Includes products that possess a distinctive, typically pleasant scent used to mask unwanted odor or to impart a clean scent.	Cologne Deodorant (stick, spray) Eau de toilette Essential oils Fragrance Perfume	
Lotions, Creams, Sunscreen and Toothpaste	Includes products used to moisturize skin (lotions and creams), to protect skin from ultraviolet rays (sunscreen), and to promote oral hygiene (toothpaste).	Body lotion Cream Eye cream Face cream Hand cream Moisturizer Sunscreen Toothpaste	
Makeup and Cosmetic Products	Includes products used for beauty enhancing purposes.	Coloured cosmetics Eye makeup Face makeup Lip balm Lip makeup Lipstick Nail polish Nail products Skin care cosmetics Skin makeup	

2.2 Chemical Families

Four major families of synthetic chemicals that are commonly found in the composition of PCPs: parabens, phenols, phthalates, and PFAS. In this section, a description of each family and their practical properties, toxicological properties, and toxicokinetics will be discussed. In connection with this section, a table containing the chemical structure and general characteristics of some of the most common compounds of each chemical family will be found at the end of the chapter (Tables II to V).

2.2.1 Parabens

The aliphatic esters of *para*-hydroxybenzoic acid are the compounds known as parabens (Petric et al., 2021). Parabens can be found naturally in the environment and are secreted by many plants and microorganisms (Nowak et al., 2018). Although, parabens found in products of commercial purpose are synthetically created (Genuis et al., 2013). These compounds have the ability to work over a large pH margin and are also known to have good stability (Petric et al., 2021). Additionally, parabens have no odour or taste and have a low financial cost (Askari & Warshaw, 2006). Within this chemical family, methyl paraben, ethyl paraben, propyl paraben, and butyl paraben are the most frequently used in PCPs (Petric et al., 2021). Since the 1920s, parabens have been incorporated in cosmetics, and even food, as preservatives in order to prevent the development of microorganisms in the products (Nowak et al., 2018). They are added as preservatives in PCPs as well (Kirchhof & de Gannes, 2013). However, some studies have raised concerns over the potential toxicity resulting from the exposure to this family of chemicals (Nowak et al., 2018). Structure and general characteristics of some of the most common parabens are found in Table II, at the end of this chapter.

2.2.1.1 Practical Properties of Parabens

Parabens possess antimicrobial activity, and this activity is known to improve as the alkyl chain of their structure gets longer (Petric et al., 2021). Indeed, it is likely that the secretion of parabens by plants protect them by preventing the development of bacteria, fungi, moulds, and yeasts (Nowak et al., 2018; Soni et al., 2005). Thus, this practical antimicrobial property explains the use of parabens as preserving agents in PCPs to prevent spoiling and to enhance shelf life and quality.

2.2.1.2 Toxic Properties of Parabens

The exposure to parabens can potentially have a negative impact on human health and various health issues have been linked to this family of synthetic chemicals. Indeed, parabens possess endocrine-disrupting properties and were reported to perturb the activities of steroidal sex hormones (Nowak et al., 2018). The principal sex hormones are testosterone, estrogen, and progesterone, all present in both men and women. Testosterone is the principal male sex hormone, whereas estrogens and progesterone are the two principal female sex hormones. Together, these hormones are involved in several physiological phenomena, including reproduction (Gildner, 2021). Parabens have the ability to imitate estrogens through their estrogenic activity (Nowak et al., 2022). Indeed, parabens copy endo-estrogens through their capacity to bind to estrogen receptors alpha (ERα) and beta (ERβ) (Nowak et al., 2022). In consequence, parabens compete with estrogens to bind ERα and ERβ (Okubo et al., 2001). Studies suggested that binding affinity of parabens augmented with increasing length of alkyl chains and increasing branching (Błędzka et al., 2014; Boberg et al., 2010; Okubo et al., 2001).

Parabens can also interfere with the activity of enzymes. Specifically, parabens can hinder the activities of 17β-hydroxysteroid dehydrogenase 1 (17β-HSD1), an enzyme that activates estrogen, and 17β-hydroxysteroid dehydrogenase 2 (17β-HSD2), an enzyme that deactivates estrogen (Engeli et al., 2017). The enzymes 17β-HSD1 and 17β-HSD2 participate in steroidogenesis – the process of steroid hormone production (Miller & Auchus, 2011) – and are integral to maintaining a hormonal balance between highly active and weakly active estrogens (Engeli et al., 2017). In addition, Prusakiewicz et al. (2007) have reported that parabens can inhibit the activity of estrogen sulfotransferases, which are enzymes expressed in the skin. Thus, parabens are suspected of having anti-androgenic (Nowak et al., 2018; Özdemir et al., 2018) and estrogenic properties (Engeli et al., 2017), in consequence disrupting sex hormones' activity.

Parabens may disrupt the functioning of thyroid hormones (Liang et al., 2022) as well. Thyroid hormones thyroxine (T4) and triiodothyronine (T3) are produced by the thyroid gland. Iodine – an indispensable element for thyroid hormones – and the pituitary gland's production of thyroid-stimulating hormone (TSH) are responsible of controlling thyroid hormones' production

(Nowak et al., 2018), among other processes. Thyroid hormones are key participants in processes such as metabolism of proteins, neural development, and brain function among many others (Mondal et al., 2016).

2.2.1.2.1 In vitro Studies on Parabens

An *in vitro* study that conducted a yeast estrogen screen has shown that the assay allowed to demonstrate the estrogenic activity of methyl, ethyl, propyl, and butyl paraben (Routledge et al., 1998). However, their estrogenicity was much weaker than estradiol's (an estrogen) (Routledge et al., 1998). The least estrogenically active paraben – methyl paraben – had an estrogenic potency that was 2,500,000 times weaker than estradiol (Routledge et al., 1998). The paraben with the strongest estrogenicity – butyl paraben – had a estrogenic potency that was 10,000 weaker than estradiol (Routledge et al., 1998).

Parabens may also affect thyroid hormones and their receptors. A study that has investigated parabens' effect on thyroid receptors through an *in vitro* assay using GH3 cells – which are rat pituitary tumour cells (van den Brand et al., 2019) – found that methyl, ethyl, propyl, and butyl paraben all exerted agonistic effects (Liang et al., 2022). Another study has shown through an *in vitro* assay that butyl paraben acted as a weak thyroid hormone receptor agonist, thus increasing GH3 cell proliferation (Taxvig et al., 2008).

2.2.1.2.2 Animal Studies on Parabens

In vivo studies have reported impacts on estrogenicity and androgenicity following paraben exposure. In male rats, sperm count and testosterone concentrations were reported to have decreased following exposure to propyl paraben and butyl paraben (Oishi, 2001; Oishi, 2002). In female Sprague-Dawley rats that were orally given different parabens daily (62.5, 250, and 1000 mg/kg body weight/day), it was reported that the onset of the vaginal opening phenomenon occurred late when given 1000 mg/kg body weight/day of methyl paraben for instance (Vo et al., 2010).

Parabens may also exert endocrine effects on thyroid hormones. One study reported that exposure to parabens in zebrafish had perturbed the production of thyroid hormones which led to negative effects on the embryos and larvae, thus affecting the early development of zebrafish (Liang et al., 2022). The exposure to parabens also had an impact on the expression of genes in the hypothalamic-pituitary-thyroid axis (Liang et al., 2022). Thyroid hormone levels also decreased following paraben exposure (Liang et al., 2022). Differently, an *in vivo* study conducted on Wistar rats reported that ethyl and butyl paraben did not have any effect on T3 and T4 levels (Taxvig et al., 2008).

Regarding other effects of paraben exposure, a study has found that parabens were involved in adipocyte differentiation in mice and that this ability increased with longer alkyl chain length, meaning this chemical family could play a role in obesity (Hu et al., 2013). Behavioural changes and developmental abnormalities in zebrafish following ethyl paraben and butyl paraben exposure were reported in another study (Merola et al., 2020).

2.2.1.2.3 Human Studies on Parabens

A study on female university students in Japan (n=128) has shown that exposure to parabens decreases the duration of the menstrual cycle (Nishihama et al., 2016). In consequence, the study suggests that parabens may be involved in infertility among females (Nishihama et al., 2016). A different study investigating the impact of paraben exposure on the ovarian reserve of women attending an infertility clinic in Poland (n=511) has reported a decrease of estradiol following the exposure to propyl paraben (Jurewicz et al., 2020). The authors suggested that long-term exposure to propyl paraben may be involved in fecundity and fertility issues (Jurewicz et al., 2020). Another study in which participants were 156 men attending a fertility clinic has found a positive association between exposure to parabens and sperm disomic for chromosomes (Jurewicz et al., 2017). Thus, such results suggest that exposure to parabens may lead to reproductive issues in women.

In concern with parabens' disruption of thyroid hormones, a study on 454 pregnant women found an association between increasing propyl paraben exposure and decreasing TSH (Berger et al., 2018). In another study also including pregnant women (n=106), it was shown that as butyl paraben exposure increased, maternal free T4 concentrations increased as well (Aker et al., 2018). This study also found that propyl paraben exposure decreased maternal free T4, and methyl paraben increased total T4 in mothers (Aker et al., 2018). A cross-sectional study involving 1,831 individuals has found a negative association between paraben exposure and thyroid hormone concentrations in adults, mainly in adult women (Koeppe et al., 2013).

2.2.1.3 Toxicokinetics of Parabens

Frequent and widespread use of parabens means human exposure is common. As PCPs are designed to be utilized externally (Harikishore Kumar Reddy, 2017), parabens contained in products are absorbed dermally after product application (Seo et al., 2017). According to an *in vitro* study, when propyl paraben was applied on rat skin, 30% penetrated the skin unaltered (Bando et al., 1997). Another *in vitro* study reported that 60% of methyl paraben, 40% of ethyl paraben, and 20% of propyl paraben penetrated rabbit skin following eight hours of contact with the skin (Pedersen et al., 2007). For human skin samples (epidermis-dermis layers, 36 hours following body lotion application), 0.057% of methyl paraben, 0.045% of ethyl paraben, 0.028% of propyl paraben, and 0.007% of butyl paraben had permeated in skin (El Hussein et al., 2007).

Following their absorption, parabens are metabolized by first undergoing hydrolysis performed by esterases (Seo et al., 2017) and are converted to *para*-hydroxybenzoic acid, thus summarizing the first phase of their biotransformation (Nowak et al., 2018). Afterwards, glucuronidation is performed by UDP-glucuronosyltransferase enzymes in the liver, therefore allowing the conjugation to sulfate, glucuronide, or glycine during this second phase of parabens biotransformation (Abbas et al., 2010; Nowak et al., 2018).

The conjugated metabolites of parabens are then excreted through urine and bile (Boberg et al., 2010). In blood and urine, it is generally unlikely to detect unaltered parabens and more common to detect metabolites of parabens (Boberg et al., 2010). Regarding excretion, Moos et al. (2016) has reported lower urinary excretion of parent parabens with a longer alkyl chain. It is reported that 17.4% of methyl paraben, 8.6% of propyl paraben, and 5.6% of butyl paraben were excreted in their free or conjugated forms – *i.e.,* unchanged – in human urine following oral intake, for instance (Moos et al., 2016; Shin et al., 2019).

Parabens' half-life in humans is less than 24 hours, which indicates that they are metabolized quickly (Leppert et al., 2020).

2.2.2 Phenols

Phenols are chemical compounds composed of a benzene ring which is substituted with at least one hydroxyl (–OH) group (Issaoui et al., 2020). It is possible to find compounds of this chemical family in plants and medicinal herbs, as well as essential oils (Floris et al., 2021; Huang et al., 2010). Phenolic compounds found in nature are known for their ability to prevent bacterial growth (Floris et al., 2021). However, most phenols used commercially in PCPs are manufactured industrially, some of the most common being triclosan and benzophenone-3 (Vindenes et al., 2021). In addition, bisphenols such as bisphenol A (BPA), bisphenol F (BPF) and bisphenol S (BPS), are also used in the production of several PCPs (Dodson et al., 2020; Fisher et al., 2019; Liao & Kannan, 2014). The chemical family of phenols is one of growing concern because it is composed of substances suspected to be EDCs and numerous studies have suggested that the exposure to phenols is harmful to humans' health , as better explained in the next sections. Structure and general characteristics of some common phenols are presented in Table III, at the end of this chapter.

2.2.2.1 Practical Properties of Phenols

Phenols are commonly used in consumer products and PCPs because of their antibacterial property. It is due to its antibacterial activity that triclosan is found in several products such as deodorants, hand soap, and toothpaste (Dodson et al., 2020) and acts as a microbicide (Nakiwala et al., 2020). Benzophenone-3, also known as oxybenzone, is a phenol incorporated in products as an ultraviolet radiation filter (Dodson et al., 2012; Nakiwala et al., 2020). Thus, it is commonly found in sunscreens, cosmetics, and various other PCPs (Wnuk et al., 2022). As for bisphenols, they are detected in PCPs primarily because of contamination by product packaging containing bisphenols (Lu et al., 2018). In fact, materials like polycarbonate plastics and epoxy resins are composed of bisphenols (Nakiwala et al., 2020).

2.2.2.2 Toxic Properties of Phenols

Exposure to substances in the chemical family of phenols may be detrimental to human health. Phenols are suspected of modulating steroidal sex hormones and thyroid hormones (Aker et al., 2016; Le Fol et al., 2017; Yang et al., 2016; Yoon & Kwack, 2021) and possessing estrogenic and anti-androgenic potencies (Le Fol et al., 2017; Yang et al., 2016; Yoon & Kwack, 2021). Phenol exposure was also reported to disrupt thyroid hormones' (Kim & Park, 2019). Since phenols are incorporated in a wide range of PCPs, their potential health toxicity is concerning.

2.2.2.2.1 In vitro Studies on Phenols

A study has reported that different phenols' were capable of activating various hormone receptors by using recombined yeast strains for their investigation (Li et al., 2010). For instance, BPA was reported to be an agonist of ERα and 2,4-dichlorophenol was found to be an antagonist for androgen receptor (Li et al., 2010).

Other *in vitro* studies have assessed the estrogenic activity of BPS and BPF. The estrogenic and androgenic activity of BPF was reported in many in vitro experiments (Molina-Molina et al., 2013; Rosenmai et al., 2014; Satoh et al., 2004). Several studies reported that BPS possessed lower estrogenicity than estradiol following assays realised with nuclear receptor models (Grignard et al., 2012; Molina-Molina et al., 2013; Teng et al., 2013). Molina-Molina et al. (2013) have also reported in their study that BPS exerted androgenic potency. Through an assay using modified human osteosarcoma cells, one study reported that both BPF (luminescence value of 125.48 ± 23.94%) and BPS (luminescence value of 98.74 ± 12.07%) have estrogenic potency that is weaker than that of BPA (luminescence value of 137.21 ± 16.62%) (Shao et al., 2021). Luminescence values were relative to estradiol's maximum activity, which represented the value of 100% (Shao et al., 2021).

For other phenols, triclosan's estrogenicity was shown through *in vitro* assay results of some studies (Huang et al., 2014; Yoon & Kwack, 2021) and benzophenone-3 was reported to be an antagonist of the estrogen receptor and androgen receptor as a result *in vitro* assays as well (Molina-Molina et al., 2008; Schreurs et al., 2005). One study has also shown that benzophenone-3 acts as an agonist towards the thyroid receptor *in vitro* (Schmutzler et al., 2007).

2.2.2.2.2 Animal Studies on Phenols

Studies conducted on mice have reported that BPA exposure decreased sperm production (Tainaka et al., 2012) and sperm motility (Rahman et al., 2017; Tainaka et al., 2012). Similarly in rats, a study found that exposure to BPA reduced sperm production and motility (Tiwari & Vanage, 2013). According to this study, an increase in damages in rat sperm DNA was observed following exposure to BPA (Tiwari & Vanage, 2013). Another animal study has shown that BPS exerted estrogenicity in rats following exposure for three days (Yamasaki et al., 2004). One study exposing neonatal female rats to BPA and BPS reported alterations in folliculogenesis, and infertility in adult female rats (Ahsan et al., 2018).

Phenol exposure can affect thyroid hormones as well. For both BPF and BPS, a study found that they alter T4 and T3 concentrations in zebrafish (S. Lee et al., 2019). In rats, exposure to BPF lowered T3 levels and increased T4 levels (Higashihara et al., 2007). In zebrafish, decreases in gonad weight were noticed following the exposure to BPS (Ji et al., 2013). BPA can act as an antagonist of the thyroid hormone receptor and be capable to bind to this receptor (Kim & Park, 2019) and exposure to triclosan was shown to reduce total serum T4 in a dose-dependent fashion in rats (Zorrilla et al., 2009).

2.2.2.2.3 Human Studies on Phenols

In humans, a study involving men (n=191) who attended a clinic for assisted reproduction reported that spermatozoa number and motility were adversely affected by BPA in semen (Vitku et al., 2016). Triclosan exposure was also linked to lesser quality of sperm and atypical sperm morphology according to a study involving Polish males attending an infertility clinic (n=315) (Jurewicz et al., 2018). In women undergoing fertility treatment (n=209), exposure to BPA was linked with follicle loss according to one study (Souter et al., 2013). BPA exposure was also associated with a reduction in estradiol levels and in the amount of typically fertilized oocytes among 174 women undergoing in vitro fertilization (Ehrlich et al., 2012). Not all studies have found associations between BPA exposure and adverse reproductive health effects. In fact, one study on 1,742 women in their first trimester of pregnancy found no association between BPA and decrease of fecundity (Vélez et al., 2015). However, this study did report an association between triclosan exposure and decrease in fecundity among 1,699 pregnant women in their first trimester (Vélez et al., 2015).

Regarding thyroid hormones, a cross-sectional study involving 2,340 adults has reported, only in men, a negative correlation between BPA exposure and serum concentrations of free (Sriphrapradang et al., 2013). Another study (n=3,394) reported that a high urinary BPA concentration was linked to increased thyroid function (Wang et al., 2013). This study equally reported that, in men and women, high urinary BPA was associated with higher serum free T3 and lower serum TSH (Wang et al., 2013). A study on pregnant women (n=439) (Aker et al., 2018) and a study on women attempting to obtain medically assisted reproduction (n=317) (Skarha et al., 2019) reported that triclosan exposure was inversely associated with T3 and T4 concentrations. For benzophenone-3, one study found that the chemical was negatively associated with T3 and T4, but positively associated with TSH (Aker et al., 2018).

2.2.1.3 Toxicokinetics of Phenols

Bisphenols, such as BPA, can be absorbed dermally in the event of a direct contact with human skin (Toner et al., 2018). A study using an *in vitro* method has shown that 8.6% of the applied BPA dose penetrated human skin after 24 hours (Demierre et al., 2012). Another study using human skin reported that the percutaneous absorption of BPA is of 1.7–3.6% after 24 hours (Toner et al., 2018).

In humans, metabolization of bisphenols involve glucuronidation and sulfation (Durcik et al., 2022). For instance, when metabolized in human skin, BPA is converted into BPA-glucuronide and BPA-sulfate during the second phase of biotransformation (Toner et al., 2018; Zalko et al., 2011). In general, for mammals, the metabolization of BPA also involves glucuronidation by UDP-glucuronosyltransferases to produce BPA-glucuronide and sulfation to produce BPA-sulfate (Jalal et al., 2018).

Following their metabolization, bisphenols are excreted in urine (Y.-X. Wang et al., 2019). In fact, it has been shown that after its metabolization, BPA metabolites are eliminated via the urine in humans (Jalal et al., 2018). One human study has shown that, following dermal exposure, 0.71-8.3% of free BPA was found in urine (Liu & Martin, 2017). In the general Canadian population, urinary total BPA concentration was reported to be 1.1 μg/L, for example (geometric mean) (Health Canada, 2015).

For triclosan and benzophenone-3, the substances undergo hydroxylation during the first phase of biotransformation followed by glucuronidation and sulfonation during the second phase of biotransformation (Wang & Kannan, 2013; Wu et al., 2010). Triclosan and benzophenone-3 are principally eliminated through urine as well (Sandborgh-Englund et al., 2006; Wang & Kannan, 2013).

Half-lives of phenols vary. For example, triclosan's half-life specific to urinary excretion was of 11 hours (Sandborgh-Englund et al., 2006). Following oral exposure in humans, the urinary excretion half-life of BPA ranged from 1 to 3 hours (Thayer et al., 2015) and the terminal half-life of BPS was of around 6 hours (Oh et al., 2018).

2.2.3 Phthalates

The esters of phthalic acid are the substances more commonly known as phthalates and are synthetic chemicals widely used as plasticizers (Koniecki et al., 2011). This chemical family is composed of low-molecular weight phthalates and high-molecular weight phthalates (Pagoni et al., 2022). These substances are included in PCPs to increase the products' lifespan and offer stability (Pagoni et al., 2022). In addition, phthalates are added to plastics because to improve pliability and softness (Karačonji et al., 2017). Phthalates can be found in PCPs that have plastic packaging (Wang & Qian, 2021) and more precisely in creams, lotions, cosmetics, hair products, nail polish, baby diapers, and feminine hygiene products, to name a few (Pagoni et al., 2022). Phthalates that can be found in PCPs are dimethyl phthalate, diethyl phthalate, di-*n*-butyl phthalate (dibutyl phthalate), and di-isobutyl phthalate (Parlett et al., 2013). For instance, dimethyl phthalate can be found in hair products, whereas dibutyl phthalate can be found in nail polishes (Wang & Qian, 2021). In addition to this, dibutyl phthalate and diethyl phthalate, are used in fragrances and to promote colour maintenance (Parlett et al., 2013). As for di-isobutyl phthalate, it is mainly used as a plasticizer (Wang & Qian, 2021). Since phthalates do not form chemical bindings with the plastics they are added to, they can easily evaporate or migrate off of the material (Karačonji et al., 2017). Despite the usefulness of plastics, phthalates are suspected to have endocrine-disrupting potency and have been linked to adverse health effects such as reproductive disorders (Hlisníková et al., 2020). Structure and general characteristics of a few common phthalates are presented in Table IV, at the end of this chapter.

2.2.3.1 Practical Properties of Phthalates

Phthalates are primarily used for their plasticizing properties. For instance, phthalates – such as di-2-ethylhexyl phthalate (Ramadan et al., 2020) – are added to plastics known as polyvinyl chloride as softeners (Wang & Qian, 2021). Other phthalates, such as diethyl phthalate and dibutyl phthalate are added to PCPs as solvents to make scents and colours durable (Cao, 2010).

2.2.3.2 Toxic Properties of Phthalates

Phthalates exert multiple adverse effects on human health and have been labelled as EDCs. It has been suggested that the chemicals of this family have estrogenic and anti-androgenic potencies, like many other EDCs (Chen et al., 2014; De Falco et al., 2015). This means that phthalates are capable of imitating estrogens (Morgan et al., 2017) and can also behave as antiandrogens (Hlisníková et al., 2020). In fact, phthalates are known to impact hormone receptors' activities by activating estrogen receptors ERα and ERβ, and inhibiting the androgen receptor (Engel et al., 2017). Phthalate exposure can also alter thyroid hormone concentrations (Meeker & Ferguson, 2011). With such impact on hormones, exposure to phthalates may increase the risk of onset of several health disorders.

2.2.3.2.1 In vitro Studies on Phthalates

A study using luciferase reporter gene assays found that dibutyl phthalate, mono-butyl phthalate, and di-2-ethylhexyl phthalate exerted antiandrogenic potency, and androgenic potency (Shen et al., 2009). Using *in vitro* techniques to study phthalates' estrogenic activity – such as estrogen receptor competitive ligand-binding, as well as mammalian and yeast-based analyses – one study found that the metabolites of di-butyl phthalate were weakly estrogenic (Zacharewski et al., 1998). Results from a different *in vitro* assay performed in this study showed that dibutyl phthalate exerted a weak estrogenic activity (Shen et al., 2009). Another study has shown that butyl benzyl phthalate and dibutyl phthalate exert estrogenicity *jn vitro* and were reported to provoke estrogen receptor transactivity (Ghisari & Bonefeld-Jorgensen, 2009).

Phthalates were equally reported to exert activity similar to that of thyroid hormones, as reported by one study (Ghisari & Bonefeld-Jorgensen, 2009). Dibutyl phthalate, mono-butyl phthalate, and di-2-ethylhexyl phthalate were also reported to act as antagonists towards thyroid receptors (Shen et al., 2009). Additionally, phthalates may induce alterations in the uptake of iodine by thyroid follicular cells, which can change the concentration of thyroid hormone T4 in consequence (Breous et al., 2005; Wenzel et al., 2005). A study that used a thyroid receptor gene assay using an African clawed frog cell line reported that benzyl butyl phthalate, dibutyl phthalate and di-2-ethylhexyl phthalate acted as antagonists for T3 (Sugiyama et al., 2005).

2.2.3.2.1 Animal Studies on Phthalates

Phthalate exposure may alter steroid sex hormone levels and lead to reproductive issues. For instance, in rats, a study reported that di-2-ethylhexyl phthalate exposure led to higher serum testosterone and estradiol levels (Akingbemi et al., 2004). One study reported that maternal di-2-ethylhexyl phthalate exposure in mice has decreased viability of sperm by 20%, daily production of sperm had by 30%, and epididymal sperm count by 70% in adult male offspring mice (Fiandanese et al., 2016). In female rats chronically treated with dibutyl phthalate from weaning to pregnancy, litter size decrease was associated with lower serum progesterone concentrations when the examination of females took place during gestational day 13 (Gray et al., 2006). The exposure to dibutyl phthalate perturbed the development of reproductive organs in male rats, along with a reduction in fertility (Mahood et al., 2007) and the apparition of benign tumours in Leydig cells (Mylchreest et al., 2002), which are cells known to produce androgens like testosterone (Zirkin & Papadopoulos, 2018).

Among Sprague-Dawley rats, exposure to di-2-ethylhexyl phthalate decreased T3 and T4 concentrations (C. Liu et al., 2015). This study suggests that di-2-ethylhexyl phthalate exposure may negatively affect thyroid hormone biosynthesis and transport for instance (C. Liu et al., 2015). Adolescent male Sprague-Dawley rats exposed to di-2-ethylhexyl phthalate (0.75 and 150 mg/kg/day) has lower concentrations of serum T4 (Kim et al., 2021). In mice, maternal exposure to di-2-ethylhexyl phthalate decreased free T3 concentrations in the brain of male fetuses (Lv et al., 2022).

Among other adverse impacts, phthalate exposure altered heart rate and decreased length of the body from head to tail in zebrafish (H. Lee et al., 2019).

2.2.3.2.2 Human Studies on Phthalates

In humans, phthalates are reported to increase the concentrations of estrogens like estradiol, a change that can induce the appearance of reproductive health disorders in females (Hlisníková et al., 2020). A study has found that the exposure to several phthalates were linked to decreased concentrations of serum testosterone not only in males, but females as well (Meeker & Ferguson, 2014). In one study involving men consulting a fertility clinic (n=425), phthalate exposure reduced not only testosterone levels, but estradiol levels equally, thus showing phthalates' impact on sex hormones (Meeker et al., 2009). Phthalate exposure was reported to decrease testosterone concentrations in a study involving 1,768 adults (Zhu et al., 2022). This study also reported a positive association between mono(2-ethylhexyl) phthalate and estradiol levels (Zhu et al., 2022). One study reported that, among postmenopausal women (n=557), di-2-ethylhexyl phthalate exposure was associated with decreased concentrations of estradiol and testosterone (Long et al., 2021).

For thyroid hormones, a study (n=2,208) has shown that metabolites of di-2-ethylhexyl phthalate were inversely associated with total T4, free T4, and total T3 (Meeker & Ferguson, 2014).

This study also reported that reduced thyroid hormone concentrations were linked to one urinary metabolite of dibutyl phthalate, mono(3-carboxypropyl) phthalate (Meeker & Ferguson, 2014). One study involving 408 adult men found that urinary mono(2-ethylhexyl) phthalate concentration was negatively associated with serum free T4 and T3 (Meeker et al., 2007). In another study involving 509 men, a negative association was reported between urinary monoethyl phthalate concentration and serum thyroid hormone levels (Wang et al., 2018). In consequence, this result was related to altered semen quality (Wang et al., 2018). One study on pregnant women (n=76) reported a negative association between concentrations of T4 and free T4, and urinary mono-butyl phthalate concentration (Huang et al., 2007).

2.2.3.3. Toxicokinetics of Phthalates

PCPs containing phthalates that are used directly on the skin are absorbed (Pagoni et al., 2022). For example, a study conducted on hairless guinea pigs determined that 62% of the applied dose of dibutyl phthalate was absorbed 24 hours following dermal application (Doan et al., 2010). For human skin, one study either covered the skin with a Teflon cap or left it uncovered following application of diethyl phthalate (Mint et al., 1994). For uncovered human skin, the absorption of diethyl phthalate was of 4.8% of the applied dose following 72 hours (Mint et al., 1994).

Once phthalates are absorbed, they undergo hydrolyzation during their first step of biotransformation (Frederiksen et al., 2007; Wang & Qian, 2021). During the second phase of their biotransformation, enzymes such as the uridine 5'-diphosphoglucuronyl transferase initiates the conjugation reaction to produce a glucuronide conjugate (Frederiksen et al., 2007).

The conjugated form is later eliminated through urinary excretion (Frederiksen et al., 2007). In humans, following dermal application, 5.79% of diethyl phthalate and 1.82% of dibutyl phthalate were found in urine in the form of metabolites (Janjua et al., 2008). Furthermore, urinary concentrations of total (*i.e.,* free and conjugated forms) monoethyl phthalate for example was of 96.2 ng/mL in humans (n=269) (Meeker et al., 2012). A metabolite of di-(2-ethylhexyl) phthalate, mono-2-ethyl-5-carboxypentyl phthalate, had a urinary concentration of 21 ng/mL for the total of its free and conjugated forms (Meeker et al., 2012).

In general, phthalates are quickly eliminated following exposure (Basso et al., 2022). The biological half-life of phthalates lasts around 12 hours (Hoppin et al., 2002). However, our exposure to these phthalates is incessant due to their widespread environmental existence (Basso et al., 2022).

2.2.4 Per- and Polyfluoroalkyl Substances (PFAS)

Per- and polyfluoroalkyl substances (PFAS), also known as the "forever chemicals" (Cao & Ng, 2021), are manmade chemicals with one or several perfluorinated methyl groups ($–CF_3$) or perfluorinated methylene group ($–CF_2–$) (Panieri et al., 2022). This chemical family can be divided into two groups: the legacy PFAS and the emerging PFAS (Meegoda et al., 2020). Legacy PFAS have a chemical structure composed of a longer chain, whereas emerging PFAS are compounds composed of a smaller and are novel substitutes to the chemicals of the legacy chemicals (Meegoda et al., 2020; Nian et al., 2022). Legacy PFAS include perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) (Meegoda et al., 2020; Zhang et al., 2022). Emerging PFAS are composed of a short chain; an example is hexafluoropropylene oxide dimer acid (GenX) (Heidari et al., 2021). Chemicals of the PFAS family are found in various products, from foam used to suppress fires to PCPs (Ragnarsdóttir et al., 2022). PFAS have been linked to several health problems in humans (Fenton et al., 2021), therefore the exposure to this group of chemicals is of high concern. Structure and general characteristics of some PFAS can be found in Table V, at the end of this chapter.

2.2.4.1 Practical Properties of PFAS

PFAS are known for being greatly stable chemicals, resistant to chemical or thermal degradation (Panieri et al., 2022). Hence, PFAS have been largely utilized in chemical processes and as surfactants in the industry (Brase et al., 2021). In addition to this, PFAS have several other useful properties such as being waterproof, greaseproof, and non-stick (Pelch et al., 2019). Therefore, they are commonly applied to cookware to ensure they are non-stick (Ramírez Carnero et al., 2021).

2.2.4.2 Toxic Properties of PFAS

PFAS are highly persistent chemicals that are worrying for human health, despite the discontinuation of the production of several substances in this group (Brase et al., 2021). Indeed, these substances are reported to have endocrine-disrupting properties and interfere with humans' hormonal system (Kar et al., 2017). Inconsistent evidence exists regarding the effect of PFAS on hormones, but it has been reported that PFAS can disrupt estrogen and androgen receptors' activity (Du et al., 2013; Kjeldsen & Bonefeld-Jørgensen, 2013). PFAS have several toxic features such as hepatotoxicity (Fenton et al., 2021; Lin et al., 2022), immunotoxicity, and reproductive toxicity (Fenton et al., 2021). Additionally, the exposure to PFAS may be toxic to the thyroid (Kar et al., 2017).

2.2.4.2.1 In vitro Studies on PFAS

An *in vitro* study using a human androgen receptor mediated luciferase reporter gene assay reported that three of five studied PFAS possessed antiandrogenic activity and affected the testosterone-stimulated androgen receptor's activation (Tachachartvanich et al., 2022). For the same three PFAS, the study equally reported that they acted as competitive antagonists of the androgen receptor (Tachachartvanich et al., 2022). Another study investigating the estrogenicity of chemical compounds has reported that both PFOA and PFOS had estrogenic potency in different assays (Henry & Fair, 2013). Differently, both PFOA and PFOS were reported to not exert estrogenicity by a study that investigated the two PFAS's estrogenic activity on hormone-dependent breast cancer cells (Sonthithai et al., 2016).

In relation to thyroid hormones, an *in vitro* study reported that PFOS had an agonistic effect on the thyroid hormone receptor in rat pituitary cancer cells (Xin et al., 2018). A different *in vitro* study found that PFOA and PFOS diminished the activity of the enzyme thyroid peroxidase – which is essential in the synthesis of thyroid hormones – in human follicular thyroid carcinoma cells (Song et al., 2012).

2.2.4.2.2 Animal Studies on PFAS

PFAS exposure can affect sex hormone levels and may engender reproductive problems in animals. Indeed, exposure to PFOS was related to a decrease in testosterone concentrations in rodents (L. Li et al., 2018; López-Doval et al., 2014). In mice, spermatogenesis was disrupted, and sperm count was decreased following exposure to PFOA (W. Liu et al., 2015; Zhang et al., 2014). One study reported that PFOA can provoke estrogenic response in rainbow trout liver; however, the mechanism behind this phenomenon is not yet known (Tilton et al., 2008).

PFOS exposure in adult male rats lowered T4 and T3 concentrations, but TSH concentrations were not impacted (Davidsen et al., 2022). Another study reported that exposure to PFOS in

Sprague-Dawley male rats lowered serum concentration of total T4 (Yu et al., 2009). One study investigated the exposure to perfluorohexane sulfonate in rat dams and their offspring and reported a dose-dependent decrease in thyroid hormone concentrations (Ramhøj et al., 2020). In male cynomologous monkeys that were fed PFOA for 6 months, lower T3 and total T3 concentrations were reported among the group that was fed the highest doses (30 and 20 mg/kg/day) (Butenhoff et al., 2002).

Among other adverse effects, exposure to PFAS may alter the metabolism of hepatocytes and allow lipids to collect in the liver (Fenton et al., 2021). In rodents, toxicological studies have shown that PFAS exposure led to apoptosis, necrosis, and increase of hepatocytes (Fenton et al., 2021).

2.2.4.2.3 Human Studies on PFAS

Steroid sex hormones and their receptors are also affected by PFAS exposure. PFAS have been reported to exert anti-androgenic properties by obstructing the binding of testosterone to the human androgen receptor (Tachachartvanich et al., 2022). In recent studies, exposure to PFAS was linked to lower estradiol concentrations in females (Xie et al., 2021) and exposure to PFOA and PFOS was associated with lower free testosterone concentrations in males' semen (Cui et al., 2020). Differently, a cross-sectional study found that elevated concentrations of testosterone were correlated to high serum concentrations of PFOA in males (n=212) (Di Nisio et al., 2018). In children (n=2,292), a study reported that PFAS exposure lowers the concentrations of sex hormones (Lopez-Espinosa et al., 2016). Reproductive issues may develop following PFAS exposure. In women, reproductive hormone concentrations and fertility are negatively impacted by PFAS, among many other reproductive health effects (Rickard et al., 2022). Indeed, many studies showed that exposure to PFOA and PFOS was associated with polycystic ovary syndrome and infertility in women (Heffernan et al., 2018; Vagi et al., 2014; W. Wang et al., 2019). In a cross-sectional study involving 383 young men, exposure to PFOA and PFAS was linked to smaller size of the penis and decreased volume of testicles (Di Nisio et al., 2018). Additionally, PFAS exposure may lead to poorer semen quality (Di Nisio et al., 2018; Pan et al., 2019).

The synthesis of thyroid hormones is also impacted by PFAS exposure, altering the concentrations of these hormones (Coperchini et al., 2020). Moreover, exposure to PFOA and PFOS has been linked to the development of hypothyroidism (Coperchini et al., 2017), which causes a deficiency of thyroid hormone (McDermott, 2020). Occupational exposure to PFOA was negatively associated with free T4 levels and positively associated with T3 levels among 506 production workers from three different production sites according to one study (Olsen & Zobel, 2007). In contrast, a study investigating exposure to PFOA in an exposed community (n=371) did not find any association between serum PFOA concentration and residents with thyroid or liver disease history (Emmett et al., 2006). Another study involving workers of two different locations who were occupationally exposed found that PFOS concentration was positively associated with T3 concentrations according to a longitudinal analysis over six years of 174 male employees (Olsen et al., 2003).

PFAS exposure can equally increase cholesterol concentrations in the circulation and restrain the immunological response through several mechanisms, such as decreasing antibody concentrations (Fenton et al., 2021). Additionally, one cross-sectional study has reported that PFAS exposure in humans can engender lipids to infiltrate hepatocytes, a health disorder also known as steatosis, which may lead to non-alcoholic fatty liver disease (Bassler et al., 2019).

2.2.4.3 Toxicokinetics of PFAS

PCPs containing PFAS, such as mascara, can easily be absorbed by the body (Whitehead et al., 2021). For human skin, one study reported that following application around 24% of the applied PFOA dose permeated through skin samples after 24 hours (Franko et al., 2012). During their metabolism, PFAS generally undergo hydrolysis (Han et al., 2021). However, numerous PFAS are difficult to metabolize due to the several, very robust carbon and fluorine bonds they possess, conferring them a great chemical stability (Brase et al., 2021; Solan et al., 2022). In consequence, it seems that PFAS are not metabolized in tissues or in the liver, which lets the chemicals stay trapped in the body (Jeddi et al., 2022).

When PFAS are metabolized, they are principally eliminated through the urine (Jeddi et al., 2022). Although, PFAS can also be excreted in feces and breast milk, although in lesser quantities (Agency for Toxic Substances and Disease Registry, 2021).

The half-lives of PFAS vary between short chain and long chain PFAS. In humans, a study estimated that the half-life of PFOS is 3.4 years and the half-life of PFOA is 2.7 years, both in blood serum (Y. Li et al., 2018). Another study reported that the serum half-life for both PFOS and PFOA ranged between two and four years in humans (Xu et al.). The half-life of one short chain

PFAS, perfluoropentane sulfonic acid, was reported to last less than a year (Nicole, 2020). Two other short chain PFAS, perfluorobutanoic acid and perfluoroheptanoic acid, have half-lives of 0.12 years and 0.17 years, respectively (Nicole, 2020).

2.2.5 Biomonitoring

The use of biomonitoring in order to study the exposure to EDCs has evolved and is the gold standard for exposure assessment nowadays. However, it is a challenge to study exposure to certain chemicals due to the rapid metabolism of parent compounds. For example, this is the case for phthalate monoesters and phthalate di/esters (Calafat, 2016). Most biomarkers used for biomonitoring only allow to study recent, short-term exposure, making it challenging to assess exposures that are long-term and to chemicals with short half-lives (Arbuckle, 2010). In consequence, the exposure assessment of several chemicals is conducted by studying their metabolites' concentrations in biological matrices such as blood or urine which are the most commonly used for population-based studies in environmental epidemiology (Calafat, 2016).

2.3 Developmental Windows of Vulnerability

Conception, early childhood and adolescence are important windows of vulnerability to chemical exposure (Robledo et al., 2019). Developmental windows of vulnerability are critical periods during which a child is overly susceptible to chemicals (Carroquino et al., 2012). Exposure to some environmental substances, such as tobacco smoke and alcohol, early pregnancy is considered a critical window of vulnerability for fetuses (Robledo et al., 2019). Indeed, infants exposed to these toxicants during this stage can develop adverse health effects, such as congenital abnormalities and low birth weight (Robledo et al., 2019). Although fetal development is an established major window of vulnerability, it is imperative to study exposures during later periods of childhood and during adolescence, as they may have varying impacts on developing youth.

2.3.1 Childhood

Childhood is an important period of growth during which a child's organs (including their function), metabolism, body, and behaviour are all undergoing growth and maturation. The exposure and metabolism of chemicals are different in children compared to adults (Etzel, 2020). For each unit of their body weight, children tend to have breathing, drinking, and ingestion rates that are considerably higher than adults (Hauptman & Woolf, 2017). Due to this, children are more significantly exposed to environmental chemicals according to the weight of their bodies (Hauptman & Woolf, 2017). Also, it is common for young kids to have hand-to-mouth habit and play near the ground, which exposes them to chemicals present in their environment through routes different than those adults are exposed through (Carroquino et al., 2012; Xue et al., 2007). In addition, children are more susceptible to chemical exposures because their metabolic capacities are not fully developed .

2.3.2 Adolescence

Adolescence refers to the period of life beginning with puberty and ending with adulthood, characterized with a myriad of biological and behavioural changes (Jaworska & MacQueen, 2015). Therefore, adolescence is a vulnerable stage for EDC exposure. All through this period, the function and structure of the brain undergo significant development (Arain et al., 2013). New habits appear with puberty and the ongoing brain development leading to the modification of an individual’s health behaviours through adolescence (Viner et al., 2012). Adolescence is known as a developmental window (Jaworska & MacQueen, 2015) and many have also suggested that it is a window of vulnerability to both environmental stressors and chemicals (Bullert et al., 2021; Gomes et al., 2016).

Adolescence is characterized by hormonal transformations and physical changes induced by puberty (Best & Ban, 2021; Sawyer et al., 2018). On average, puberty will begin around 11 years of age for girls and 12 years of age for boys (Blakemore et al., 2010). Pubertal hormonal phenomena consist of the adrenal stress hormones’ stimulation, the growth spurt, and the gonadotrophin-induced transformations in the ovaries or testicles (Sawyer et al., 2018). During adolescence, neuroendocrine development takes place due to puberty, making adolescents susceptible to chemical substances that imitate or inhibit hormones (Moorman et al., 2000; Romeo, 2018). The hypothalamic-pituitary-adrenal axis and the hypothalamic-pituitary-gonadal axis are also activated during this period of life through processes known as adrenarche and gonadarche (Blakemore et al., 2010; Romeo, 2005). In both boys and girls, the hypothalamus synthesizes the gonadotrophin hormone (GnRH) which leads to the luteinizing hormone’s (LH) and the follicle stimulating hormone’s (FSH) release (Best & Ban, 2021). Throughout the maturation stimulated by LH and FSH, the gonads produce the steroidal sex hormones estrogen (ovaries) and testosterone (testes) and start producing gametes, hence reaching reproductive competency (Blakemore et al., 2010).

These hormonal changes lead to several physical and biological changes equally in young people entering adolescence, such as the appearance of pubic hair; the beginning of menstruations and the appearance of breasts in females; the transformation of testicles in males; changing voice; and acne (Best & Ban, 2021; Blakemore et al., 2010). Many neurological changes occur as well, such as brain maturation (Best & Ban, 2021). Estrogen, progesterone, and testosterone hormones influence brain maturation in adolescents (Arain et al., 2013). Modulated by the increased concentrations of steroid sex hormones, the development of myelin sheaths and the neurocircuitry of the brain – both processes taking place in the central nervous system (CNS) – continue maturing during puberty (Arain et al., 2013).

With the knowledge that endocrine-disrupting chemicals can perturb hormonal activities, it is understandable that exposure to such toxicants during this sensitive period of life may be detrimental to young peoples' health and development.

2.3.2.1 Sociocultural standards and PCP use

Throughout adolescence, the sociocultural standards related to appearance and the concept of social acceptance greatly influence youth (Gustafsson et al., 2011). Such preoccupations can shape adolescents' behaviour and preferences as they seek to define themselves (McCaleb & Cull, 2000). For example, one study showed that sociocultural standards help shape self-care practices in adolescents aged 15 and 16 years (McCaleb & Cull, 2000). Marcoux (1999) mentions that an adolescent starts caring about their looks following their thirteenth birthday. Sociocultural pressure can stem from various sources such as parents, peers, significant others, and the media (Anić et al., 2022).

A common behaviour among adolescents is the use of PCPs such as cosmetics to beautify their appearance (Marcoux, 1999). With the knowledge that adolescents commonly develop skin problems such as acne due to puberty, it was revealed in a study that 64% of adolescents suffering from acneic skin were self-conscious about this condition (Ritvo et al., 2011). Indeed, 48% of the teenagers surveyed in Ritvo et al.'s (2011) study reported using concealer or makeup products to hide their acne. Applying cosmetics to hide imperfections may help adolescents meet the sociocultural standards concerning appearance. However, teenagers' behaviour in relation to PCP use to better their attractiveness contributes to their exposure to chemicals found in PCPs.

2.5 Relevance of a Review

As described in the present review of literature, many chemicals possess endocrine-disrupting properties that are detrimental to human health. Children and adolescents may be particularly susceptible to the adverse effects of EDCs due to the physiological changes and maturation of their metabolic capacities that take place during these periods. However, few studies investigate the extent to which PCP usage contributes to the exposure to chemicals, especially in children and adolescents. Most human studies assess exposure patterns among adults. Experimental studies conducted on animal models do not reflect chemical exposure pathways among humans as these can be: 1) exposures to a mixture of chemicals; 2) exposures that are irregular; 3) to our knowledge, no animal study has attempted to study PCP use that is reflective of real-life usage of these products, which is characterized by multiple different products with complex and varied chemical concentrations. To add, findings of studies conducted on laboratory animals cannot be applied to humans due to interspecies biological differences.

PCPs are consumer products used by a wide range of individuals and various population groups. PCPs harbour chemicals such as parabens, phenols, phthalates, and PFAS, all potential EDCs. A myriad of scientific studies has shown that EDCs can mimic many endogenous hormones – thus negatively affecting the nervous system and the reproductive system, for instance – and may trigger the development of critical health disorders, such as cancer, in humans.

Table II. Chemical structure and general characteristics of most common parabens

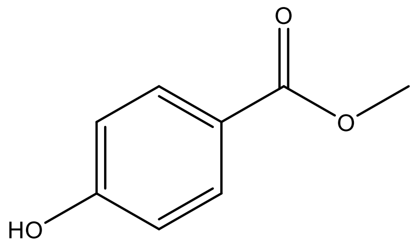
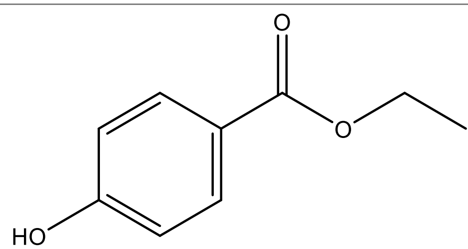
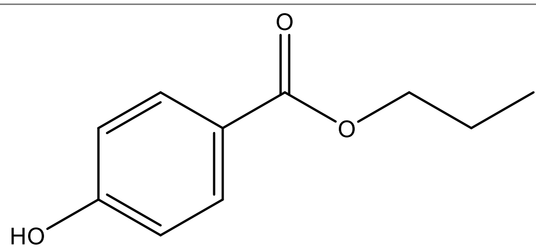
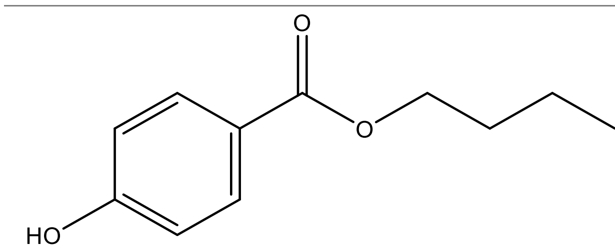
Chemical Structure and Common Name	PubChem CID	Other Names	Sources of Exposure	Properties
 Methylparaben	7456	Methyl 4-hydroxybenzoate, methyl p-hydroxybenzoate, 4-hydroxybenzoic acid methyl ester, Nipagin (National Center for Biotechnology Information, 2022k)	Shampoo, sunscreen, mascara, hair products, creams, baby products, lotions, cleansers, foundation, shaving gel (Consumer Product Information Database, n.d.-g)	Antimicrobial (Petric et al., 2021)
 Ethylparaben	8434	Ethyl 4-hydroxybenzoate, Ethyl p-hydroxybenzoate, 4-hydroxybenzoic acid ethyl ester, Nipagin A (National Center for Biotechnology Information, 2022l)	Shampoo, creams, cleansers, cleansing pads, lotions, sunscreen, shaving gel/balm, mascara, foundation, hair dye (Consumer Product Information Database, n.d.-f)	
 Propylparaben	7175	Propyl 4-hydroxybenzoate, propyl p-hydroxybenzoate, 4-hydroxybenzoic acid propyl ester, Nipasol (National Center for Biotechnology Information, 2022i)	Shampoo, sunscreen, mascara, creams, lotions, cleansers, cleansing pads, shower gel (Consumer Product Information Database, n.d.-h)	
 Butylparaben	7184	Butyl 4-hydroxybenzoate, Butyl p-hydroxybenzoate, 4-hydroxybenzoic acid butyl ester, Nipabutyl (National Center for Biotechnology Information, 2022j)	Creams, cleansers, face wash, shaving gel/balm, lipstick, sunscreen, cleansing pads, shampoo (Consumer Product Information Database, n.d.-b)	

Table III. Chemical structure and general characteristics of common phenols

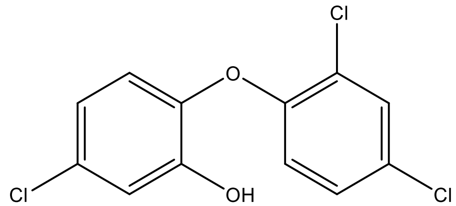
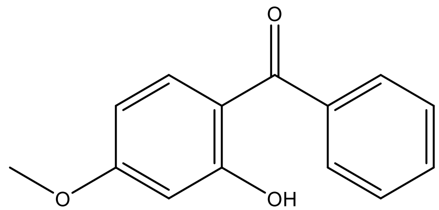
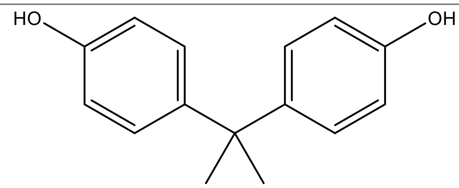
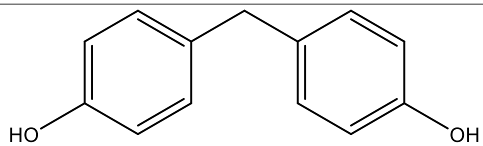
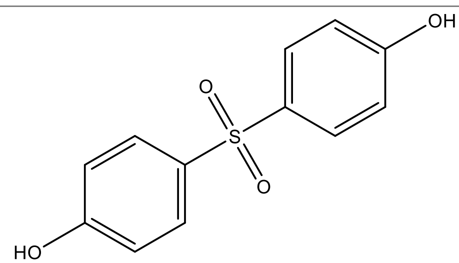
Chemical Structure and Common Name	PubChem CID	Other Names	Sources of Exposure	Properties
 Triclosan	5564	5-Chloro-2-(2,4-dichloro-phenoxy)-phenol, 2,4,4'-Trichloro-2'-hydroxydiphenyl ether, Cloxifenol (National Center for Biotechnology Information, 2022d)	Hand soap, soap bar, deodorant, body spray, toothpaste, shaving gel, cleansers, lipcolor, body wash (Consumer Product Information Database, n.d.-i)	Antimicrobial (Dodson et al., 2020; Nakiwala et al., 2020)
 Benzophenone-3 (also known as Oxybenzone)	4632	Oxybenzone, 2-hydroxy-4-methoxybenzophenone, (2-hydroxy-4-methoxyphenyl)(phenyl)methanone (National Center for Biotechnology Information, 2022c)	Sunscreen, lipstick, cleansing scrub, perfume, body spray, cologne, lip balm, face wash, creams, lipcolor (Consumer Product Information Database, n.d.-a)	Ultraviolet rays filter (Dodson et al., 2012; Nakiwala et al., 2020)
 Bisphenol A	6623	2,2-bis(4-hydroxyphenyl)propane, 4,4'-isopropylidenediphenol (National Center for Biotechnology Information, 2022e)	Bath gels, body lotions, face cleansers, hand lotions, lipsticks, masks, shampoos, sunscreens, toothpastes (Lu et al., 2018)	Plasticizer (Nakiwala et al., 2020)
 Bisphenol F	12111	4,4'-methylenediphenol, Bis(4-hydroxyphenyl)methane (National Center for Biotechnology Information, 2022o)		
 Bisphenol S	6626	4,4'-sulfonyldiphenol, Bis(4-hydroxyphenyl) sulfone (National Center for Biotechnology Information, 2022f)		

Table IV. Chemical structures and general characteristics of common phthalates

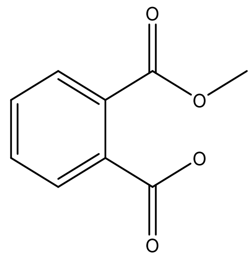
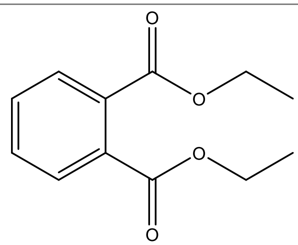
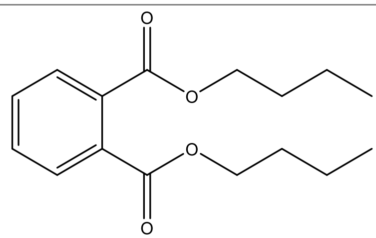
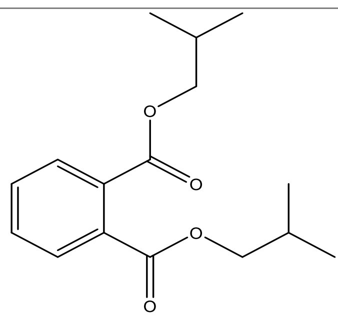
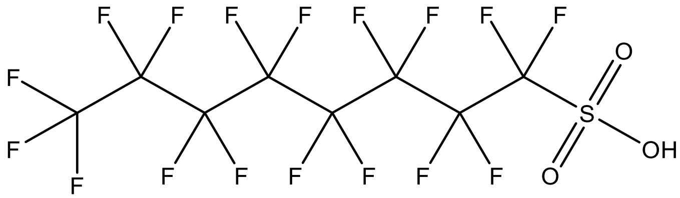
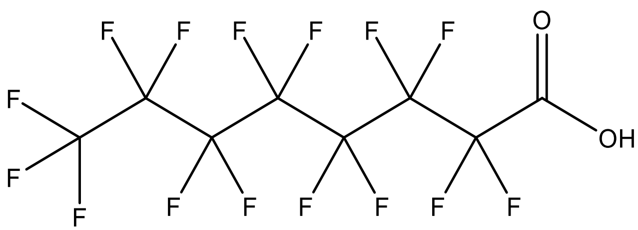
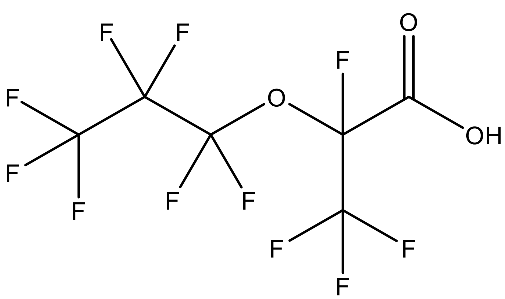
Chemical Structure and Common Name	PubChem CID	Other Names	Sources of Exposure	Properties
 Dimethyl phthalate	8554	Methyl phthalate (National Center for Biotechnology Information, 2022m)	Fragrance, insect repellents (for skin), plastics, molding powders, pesticides, solvents (Consumer Product Information Database, n.d.-e)	Plasticizer (Koniecki et al., 2011)
 Diethyl phthalate	6781	Ethyl phthalate, Di-*n*-ethyl phthalate (National Center for Biotechnology Information, 2022g)	Cleansers, fragrance oils, plastics, air deodorizing products, laundry and dishwashing products, cleaning products (Consumer Product Information Database, n.d.-d)	
 Di-*n*-butyl phthalate	3026	Dibutyl phthalate (National Center for Biotechnology Information, 2022b)	Nail polish, fragrance, plastics, solvents, cleaning products, colorant products (Consumer Product Information Database, n.d.-c)	
 Diisobutyl phthalate	6782	Di(*i*-butyl)phthalate, di-*l*-butyl phthalate, isobutyl phthalate (National Center for Biotechnology Information, 2022h)	Nail polish, cosmetics, clothing treatments, lacquers, paint pigments (National Center for Biotechnology Information, 2022a)	

Table V. Chemical structure and general characteristics of common PFAS

Chemical Structure and Common Name	PubChem CID	Other Names	Sources of Exposure	Properties
 PFOS	74483	Perfluorooctane sulfonate, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluorooctane-1-sulfonic acid, heptadecafluorooctanesulfonic acid (National Center for Biotechnology Information, 2022p)	Cosmetics, fire-fighting foams, lubricants, paper coatings, surfactant, textiles (Li et al., 2022)	
 PFOA	9554	Perfluorooctanoic acid, 2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-Pentadecafluorooctanoic acid, pentadecafluorooctanoic acid (National Center for Biotechnology Information, 2022n)	Foundation, liquid makeup base, manicure products, lip rouge, lip gloss, lip balm, sunscreen (Fujii et al., 2013; Thépaut et al., 2021)	Waterproof, greaseproof, non-stick (Pelch et al., 2019)
 GenX	114481	2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propanoic acid, ammonium 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propopoxypropanoic acid, hexafluoropropylene oxide dimer acid (National Center for Biotechnology Information, 2022q)	Fluoropolymer resins, wire cables, coatings (Hale et al., 2020)	

III
Objective

The objective of the present research is to provide an overview of biomonitoring studies that describe the concentrations of parabens, phenols, phthalates, and PFAS following PCP use among children and adolescents aged 5 to 19 years old. Another aim was to identify if there are any gaps in knowledge in this area of research.

IV
Methods

4.1 Scoping Review

Scoping reviews are described as an approach aimed at synthesizing evidence and establish the scope of available scientific studies on a particular subject (Munn et al., 2018). Following, is a recommended definition for this type of review:

> A scoping review or scoping study is a form of knowledge synthesis that addresses an exploratory research question aimed at mapping key concepts, types of evidence, and gaps in research related to a defined area or field by systematically searching, selecting, and synthesizing existing knowledge. (Colquhoun et al., 2014, pp. 1292-1294)

Another definition by Grant and Booth (2009) describes the scoping review as a "preliminary assessment of potential size and scope of available research literature. Aims to identify nature and extent of research evidence (usually including ongoing research)" (p. 95). The exhaustiveness of the research conducted for a scoping review is influenced by limits on the available time and the range of studies, in addition there is no formal evaluation of the review's quality (Grant & Booth, 2009). Indeed, the time needed to complete a scoping review fluctuated from 2 weeks to 20 months and quality evaluation was rarely accomplished for this type of review according to the findings of Pham et al. (2014).

Alternatives to conducting a scoping review would be the systematic review, for example, which also has a rigorous methodology and allows to assess the quality of retained studies, thus increasing the quality of the review itself. Combined with a meta-analysis, a systematic review can provide a more quantitative analysis based on findings reported by the included publications. However, due to not knowing how diverse the existing studies on this rather recent subject are in terms of their characteristics, a scoping review was deemed as the adequate type of review. A scoping review allows to grasp the scope and nature of literature on this fairly novel topic and is a valuable method to provide an overview on this subject, which suits our study objective.

4.1.1 Framework for the scoping review

Five steps inspired by the methodology proposed by Arksey and O'Malley (2005) were followed for this scoping review: (1) identifying the research question, (2) identifying relevant studies, (3) study selection, (4) charting the data, and (5) collating, summarizing, and reporting the results. A supplementary step was also suggested by the authors of this framework: consultation exercise (Arksey & O'Malley, 2005). Since this stage was defined as optional by the authors (Arksey & O'Malley, 2005), it was not included in our scoping review's framework.

4.2 Research Question

We based our aim on the question "What is the exposure to chemicals found in PCPs among children and adolescents?". The aim of our research was to identify biomonitoring studies that describe the PCP use patterns of children and adolescents ages 5 to 19 years and their exposure to chemicals found in such products. Supplementary aims were to describe the characteristics of identified publications and identify if there are gaps in knowledge in this area of research.

4.3 Search Strategy

We conducted a systematic literature search on the three following databases: MEDLINE, Embase, and Global Health. Our goal was to identify studies that investigated parabens, phenols, phthalates, and PFAS exposure via PCPs in participants in the age range of 5 to 19 years old. The search on each database identified literature that was published prior to September 2022. No restriction criteria were applied for the location, and date. Results retrieved from the search – which included the reference, title and abstract for each article – were imported into a screening and data extraction tool for systematic reviews: Covidence (Veritas Health Innovation). This programme removes identical duplicates following the import of references. Non-identical duplicates may not be removed. Therefore, verification during screening was important.

4.4 Study Selection

4.4.1 Inclusion Criteria and Exclusion Criteria

The following *a priori* inclusion criteria were applied: human studies including non-pregnant and not severely ill (*e.g.*, cancer) participants of ages 5 to 19 years old; studies that contained biomonitoring data on parabens, phenols, phthalates, PFAS, and PCP use data. No limits were applied regarding the language of articles or study design.

Articles with focus on maternal exposures, as well as reviews, commentaries, and abstracts only (such as conference abstracts) were excluded.

4.4.3 Screening

Screening of titles and abstracts was conducted to select articles focusing on the mentioned *a priori* inclusion criteria. When an article could not be excluded with certitude based on the examination of the title and abstract, it was considered as part of the eligible articles and its full-text was thoroughly analyzed. Following this, the full-texts of each study were assessed to determine its eligibility. During this step, we carefully excluded articles according to the exclusion criteria.

4.5 Charting the Data

For this scoping study, data charting refers to the organization and summarization of the key findings and data reported following the review of the final selected studies. For each retained study, both general and key information was entered in a form created with Microsoft Excel®. General information consisted of the name of the authors, the title and date of the article, the country or region of the study, the aim of the study, and the study design. Key information included characteristics of participants of interest, the biological matrix used to collect biomonitoring data, data collection methods (*e.g.*, interview, questionnaires, 24-hour recall), the measured chemicals and/or their metabolites, the studied PCPs, and a summary of the key findings.

V
Results

Scientific Article

Childhood and Adolescent Exposure to Chemicals Found in Personal Care Products

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Conflicts of interest:

The authors declare that they have no known competing financial interests.

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*Article in preparation for publication

Abstract

Background: Personal care products (PCPs) contain a variety of chemicals including parabens, phenols, phthalates, and per- and polyfluoroalkyl substances (PFAS). Exposure to these chemicals are of concern for children and adolescents, as they are known possess an increased susceptibility to chemical exposures. To date, no published review has explored youth exposure to chemicals found in PCPs.

Objective: This scoping review aimed to provide an overview of biomonitoring studies that describe the concentrations of parabens, phenols, phthalates, and PFAS following PCP use among children and adolescents of any age from 5 to 19 years old.

Methods: The search was conducted in MEDLINE, Embase, and Global Health. Articles were screened and assessed for eligibility. From eligible studies, data were extracted to summarize and describe the findings.

Results: Thirty-seven studies were included, the first of which appeared in 2013. The majority of studies were cross-sectional (n=35) and included more than 100 participants (n=27). The most frequently studied chemicals were phthalates (n=23), followed by parabens and phenols (each n=18), and then PFAS (n=1). The biological matrix mainly used was urine (n=36). Thirty-one studies reported at least one positive association between personal care products and certain chemical classes, such as between makeup and parabens; lotion and phenols; and perfume and phthalates.

Conclusion: More rigorous studies on the exposure to chemicals found in PCPs among youth are needed to document the relative importance of PCP use with regard to total chemical exposure.

Moreover, uniformity throughout data collection questionnaires may help to reduce heterogeneity between study findings.

Keywords: personal care products, parabens, phenols, phthalates, perfluoroalkyl substances, polyfluoroalkyl substances, children, adolescents, exposure

1. Introduction

Personal care products (PCPs) are household products used for beautifying purposes and maintaining personal hygiene (Lang et al., 2016; Montes-Grajales et al., 2017), these include products such as shampoo, cosmetics, fragrances, lotions, toothpaste, hair dyes, deodorants, and skin care products (*e.g.,* sunscreens). A wide range of chemicals are used as ingredients in PCPs including chemicals from the families of parabens, phenols, phthalates, and per- and polyfluoroalkyl substances (PFAS). Parabens and phenols are broad-spectrum antimicrobial phenolic compounds that are incorporated in various products, from cosmetics to food, to prevent bacterial and fungal growth (Murphy et al., 2021; Nowak et al., 2018). Phthalates are commonly used as plasticizers (Rael et al., 2009) but may be used as solvents that help scents and colour last longer (Cao, 2010). PFAS are generally used for their waterproof and greaseproof abilities (Pelch et al., 2019).

Children and adolescents are an important group of PCP users. For instance, in the United States, 80% of youth from 9 – 11 years were PCP and beauty product users in 2016 (Mintel Press Office, 2016). In total, 90% of American girls and 69% of American boys of ages 9 – 17 years were beauty product users (Mintel Press Office, 2016). Beauty products used by over 40% of 12 – 17-year-old American boys were face cleansing products, perfume and/or cologne, and lip care products (Mintel Press Office, 2016). Over 50% of American youth 12 – 14 years old use eyeliner, eyebrow pencils, eye shadow, and mascara (Mintel Press Office, 2016). Cologne, spray, and perfume were used by 39% of girls and 25% of boys of aged 6 – 8 years (Mintel Press Office, 2016). Among Swiss-German children and adolescents (n=397), a study that has investigated the usage patterns of leave-on PCPs reported that prevalent sunscreen use was the highest (100% for females, 99.0% for males) (Manová et al., 2013). Among female youth, 84.3% frequently used body lotion and among male youth, 68.9% frequently used lip care products (Manová et al., 2013). Aftershave, hand cream, lip care, lip stick, and makeup foundation were more commonly used by adolescents 13 – 17 years (Manová et al., 2013). Among children aged 4 years or younger, face cream and body lotion were reported to have the highest prevalence of use (Manová et al., 2013).

The potential adverse effects of chemicals used in PCPs – such as parabens, phenols, phthalates, and PFAS – creates concerns as it is suggested that they have a connection with a range of health problems in youth. Indeed, childhood and adolescent exposure to these chemicals have been linked with neurodevelopmental delays (Bennett et al., 2022); negative cognitive development (Ejaredar et al., 2015); behavioural changes and allergic illnesses, such as asthma and eczema (Braun et al., 2013); altered sex hormone (Boas et al., 2010; Hu et al., 2022) and thyroid hormone levels (Lopez-Espinosa et al., 2016); and hypertension and obesity (Averina et al., 2021) among many others. Since children and adolescents are particularly vulnerable to the chemical exposures due to their developing organ systems and metabolic capacities (Makri et al., 2004), exposure to chemicals found in PCPs is concerning.

To our knowledge, there is no existing review that highlights the exposure to chemicals following PCP use among young people. Thereby, we undertook the following review to provide an overview of existing biomonitoring studies that describe the concentrations of parabens, phenols, phthalates, and PFAS following PCP use among children and adolescents aged 5 to 19 years old. As secondary objectives, we aimed to describe the characteristics of the selected studies and identify gaps in knowledge on this subject.

2. Methods

Framework

The framework for this review was inspired by the five key steps in the methodology proposed by Arksey and O'Malley (2005) for scoping reviews: (1) identifying the research question, (2) identifying relevant studies, (3) study selection, (4) charting the data, and (5) collating, summarizing, and reporting the results. This framework also proposed an additional step requesting to consult experts (Arksey & O'Malley, 2005). This sixth step is optional (Arksey & O'Malley, 2005) and, therefore, was not applied in our study.

Literature Search and Selection of Relevant Articles

A systematic literature search was conducted on three databases in Ovid: Medline, Embase, and Global Health. We intended to identify original studies that investigated concentrations of parabens, phenols, phthalates, and PFAS in a biological matrix in relation with PCP use in participants of any age from 5 to 19 years old. The search was conducted on September 19th, 2022. Thus, papers available up until this date were included in the present review. We did not restrict results with respect to location, year of publication, or language. The search is provided in the Supplementary Material (Tables S1, S2, and S3).

We screened titles and abstracts to select articles that met the following *a priori* inclusion criteria: human studies including non-pregnant participants of any age ranging from 5 to 19 years old; studies that included biomonitoring data on parabens, phenols, phthalates, PFAS, and PCP use data. When it was not possible to exclude a study based on the title or abstract with certainty, the full-text was thoroughly analyzed. Exclusion criteria were the following: participants with severe illness and focus on maternal exposures. We excluded reviews, commentaries, and abstracts only (conference abstracts or other).

3. Results

Characteristics of Retained Studies

The literature search has yielded 521 potentially pertinent studies. Following deduplication of 229 studies, inclusion criteria was applied and a total of 292 studies were screened by their title and abstract. 154 from these did not match the inclusion criteria resulting in full-text screening of 138 studies. In total, 37 studies were selected for this scoping review (Figure 1). All retained studies' general characteristics are presented in Table 2.

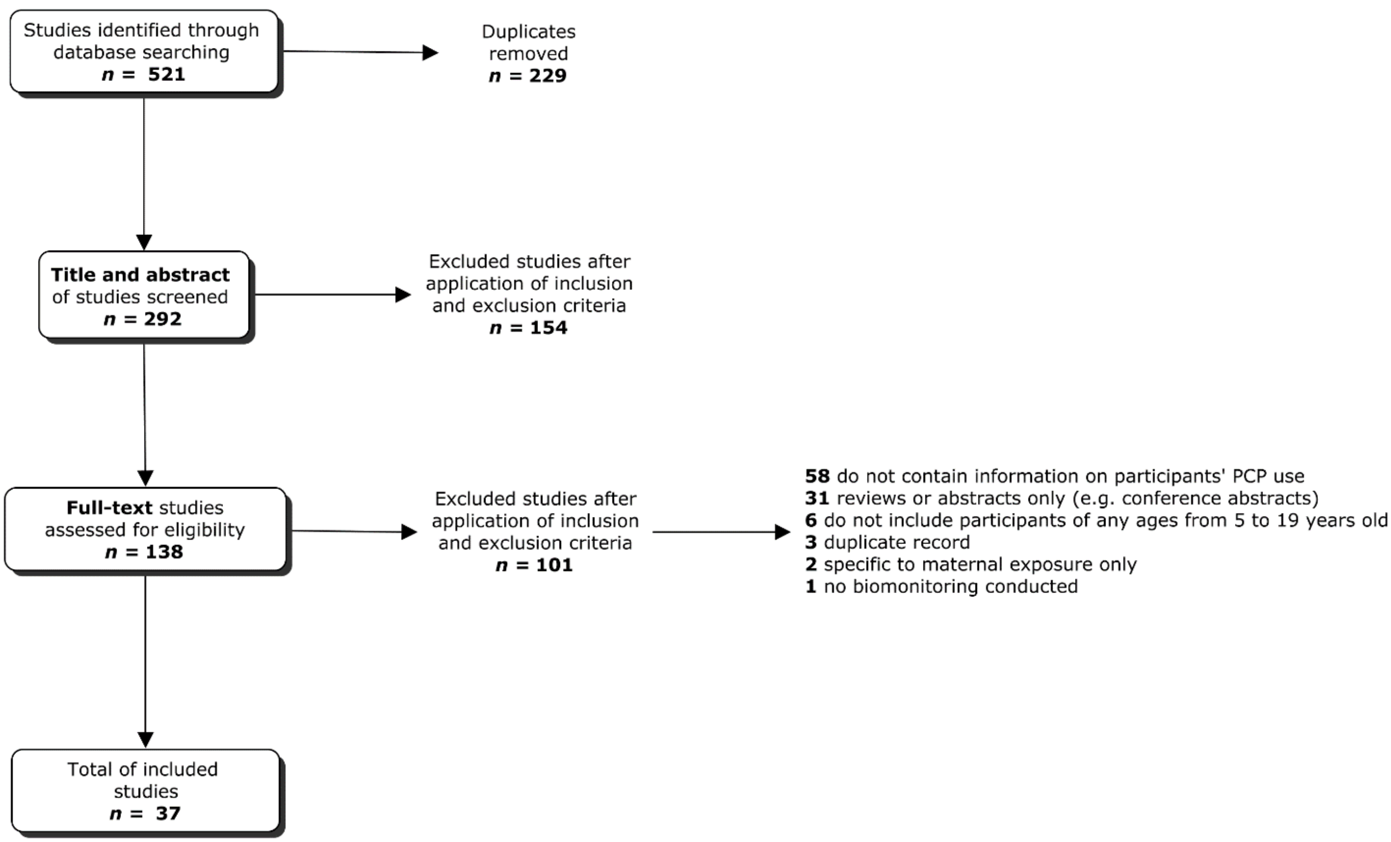

Figure 1. Study selection flow diagram representing the steps to select studies for inclusion in the scoping review, and the number of studies excluded at each step.

The retained studies were published between 2013 (Den Hond et al., 2013; Lewis et al., 2013) and 2022 (Huang et al., 2022; Jala et al., 2022; Stuchlík Fišerová et al., 2022), as shown in Figure 2. Studies were mostly conducted in Europe (n=19) followed by Asia (n=14) and North America (n=7) (Table 1). In Europe, studies were mostly carried out in Norway (n=3). In Asia and in North America, studies were mainly undertaken in China (n=9) and in the United States (n=6), respectively. One study was conducted in Czechia, Hungary, and Slovakia (Černá et al., 2015). One study focused on Flemish participants in the region of Flanders, in Europe (Den Hond et al., 2013). The majority of included studies had a cross-sectional design (n = 35). Of the remaining two studies, one had an interventional design (Berger et al., 2019) and the other was a case study (Černá et al., 2015). Some studies were conducted at a national level and included general population (Fillol et al., 2020; Huang et al., 2015; Huang et al., 2022; Lim, 2020), while others focused on a limited range of participants (*e.g.*, mother and child pairs, children only, adolescents only, or young adults). Study sample size ranged from n=30 (Chen et al., 2015) to n=5962 (Lim, 2020). Ten studies included 100 participants or less, remaining studies included over 100 participants (n=27). Most studies included participants of both biological sexes (n=35). In one study (Fillol et al., 2020), the number of participants varied depending on the chemicals measured. For biomonitoring, thirty-six studies used urine as a matrix from which one study (Fillol et al., 2020) used serum as well. One study measured chemical concentrations in participants' fingernails (Li et al., 2020). The included studies measured concentrations of phthalates (n=23), concentrations of parabens (n=18), concentrations of phenols (n=18), and concentrations of PFAS (n=1) (Figure 3). Retained studies have investigated one class of chemicals (n=20), two classes of chemicals (n=11), and three classes of chemicals (n=6) (Figure 4).

Data Collection

The surveying methods applied by the included studies were traditional self-administered questionnaires (n=25), 24-hour recalls (n=2), and structured interviews with participants (n=11) to collect information on PCP use, such as the products used, number of products used, frequency of use, among other relevant information (*e.g.,* age, gender, sociodemographic characteristics, residential environment, diet). One study (Fillol et al., 2020) used either a structured interview, and online questionnaire, or a self-administered questionnaire for data collection. One study used both a questionnaire and a 24-hour recall to collect participants' information (Šidlovská et al., 2017), while another study just used a 24-hour recall (Sakhi et al., 2018). Few studies applied novel data collection methods. Fillol et al. (2020) administered their questionnaire online as an option, Watkins et al. (2014) administered a computer-assisted questionnaire, and Zhang et al. (2018) offered their questionnaire in the option of a mobile phone application. In general, most of the included studies collected data on participants' product use frequency. However, certain studies uniquely assessed the use/no-use data of all studied PCPs (n=7). Some studies collected use/no-use data for certain products only (n=4). Four studies assessed the cumulative number of PCPs used by participants, instead of collecting PCP use data for products individually. Low, moderate/medium or high PCP use was assessed by three studies. Each retained study collected data differently; characteristics of each study's data collection methods are provided in Table III.

Table I. Geographic provenance of included studies (n=37).

Region	Country		
Asia (n=14)	China [a] (n=9)	India (n=1)	Iran (n=1)
	South Korea (n=3)		
Europe (n=19)	Belgium (n=1)	Czechia (n=1)	Czechia, Hungary, Slovakia [b] (n=1)
	Denmark (n=1)	France (n=1)	Flanders [c] (n=1)
	Germany (n=2)	Ireland (n=1)	Norway (n=3)
	Slovakia (n=1)	Slovenia (n=2)	Spain (n=1)
	Sweden (n=1)		
North America (n=7)	United States (n=6)	Mexico (n=1)	

[a] Also includes studies conducted in Taiwan (n=4)
[b] One study (Cerna et al. (2014)) was conducted in Czechia, Hungary, and Slovakia
[c] Flemish region in Europe

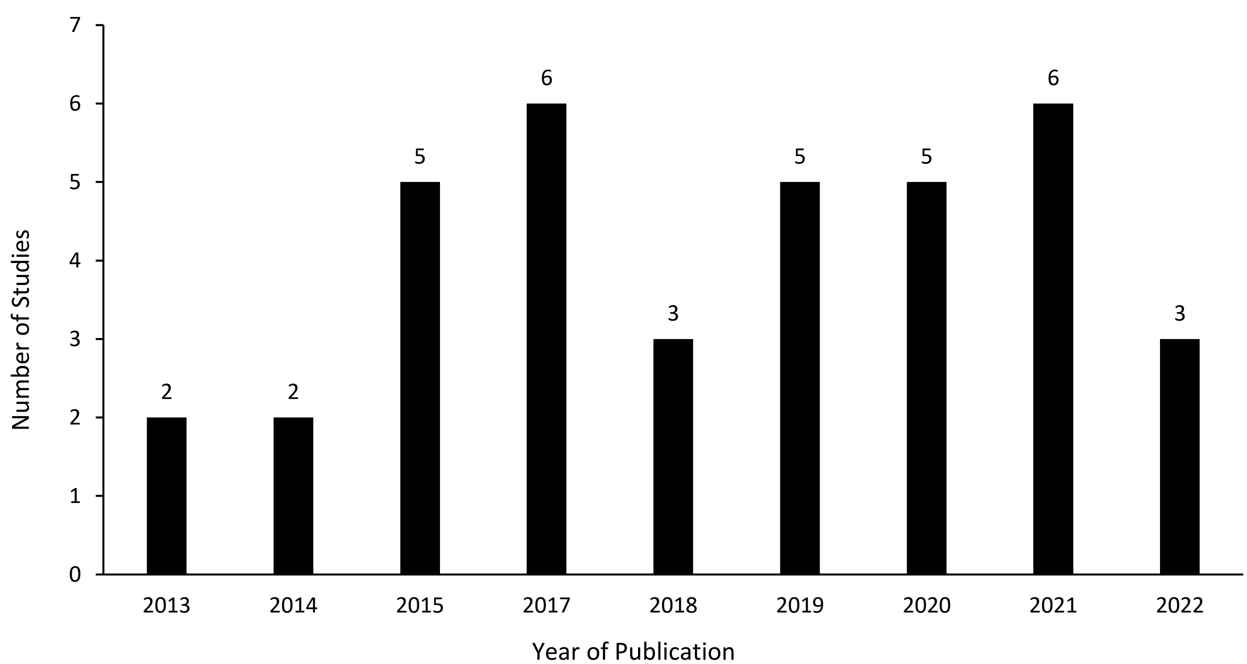

Figure 2. Number of included studies published from 2013 (earliest study published on the studied topic) to September 19th, 2022.

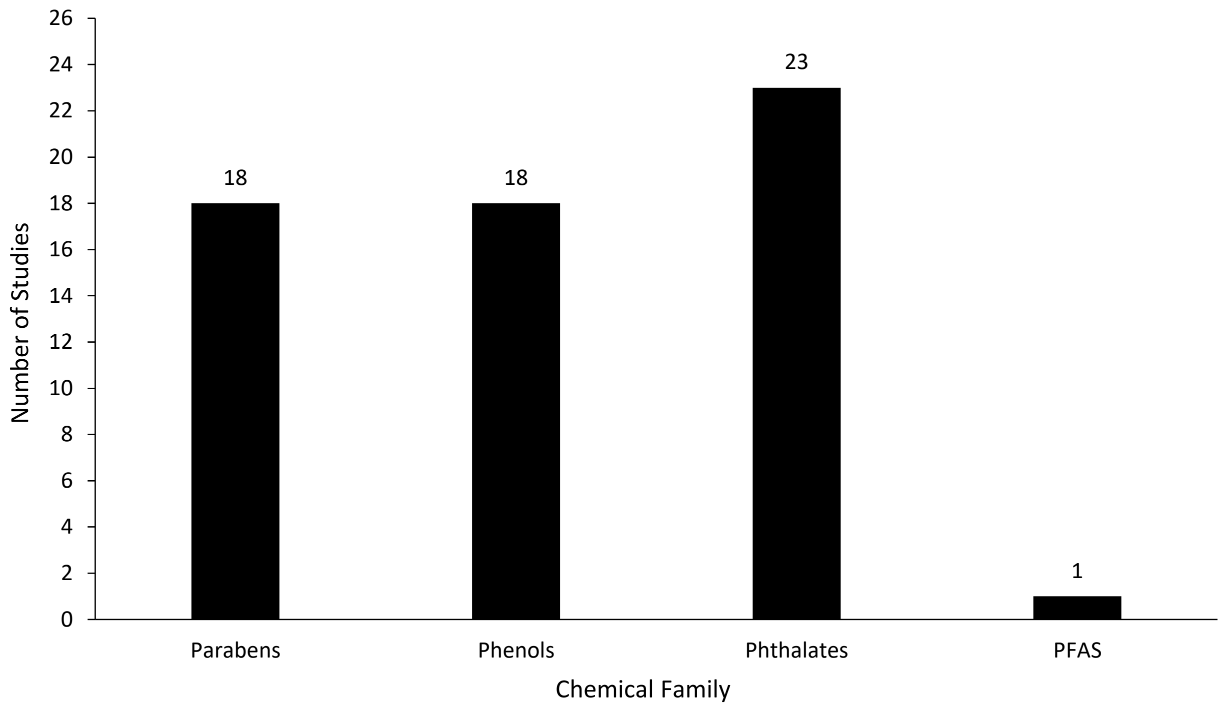

Figure 3. Number of included studies per each chemical family of interest studied.

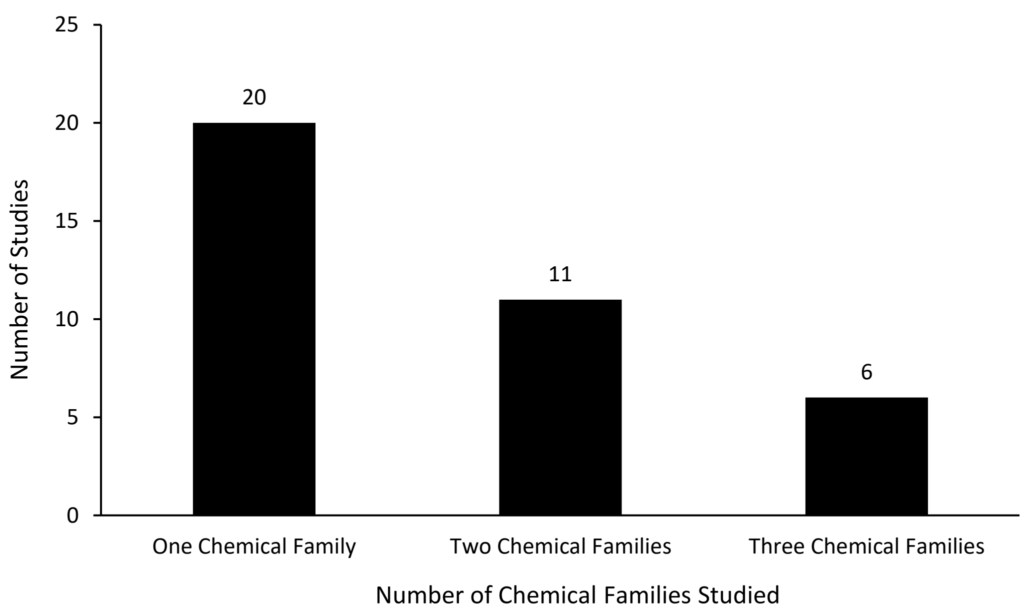

Figure 4. Number of included studies per number of chemical families of interest studied.

Table II. General characteristics of included studies, and the investigated chemical families and personal care products.

Author (Year)	Title	Participants of Interest	Investigated Chemical Families [a]	Personal Care Products
Berger et al. (2019)	Personal care product use as a predictor of urinary concentrations of certain phthalates, parabens, and phenols in the HERMOSA study	Latina girls aged 14 to 18 years old (n=100)	- Parabens - Phthalates - Phenols	- Makeup products - Other facial products - Oral hygiene products - Sunscreen - Deodorants and perfumes - Soaps - Nail products - Hair products
Černá et al. (2015)	Case study: Possible differences in phthalates exposure among the Czech, Hungarian, and Slovak populations identified based on the DEMOCOPHES pilot study results	Children 6 to 11 years old (n=120 for Czech Republic and Hungary, n=129 for Slovakia)	Phthalates	- Shampoo - Body lotions and creams
Chen et al. (2017)	Exposure sources and their relative contributions to urinary phthalate metabolites among children in Taiwan	Children aged 1 to 11 years old (n=226 for Wave 1; n=181 for Wave 2)	Phthalates	- Shower gel - Shampoo - Lotion - Face wash - Hand wash - Soap - Skin makeup - Essential oils - Lip balm - Nail polish
Chen et al. (2015)	Developing an intervention strategy to reduce phthalate exposure in Taiwanese girls	Girls aged 4 to 13 years old (n=30)	Phthalates	- Essential oils - Perfumes - Skin lotions - Nail polish - Shampoo - Shower gel

Author (Year)	Title	Participants of Interest	Investigated Chemical Families [a]	Personal Care Products
Cullen et al. (2017)	Urinary Phthalate Concentrations in Mothers and Their Children in Ireland: Results of the DEMOCOPHES Human Biomonitoring Study	Children aged 5 to 11 years old (n=120)	Phthalates	- Makeup - Eye makeup - Shampoo - Hair styling products - Body lotion (e.g. hand creams, lip balsam etc.) - Fragrances (perfume, eau de toilette etc.) - Deodorants - Massage oil - Nail polish
Cutanda et al. (2014)	Urinary concentrations of eight phthalate metabolites and bisphenol A in mother-child pairs from two Spanish locations	Children aged 6 to 11 years old (n=120) and mothers aged 18 to 45 years old	Phthalates	- Makeup - Eye makeup - Shampoo - Hair styling products - Body lotion and crèmes - Fragrances - Deodorants - Massage oil - Nail polish (*Supplementary Data, Table 1s*)
Den Hond et al. (2013)	Biomarkers of human exposure to personal care products: results from the Flemish Environment and Health Study (FLEHS 2007-2011)	Flemish adolescents aged 14 to 15 years old (n=210)	- Parabens - Phenols	- Cream - Lip balm - Body lotion - Hand cream - Shampoo - Hair care products (hair balm or conditioner) - Makeup - Bath or shower products - Deodorant - Perfume - Eau de toilette
Ding et al. (2019)	Urinary concentrations of phthalate metabolites and their association with lifestyle behaviors in Chinese adolescents and young adults	Chinese adolescents and young adults aged 16 to 20 years old (n=478)	Phthalates	- Cleansing cosmetics - Skin care cosmetics - Color cosmetics - Hair dye (*Supplementary Data, Table S8*)

Author (Year)	Title	Participants of Interest	Investigated Chemical Families [a]	Personal Care Products
Fillol et al. (2019)	Exposure to pollutants in the daily life of the French population in 2014-2016 from the esteban study	French population aged 6 to 74 years old *n varies with measured chemicals*	- Phenols - Phthalates - PFAS	*List of studied PCPs not provided in article. Listed are determinants identified for parabens (*) and phthalates (**):* - Cream or body care products * - Nail polish and nail polish remover * - Cosmetic products ** - Hair products **
Hajizadeh et al. (2020)	Dietary Habits and Personal Care Product Use as Predictors of Urinary Concentrations of Parabens in Iranian Adolescents	Iranians aged 15 to 20 years old (n=100)	Parabens	- Liquid soap - Toothpaste - Shampoo - Perfume/Cologne - Sunscreen - Lotion - Deodorant - Lip makeup - Bar soap - Body wash - Eye makeup - Hair care products - Softener - Makeup base - Makeup remover - Nail products - Mouthwash - Shaving cream - Coloring products
Hammel et al. (2019)	Children's exposure to phthalates and non-phthalate plasticizers in the home: The TESIE study	Children aged 3 to 6 years old (n=203)	Phthalates	- Baby wipes (scented, unscented) - Nail polish - Lotion
Hong et al. (2021)	Urinary parabens and their potential sources of exposure among Korean children and adolescents: Korean National Environmental Health Survey 2015-2017	Children and adolescents aged 3 to 18 years old (n=2355)	Parabens	- Liquid soap - Color cosmetics - Fragrance products - Nail polish - Antiseptic products - Hair care products

Author (Year)	Title	Participants of Interest	Investigated Chemical Families [a]	Personal Care Products
Huang et al. (2015)	Age and Gender Differences in Urinary Concentrations of Eleven Phthalate Metabolites in General Taiwanese Population after a DEHP Episode	Minors aged 7 to 17 years old (n=98) and adults aged 18 to >65 (n=296)	Phthalates	- Body wash - Lotion - Perfume - Nail polish
Huang et al. (2022)	Cumulative risk assessment and exposure characteristics of parabens in the general Taiwanese using multiple hazard indices approaches	Adults aged 18 to 97 years old (n=271) and minors aged 7 to 17 years old (n=95)	Parabens	- Body wash - Lotion - Perfume - Nail polish
Jala et al. (2022)	Concentrations of parabens and bisphenols in personal care products and urinary concentrations in Indian young adult women: Implications for human exposure and health risk assessment	Young female adults aged 18 to 31 years old (n=52)	- Parabens - Phenols	- Body lotion - Foundation - Face water - Face mask - Toner - Primer - Face serum - Face gel - Sunscreen - Lipstick - Hair serum - Face cream - Shampoo - Face wash - Body wash - Conditioner - Bactericidal solution

Author (Year)	Title	Participants of Interest	Investigated Chemical Families [a]	Personal Care Products
Kim et al. (2018)	Urinary parabens and triclosan concentrations and associated exposure characteristics in a Korean population-A comparison between night-time and first-morning urine	- Toddlers aged 3 to 6 years old (n=45) - Children aged 7 to 12 years old (n=48) - Adolescents aged 13 to 18 years old (n=46) - Adults aged 19 years and above (n=91)	- Parabens - Phenols	- Skin care products - Body lotion - Fragrance - Nail polish - Colored products (facial makeup, eye makeup, lipsticks, etc.) - Sunscreen - Hand cream - Bath products (shampoo, hair conditioner or body wash) - Liquid soap - Hair spray or hair gel - Toothpaste - Mouthwash .
Koppen et al. (2019)	Mothers and children are related, even in exposure to chemicals present in common consumer products	Children aged 6 to 11 years old (n=129)	- Phenols - Phthalates	- PCPs (makeup, shampoo, eye makeup, hair styling products, body lotion, creams, fragrances, deodorants, nail polish, massage oil) - Skin bleaching - Hair dye/tone - Chemical hair structure treatment - Anti-lice shampoo - Sunscreens
Larsson et al. (2014)	Exposure determinants of phthalates, parabens, bisphenol A and triclosan in Swedish mothers and their children	Swedish children aged 6 - 11 years old (n=97)	- Parabens - Phenols - Phthalates	- Lotion - Skin makeup - Eye makeup - Sunscreen - Hair styling products - Deodorant - Fragrance - Shampoo - Mouthwash - Hand or body disinfectant
Levasseur et al. (2021)	Young children's exposure to phenols in the home: Associations between house dust, hand wipes, silicone wristbands, and urinary biomarkers	Children aged 3 to 6 years old (n=203)	- Parabens (categorized as phenols) - Phenols	- Baby wipes - Nail polish - Lotion

Author (Year)	Title	Participants of Interest	Investigated Chemical Families [a]	Personal Care Products
Lewis et al. (2013)	Predictors of urinary bisphenol A and phthalate metabolite concentrations in Mexican children	Children aged 8 to 13 years old (n=108)	- Phenols - Phthalates	- Aftershave - Bar soap - Cologne/perfume - Coloured cosmetics - Conditioner - Deodorant - Fingernail polish - Hair cream - Hair spray/hair gel - Laundry products - Liquid soap - Lotion - Mouthwash - Other hair products - Other toiletries - Shampoo - Shaving cream
Li et al. (2020)	Paraben concentrations in human fingernail and its association with personal care product use	Chinese participants aged 4 - 62 years old (n=50) (n=11 for juvenile participants aged 4 to 18 years old) *(Supplementary Data, Table S4)*	Parabens	- Face cream (samples collected from participants) *Participants reported using face cream 1 – 2 times/day.*
Li et al. (2019)	Ultraviolet filters in the urine of preschool children and drinking water	Children aged 4 to 6 years old (n=53)	Phenols	- Sunscreen - Face cream - Body lotion - Shampoo - Bath cream - Soap
Lim (2020)	The associations between personal care products use and urinary concentrations of phthalates, parabens, and triclosan in various age groups: The Korean National Environmental Health Survey Cycle 3 2015-2017	- Preschoolers aged 3 – 5 years old (n=557) - School-aged children aged 6 – 11 years old (n = 839) - Adolescents aged 12 – 17 years old (n = 807) - Adults aged 19 – 86 years old (n=3759)	- Parabens - Phenols - Phthalates	- Fragrance products - Hair care products - Body cleansers - Makeup - Nail polishes - Antiseptic products - Air fresheners

Author (Year)	Title	Participants of Interest	Investigated Chemical Families [a]	Personal Care Products
Murawski et al. (2021)	Parabens in urine of children and adolescents in Germany - human biomonitoring results of the german environmental survey 2014-2017 (GerES V)	German children and adolescents aged 3 – 17 years old (n=516; n=490 for measurement of methyl paraben only)	Parabens	- Shampoo - Body wash or shower gel - Sunscreen - Body lotion and cream - Deodorant - Facial makeup - Eye makeup
Overgaard et al. (2017)	Children with atopic dermatitis and frequent emollient use have increased urinary concentrations of low-molecular-weight phthalate metabolites and parabens	Danish children aged 4 to 9 years old (n=845)	- Parabens - Phthalates	- Emollient/moisturizer
Philippat et al. (2015)	Exposure to select phthalates and phenols through use of personal care products among Californian adults and their children	Children aged 3 to 7.9 years old and above (n=90)	- Parabens (categorized as phenols) - Phenols - Phthalates	- Shampoo - Other haircare products - Bar soap - Liquid soap - Hand sanitizer - Hand/body lotion - Chapstick or lipbalm - Suntan lotion
Runkel et al. (2020)	Urinary phthalate concentrations in the slovenian population: An attempt to exposure assessment of family units	Children aged 6 to 11 years old (n=155)	Phthalates	- Eye makeup - Hair styling - Lotions - Fragrances - Deodorant - Nail polish - Sunscreen - Mouthwash - Disinfectant

Author (Year)	Title	Participants of Interest	Investigated Chemical Families [a]	Personal Care Products
Sakhi et al. (2017)	Phthalate metabolites in Norwegian mothers and children: concentrations, diurnal variation and use of personal care products	Children aged 6 to 11 years old (n=56)	Phthalates	- Hand soap - Hand cream - Shower soap - Face cream - Deodorant - Body lotion - Perfume - Shampoo - Hair spray - Hair gel - Nail polish - Nail polish remover *(Supplementary Data, Table S2)*
Sakhi et al. (2018)	Concentrations, variability and determinants of environmental phenols in pairs of Norwegian mothers and children	Children aged 6 to 12 years old (n=54)	- Parabens - Phenols	- Body and face creams: Hand cream, body lotion, face cream - Soaps: Hand soap, shower soap, shampoo - Hair products: Hair spray, hair gel, any hair product - Nail products: Nail polish, nail polish remover, any nail product - Others: deodorant, perfume
Sidlovska et al. (2017)	Exposure of children to phthalates and the impact of consumer practices in Slovakia	Children aged 10 – 12 years old (n=107)	Phthalates	- Body lotion - Nail polish
Stacy et al. (2017)	Patterns, Variability, and Predictors of Urinary Triclosan Concentrations during Pregnancy and Childhood	Children aged 1 to 8 years old (n=389) (At 8-year visit, n=218 children provided a urine sample)	- Phenols - Phthalates	- Toothpaste - Hand soap - Bar soap - Hand sanitizer - Mouthwash - Shampoo - Lotion or sunscreen - Liquid soap or body wash - Deodorant - Hair treatments - Conditioner - Hair spray or gel

Author (Year)	Title	Participants of Interest	Investigated Chemical Families [a]	Personal Care Products
Stuchlík Fišerová et al. (2022)	Personal care product use and lifestyle affect phthalate and DINCH metabolite concentrations in teenagers and young adults	Teenagers aged 12 to 17 years old (n=300) Young adults aged 18 to 37 years old (n=300)	Phthalates	- Shampoo - Scented products (deodorants and perfumes) - Lotions - Nail polish - Makeup/foundation creams - Lip balms - Eye makeup
Tkalec et al. (2021)	Exposure of Slovenian children and adolescents to bisphenols, parabens and triclosan: Urinary concentrations, exposure patterns, determinants of exposure and susceptibility	Slovenian children aged 6 – 9 years old (n = 149) and adolescents aged 11 – 15 years old (n = 97)	- Parabens - Phenols	- Lipstick - Cream - Hair balsam - Hair styling products - Perfume - Deodorant - Body oil - Nail polish
Tschersich et al. (2021)	Bisphenol A and six other environmental phenols in urine of children and adolescents in Germany - human biomonitoring results of the German Environmental Survey 2014-2017 (GerES V)	Children and adolescents aged 3 to 17 years old (n=515 for bisphenol A and n=516 for other phenols)	Phenols	- Fragrances (fragrance lamps, incense sticks, fragrance spray, fragrance dispenser) - Sunscreen - Body lotion and cream - Body wash and shower gel - Deodorant - Facial makeup - Eye makeup
Vindenes et al. (2021)	Exposure to environmental phenols and parabens, and relation to body mass index, eczema and respiratory outcomes in the Norwegian RHINESSA study	Adults aged 18 to 47 years (n=496) and adolescents aged 10 to 17 years (n=90)	- Parabens - Phenols	- Perfume spray - Perfume (not spray) - Deo-spray - Deostick - Moisturizing cream - Lotions - Cleansing cream - Makeup - Nail-care - Shaving-products - After-shave - Hairspray - Hair-styling products - Hair-color - Hair-bleach

Author (Year)	Title	Participants of Interest	Investigated Chemical Families [a]	Personal Care Products
Watkins et al. (2014)	Variability and predictors of urinary concentrations of phthalate metabolites during early childhood	Children aged 1 to 5 years old (n=327) (At age 5, 190 children provided urine sample)	Phthalates	- Shampoo - Conditioner - Bar soap - Liquid soap or body wash - Hand sanitizer - Hairspray or gel - Sunscreen or lotion - Makeup - Nail polish
Zhang et al. (2018)	Urinary phthalate metabolites and environmental phenols in university students in South China	Students aged 19 to 34 years old (n=169) *(Supplementary Data, Table S1)*	- Parabens - Phenols - Phthalates	- Sunscreen - Shower gel - Shampoo - Facial cleanser - Body lotion - Toner - Face cream - Facial mask - Eye cream - Hand creams - Liquid makeup - Nail polish - Lipstick - Perfume - Feminine hygiene products

[a] Including metabolites of investigated chemicals.

Table III. Included studies' data collection methods and characteristics

First Author (Year)	Data Collection Characteristics
Berger et al. (2019)	• Interviewer guided questionnaire assessing PCPs used on hair, face, body, and teeth • Total number of PCPs used assessed.
Černá et al. (2014)	• Questionnaire on sources of phthalate exposure: household equipment (PVC floor, renovation of home), nutrition (convenience or fast food, ice cream, local food, etc), use of PCPs, use of plastic gloves, playing with plastic toys, lifestyle factors (smoking, alcohol consumption, sources of drinking water)
Chen et al. (2017)	• Questionnaire on sources of phthalate exposure: food consumption, toys, PCPs, parents' working or neighbourhood living environment, eating out etc • Whether child liked to use nail polish or perfume (yes, no, unnoticed) • Frequency and amount of use (0.5 – 1.5ml) of various PCPs • Completed by parents/caregivers
Chen et al. (2015)	• Questionnaire to record frequency and use of PCPs, and compliance to intervention • Amount used expressed in fraction of new Taiwan $50 coin (less than ½ a coin, ¾ of a coin, etc.)
Cullen et al. (2017)	• Interviewer guided questionnaire on possible sources of phthalate exposure, socio-demographic information, and diet • PCP use: high, moderate, low • Only use/no use of skin bleaching treatments assessed *(Supplementary Material)* • Completed by mother and interviewer
Cutanda et al. (2014)	• Interviewer guided questionnaire assessing environment, lifestyle, personal features, and others
Den Hond et al. (2013)	• Self-administered questionnaires assessing information about socioeconomic status, lifestyle, living conditions, food intake, tobacco smoke, diseases and medication, PCP use • Short questionnaire assessing exposure during the previous three days • Low, medium, and high use of PCPs assessed based on use frequency of certain products. • Partly completed by parents for their adolescent
Ding et al. (2019)	• Questionnaires assessing personal characteristics and lifestyle behaviors • Frequency of cleansing cosmetics/skin care cosmetics, color cosmetics use (< 3 times/week or ≥ 3 times/week) and the use of hair dyes (yes or no)
Fillol et al. (2019)	• Questionnaires (face-to-face with interviewer, online or auto-administered questionnaire) assessing socio-demographic characteristics, diet, physical activity, sedentariness, residential environment, professional exposure, general health, consumption of health care
Hajizadeh et al. (2020)	• Questionnaire assessing PCP use, food consumption, demographic information and lifestyle variables • User/non-user status for each product used in the past 24h • Total PCPs used assessed (for past 24h) • Categorization of participants as low user (0-3 products), medium users (4-7 products) and high users (8-19 products)
Hammel et al. (2019)	• Questionnaires assessing housing characteristic, children's health and behavior, and children's PCPs use • Frequency of the child's product use (e.g., wipes, lotion) • Use/no use assessed for baby wipes (scented and unscented) and nail polish.
Hong et al. (2021)	• Questionnaire assessing demographic and socioeconomic information; other information on factors related to environmental chemical exposure • Completed by parents/guardians
Huang et al. (2015)	• Interviewer guided questionnaire assessing demographic information, exposure, lifestyle (plastic products usage, personal care product) and other factors (disease history) • Only participants reporting use of products once a day during past month considered users *(Supplementary Data, Table S4)*
Huang et al. (2022)	• Questionnaire assessing demographic information (anthropometry index, socioeconomic status, smoking and drinking habits, and habitation) • Total number of PCPs used assessed • Less than once a month/once a month and more/never use assessed for studied PCPs *(Supplementary Data, Table S1)*

First Author (Year)	Data Collection Characteristics
Jala et al. (2022)	• Interviewer guided questionnaires assessing demographic characteristics and PCP use • Face-to-face interviews • Estimated daily intake calculated for parabens and bisphenols from the use of PCPs.
Kim et al. (2018)	• Questionnaire (self-administered) assessing demographic information, frequency of PCP use during the last 1-2 months, and food consumption frequency within a year • Only use/no use assessed for fragrance, nail polish, hair spray or hair gel, and mouthwash • Completed by parents/guardians for infants, toddlers, and children
Koppen et al. (2019)	• Interviewer guided questionnaire assessing mothers' and children's environment at home and residence, smoking behaviour, alcohol consumption, professional occupation, household income, nutrition during past 4 weeks • Face-to-face interviews • Low, moderate, and high use of PCPs assessed • Use/no use of skin bleaching, hair dye/tone in past 6 months, anti-lice shampoo in past 6 months, and sunscreen assessed *(Supplementary Data, Table SI-2)* • Completed by mothers for their children
Larsson et al. (2014)	• Questionnaire answered face-to face with a field worker or online assessing living environment, food consumption, personal care products use, smoking, lifestyle and sociodemographic information • Completed by mothers
Levasseur et al. (2021)	• Questionnaires assessing housing characteristics, children's health and behavior, use of PCPs at home (assessed the frequency of child's product use such as the use of nail polish, baby wipes, and lotion) • Only use/no use assessed for baby wipes (scented and unscented) and nail polish • Completed by parents/guardians
Lewis et al. (2013)	• Questionnaire assessing information on participants' external environment, use of water, use of containers for food and use of personal care products • Personal care product section contained yes/no questions about the use of 17 different products in the past 48h and frequency of use of each product (not at all, < once/month, 1-3 times/month, once/week, few times/week, every day)
Li et al. (2020)	• Questionnaires to assess demographic information, age height, and weight and face cream use • Collection of face creams sample • Children's questionnaire completed by parents
Li et al. (2019)	• Questionnaire assessing personal information (name, age, gender, weight, height), water consumption, frequency of hand washing, application of sunscreen, face cream, body lotion, shampoo, bath cream, and soap on the children every day • Family income and parents education included in questionnaire
Lim (2020)	• Household questionnaire and individual questionnaire • Individual questionnaire: personal information, transportation, food intake, and lifestyle habits including PCP use, health related information • 4 versions of questionnaires were developed for each age group (preschool, school-age, adolescent, adult) • Survey questionnaires for children and self-administered questionnaires for adolescents assessing personal care products frequency of use during the past three months • 6 categories of frequency of use assessed: not used, once a month and less, two or three times a month, one or two times a week, three to five times a week, and daily • **Frequency of use was reclassified for this study:** not used, less than once a week, once a week and more • Parents or guardians completed questionnaire for preschoolers and school-age children • Parents or guardians completed household section of questionnaire for adolescents • Adolescents completed individual questionnaire themselves
Murawski et al. (2021)	• Interviewer guided questionnaires given to parents/guardians **and children if 11 years or older** assessing practices relevant to exposure, habits, and behaviours (dietary habits, use of cosmetics and consumer products, residential environment information) • Only use/no use assessed for sunscreen
Overgaard et al. (2017)	• Questionnaires assessing medical history, psychomotor development, diet, and lifestyle • PCP use frequency assessed for emollient/moisturizer (daily, several times a week, several times a month, rarely, never • **Dichotomization of frequency of use:** "Frequent application" for *daily* or *several times a week* application of emollients; "Uncommon application" for *several times a month*, *rarely*, or *never* application of emollients • Completed by parents
Philippat et al. (2015)	• Questionnaire assessing PCPs use in the past 24h before urine collection in adults and their children • Only use/no use assessed for all PCPs • Total number of PCPs used in past 24h assessed for each individual • Total number of scented PCP in past 24h used assessed for each individual

First Author (Year)	Data Collection Characteristics
	• Completed by parents for their child and themselves
Runkel et al. (2020)	• Interviewer guided questionnaire assessing residential environment, diet, smoking habits, occupation, sociodemographic information, exposure-related lifestyle factors (questions on PCP use, presence of PVC in indoor environment)
Sakhi et al. (2017)	• Questionnaire assessing use of 12 different PCPs during the 24h sampling period • Completed by both mothers and children
Sakhi et al. (2018)	• 24-hour recall conducted by an expert registering food consumption and use of 12 different PCPs during study period • Only users/non-users assessed for studied PCPs *(Supplementary Data, Table S9)*
Sidlovska et al. (2017)	• Questionnaire assessing eating and drinking habits, and PCPs use • Only use/no use assessed for studied PCPs • 24-hour recall assessing dietary intakes • Completed by parents/guardians
Stacy et al. (2017)	• Questionnaire administered during children's 8-year visit assessing children's PCP use during the last 24 hours and children's handwashing frequency • Only use/no use assessed for studied PCPs • Frequency of handwashing assessed *(Supplementary Data, Table S6)* • Completed by mothers for their children
Stuchlík Fišerová et al. (2022)	• Questionnaire assessing information such as age, gender, number of siblings, education, household income, time spent indoors, home environment, diet, smoking (active and passive), PCP use, chronic illnesses • Completed by each participant
Tkalec et al. (2021)	• Interviewer guided questionnaires assessing living environment, food consumption, nutritional habits, lifestyle, socioeconomic status, PCP use • Only use/no use assessed for studied PCPs • Completed by the participants and their families
Tschersich et al. (2021)	• Interviewer guided questionnaires to collect exposure relevant behavior • Only use/no use assessed for fragrances and sunscreen *(Supplementary Data, Tables S1 – S6)*
Vindenes et al. (2021)	• Questionnaires, interviews, and clinical examination • History of diseases, smoking habits, and home environment information collected • Separate questionnaire answered by participants about frequency of use of 15 PCPs • Completed by participants
Watkins et al. (2014)	• Questionnaire (computer-assisted) assessing demographic characteristics • At 5-year follow-up visit : questions asked to mothers on child's use of plastic-food packaging and use of PCPs in the past 48h prior visit • Only users/non-users assessed *(Supplementary Data, Tables S4)*
Zhang et al. (2018)	• Questionnaire assessing daily lifestyle of students • Similar questionnaire also answered on hard copy by students in classrooms or via mobile application

Overview of Results

Among all retained studies, thirty-one have reported at least one positive association between PCP use and chemical concentrations (Summarized in Table IV). Among these, two studies reported at least one positive correlation between PCP use and chemical concentrations (Cullen et al., 2017; Larsson et al., 2014). Positive correlations were also found between face cream and paraben concentrations in human fingernails (Li et al., 2020). To determine the risks of exposure to chemicals found in PCPs, one study used logistic regression models to obtain odds ratios (Lim, 2020). This study reported associations between the use of certain PCPs and the exposure risk to some of the studied chemicals (Lim, 2020). Among children, PCP use frequency and mono-ethyl phthalate concentrations were associated (Černá et al., 2015). PCP use was also associated with higher urinary concentrations of two phthalate metabolites in children: mono-benzyl phthalate and mono-isobutyl phthalate (Koppen et al., 2019). This study equally reported an association between use of PCPs and higher triclosan concentrations in children (Koppen et al., 2019). One study reported on the determinants that influence chemical concentrations and it was the only article to have investigated PFAS concentrations (Fillol et al., 2020). However, in this study, PCP use or the use of particular PCPs was not listed as determinants that influence PFAS concentrations (Fillol et al., 2020). Six studies reported a negative association (Berger et al., 2019; Chen et al., 2015; Huang et al., 2022; Philippat et al., 2015; Sakhi et al., 2017; Sakhi et al., 2018).

Three studies found no associations between the use of PCPs and chemical concentrations (Hammel et al., 2019; Huang et al., 2015; Zhang et al., 2018). One of these studies investigated use frequency of various PCPs among its participants but did not find any significant associations between parabens, phenols, bisphenol A, and triclosan concentrations and PCPs (Zhang et al., 2018). However, they did observe greater urinary phthalate concentrations in female students than male students and the authors have stated that this result corroborates that phthalate concentrations are affected by PCP use which is greater in females (Zhang et al., 2018).

Table IV. Overview of findings presented in this scoping review

First Author (Year)	Overview of Findings
Berger et al. (2019)	• Greater urinary methyl and propyl paraben concentrations among participants who were everyday users of makeup than in non-users and rare users • Positive association between use of foundation, blush, mascara and urinary mono-ethyl phthalate concentrations • Positive association between sunscreen and benzophenone-3 • Positive association between deodorant use and urinary mono-ethyl phthalate concentrations • Positive association between use of Colgate Total® toothpaste and urinary concentrations of triclosan • Negative association between bar soap use and urinary mono-isobutyl phthalate concentration
Černá et al. (2014)	• Association between PCP use frequency and urinary phthalate concentrations in children of Czechia, Hungary, and Slovakia • Slovak children had the highest body lotion and cream use
Chen et al. (2017)	• Positive association between nail polish use and urinary mono-ethyl phthalate concentration
Chen et al. (2015)	• Association between lower shampoo use and lower urinary mono-n-butyl phthalate concentrations • Negative association between regular handwashing and urinary mono-n-butyl phthalate concentrations • Decreased shower gel use led to lower urinary mono-ethyl phthalate concentrations
Cullen et al. (2017)	• Positive correlation between PCP use and urinary concentration of methyl paraben
Cutanda et al. (2014)	• Positive associations between body lotion and creams use and urinary mono-ethyl phthalate concentrations • Association between fragrance use and urinary mono-2-ethylhexyl phthalate, mono-ethyl phthalate, mono-n-butyl phthalate, 7-carboxy-(mono-methylheptyl) phthalate concentrations
Den Hond et al. (2013)	• Positive associations between lip balm, makeup, shampoo, hair care products, bath products, day or night cream, and perfume use and urinary triclosan concentrations
Ding et al. (2019)	• Positive association between skin care cosmetics use and urinary mono-ethyl phthalate concentrations
Fillol et al. (2019)	• PCP use reported to be a determinant of paraben concentrations • Use of cosmetics and of hair products reported to be determinants of phthalate concentrations in children • PCP use or use of particular PCPs not listed as determinants that influence PFAS concentrations
Hajizadeh et al. (2020)	• Positive associations between makeup base, eye makeup, and lip makeup use and urinary methyl paraben concentrations • Participants who used a high cumulative number of PCPs had higher paraben concentrations • Positive associations between body wash, shaving gel, bar soap, and shampoo use and urinary methyl and propyl paraben concentrations • Positive associations between lotion, toothpaste, and sunscreen use and urinary propyl paraben concentrations
Hammel et al. (2019)	• No associations found between PCP use and chemical concentrations
Hong et al. (2021)	• Positive associations between liquid soaps use (e.g., shampoo and shower gel) and urinary ethyl paraben concentrations • Positive associations between fragrance use and urinary propyl paraben concentrations
Huang et al. (2015)	• No associations found between PCP use and chemical concentrations
Huang et al. (2022)	• Participants who used a high cumulative number of PCPs had higher paraben concentrations • Negative association between frequent body wash use and methyl and propyl paraben concentrations • Positive association between lotion use and urinary butyl paraben concentrations • Positive associations between perfume use and urinary ethyl paraben concentrations
Jala et al. (2022)	• Paraben exposure among young female adults mostly occurred through the use of body lotion, face cream, foundation and sunscreen
Kim et al. (2018)	• Positive association between coloured cosmetics use and urinary propyl paraben concentrations • Positive association between bath products use and methyl, ethyl, and propyl paraben concentrations

First Author (Year)	Overview of Findings
	• Positive association between bath products use and urinary triclosan concentrations • Positive association between toothpaste use and urinary methyl, ethyl, and propyl paraben concentrations • Positive association between fragrance use and urinary propyl paraben concentrations
Koppen et al. (2019)	• Positive association between PCP use and urinary concentrations of mono-benzyl phthalate, mono-isobutyl phthalate, and triclosan in children • Urinary triclosan concentrations in participants aged 6 – 11 years were affected by sunscreen use
Larsson et al. (2014)	• Positive correlation between use of eye makeup and urinary propyl paraben concentrations in participants 6 – 11 years • Positive correlation between eye makeup use and urinary mono-ethyl phthalate concentrations • Positive correlations found between lotion use and urinary concentrations of methyl paraben and propyl paraben
Levasseur et al. (2021)	• Positive association between lotion use and urinary methyl, ethyl, and propyl paraben concentrations
Lewis et al. (2013)	• Positive association between coloured cosmetics use and urinary mono-n-butyl phthalate, mono(2-ethylhexyl) phthalate, mono(2-ethyl-5-hydroxyhexyl) phthalate, mono(2-ethyl-5-oxohexyl) phthalate, and mono(2-ethyl-5-carboxypentyl) concentrations in girls • Positive association between use of hair products different from hair cream, hair spray or gel, or shampoo and concentrations of mono-n-butyl phthalate, mono-isobutyl phthalate, and mono(3-carboxypropyl) phthalate in girls • Positive association between use of conditioner and urinary mono-ethyl phthalate concentrations in girls • Positive association between lotion use and urinary mono(2-ethylhexyl) phthalate concentrations in boys • Positive association between perfume use and urinary mono-ethyl phthalate, mono(3-carboxypropyl) phthalate, mono(2-ethyl-5-hydroxyhexyl) phthalate, mono(2-ethyl-5-oxohexyl) phthalate concentrations in boys • Positive association between use of deodorant and mono-ethyl phthalate concentrations in girls
Li et al. (2020)	• Positive correlations between face cream use and fingernail concentrations of ethyl and butyl paraben
Li et al. (2019)	• Positive association between body lotion use and urinary benzophenone-2 concentrations
Lim (2020)	• Positive association between nail polish use and the risk of exposure to mono(3-carboxypropyl) phthalate • Risk of exposure to ethyl paraben was enhanced by the use of fragrance
Murawski et al. (2021)	• Positive associations between eye makeup and facial makeup use and urinary methyl and ethyl paraben concentrations • Positive associations between lotion and cream use and urinary methyl, ethyl, n-propyl paraben concentrations
Overgaard et al. (2017)	• Positive association between emollient use and methyl, ethyl, propyl, and butyl paraben concentrations • Positive association between emollient use and urinary mono-ethyl phthalate and mono-butyl phthalate concentrations
Philippat et al. (2015)	• Negative association between bar soap use and methyl, propyl, and butyl paraben concentrations • Positive association between liquid soap use and urinary mono-ethyl phthalate concentrations • Positive association between sunscreen use and benzopheone-3 concentrations • Positive association between use of Colgate Total® toothpaste and urinary concentrations of triclosan • Positive association between sunscreen use and urinary mono-n-butyl phthalate concentrations
Runkel et al. (2020)	• Positive associations between styling products and nail polish use and urinary phthalate concentrations • Positive associations between lotion and sunscreen use and urinary phthalate concentrations • Positive association between fragrance and deodorant use and urinary phthalate concentrations
Sakhi et al. (2017)	• Positive association between hairspray and hair gel use and urinary mono-ethyl and mono-n-butyl phthalate concentrations • Negative association between hand soap use and urinary di-(2-ethyl-5-hexyl) phthalate concentrations • Positive association between face cream use and urinary mono-ethyl phthalate, mono-n-butyl phthalate, di(2-ethyl-5-hexyl) phthalate, di-iso-nonyl phthalate concentrations
Sakhi et al. (2018)	• Positive associations between hair products use and urinary benzophenone-3 concentrations • Negative association between hand soap use and urinary bisphenol A concentrations • Positive association between face cream use and urinary ethyl paraben concentrations • Positive association between cream use and urinary benzophenone-3 concentrations

First Author (Year)	Overview of Findings
Sidlovska et al. (2017)	• Positive association between nail polish use and urinary mono-ethyl phthalate concentrations • Positive association between body lotion use and urinary mono(2-ethylhexyl) phthalate concentrations
Stacy et al. (2017)	• Positive association between hand soap and toothpaste use and urinary triclosan concentrations
Stuchlík Fišerováet al. (2022)	• Positive association between nail polish use and urinary mono(2-ethyl-5-carboxy-pentyl) phthalate and 7-hydroxy(monomethyl-octyl) phthalate concentrations
Tkalec et al. (2021)	• Positive association between lipstick and perfume use and urinary methyl paraben concentrations
Tschersich et al. (2021)	• Positive association between fragrance use and urinary benzophenone-1 and benzophenone-3 concentrations
Vindenes et al. (2021)	• Positive association between use frequency of moisturizer use and methyl paraben concentrations
Watkins et al. (2014)	• Positive association between hairspray or hair gel use and urinary mono-ethyl phthalate concentrations
Zhang et al. (2018)	• No associations found between PCP use and chemical concentrations

Makeup and Cosmetic Products

Several included studies have reported a positive association between makeup and cosmetic products such as coloured cosmetics, foundation (Kim et al., 2018), makeup base (Hajizadeh et al., 2020), eye makeup (Hajizadeh et al., 2020; Murawski et al., 2021), facial makeup (Murawski et al., 2021), lip makeup (Hajizadeh et al., 2020), and lipstick (Tkalec et al., 2021) and urinary paraben concentrations. Lip makeup and lipstick were not grouped together in this summary of findings, as lip makeup may also include lip products other than lipstick. One study reported greater urinary methyl and propyl paraben concentrations among participants who were everyday users of makeup than in non-users and rare users (Berger et al., 2019). According to two studies, participants who used a high cumulative number of PCPs had higher paraben concentrations (Hajizadeh et al., 2020; Huang et al., 2022). One study reported that the use of eye makeup was correlated to urinary propyl paraben concentrations in participants 6 – 11 years (Larsson et al., 2014) and another study reported that PCP use was correlated with participants' urinary concentration of methyl paraben (Cullen et al., 2017). Use of foundation was reported as an important source for paraben exposures (Jala et al., 2022). PCP use was reported to be a determinant of paraben concentration in one study (Fillol et al., 2020). Regarding phenol concentrations, use of lip balm and makeup was positively associated with urinary concentrations of triclosan according to one study (Den Hond et al., 2013).

The use of foundation, blush, mascara (Berger et al., 2019), colour cosmetics (Ding et al., 2019; Lewis et al., 2013), skin care cosmetics (Ding et al., 2019), styling products (Runkel et al., 2020), and nail polish (Chen et al., 2017; Runkel et al., 2020; Šidlovská et al., 2017; Stuchlík Fišerová et al., 2022) was positively associated with phthalate concentrations in urine. One study found an association between nail polish use among adults and preschoolers and the risk of exposure to mono(3-carboxypropyl) phthalate (Lim, 2020). In girls, use of coloured cosmetics led to higher levels of certain phthalate metabolites (Lewis et al., 2013). Another study reported a correlation between eye makeup use in children and mono-ethyl phthalate concentrations (Larsson et al., 2014). The use of cosmetics and of hair products were reported to be determinants of phthalate concentrations in children in a study by Fillol et al. (2020).

Bath, Shower, Hair and Soap Products

Positive associations have been reported between body wash, shaving gel, bar soap, and shampoo (Hajizadeh et al., 2020) and urinary paraben concentrations. Bath products (Kim et al., 2018) and liquid soaps (*e.g.,* shampoo, shower gel) (Hong et al., 2021) as PCP categories were equally positively associated with paraben concentrations. Negative associations between body wash (Huang et al., 2022) and bar soap (Philippat et al., 2015) use and paraben concentrations have also been reported. One study measured lower methyl and propyl paraben concentrations among frequent users of body wash (Huang et al., 2022). Similarly, another study reported that children who used bar soaps had lower urinary concentrations of methyl, propyl, and butyl paraben (Philippat et al., 2015).

Participants' use of shampoo (Den Hond et al., 2013), hand soap (Stacy et al., 2017), hair care products (Den Hond et al., 2013), and hair products (Sakhi et al., 2018) were also positively associated with urinary concentrations of phenols. For instance, higher urinary concentrations of triclosan have been measured in regular bath product users (Den Hond et al., 2013; Kim et al., 2018). One study reported that a high frequency of handwashing led to increased concentrations of triclosan in children (Stacy et al., 2017). In contrast, another study reported that hand soap use among children lowered the urinary concentrations of bisphenol A (Sakhi et al., 2018).

The use of hairspray and hair gel (Sakhi et al., 2017), as well as liquid soap (Philippat et al., 2015), was positively associated with urinary concentrations of phthalates. In one study, an association was found between the use of hairspray or hair gel among 5 year-old participants and high concentrations of mono-ethyl phthalate (Watkins et al., 2014). In girls, the use of conditioner was associated with increased mono-ethyl phthalate concentrations (Lewis et al., 2013). To add, the use of other hair products – different from hair cream, hair spray or gel, or shampoo – led to higher concentrations of mono-n-butyl phthalate, mono-isobutyl phthalate, and mono(3-carboxypropyl) phthalate in girls (Lewis et al., 2013). Different from these findings, one study reported an association between hand soap use among children and a 40% decrease in di-(2-ethyl-5-hexyl) phthalate concentrations in urine (Sakhi et al., 2017). Another study found that regular handwashing and lower use of shampoo were associated with lower concentrations of urinary mono-n-butyl phthalate (Chen et al., 2015). This study also found that decreased shower gel use lowered urinary concentrations of mono-ethyl phthalate (Chen et al., 2015). One study reported a negative association between bar soap use and urinary mono-isobutyl phthalate concentration (Berger et al., 2019).

Lotions, Creams, Sunscreen, and Toothpaste

Several retained studies reported a positive association between emollient (Overgaard et al., 2017), lotion (Hajizadeh et al., 2020; Huang et al., 2022; Levasseur et al., 2021; Murawski et al., 2021), cream (Murawski et al., 2021), face cream (Li et al., 2020; Sakhi et al., 2018), toothpaste (Hajizadeh et al., 2020; Kim et al., 2018), and sunscreen (Hajizadeh et al., 2020) use and paraben concentrations. One study reported that paraben exposure among young female adults mostly occurred through the use of body lotion, face cream, and sunscreen (Jala et al., 2022). Among children, a positive correlation has been reported between lotion use and concentrations of methyl paraben and propyl paraben (Larsson et al., 2014). One study reported that face cream use is a principal exposure pathway for humans (Li et al., 2020). In this study, face cream samples were correlated with fingernail concentrations of ethyl and butyl paraben (Li et al., 2020). Another study found that the use frequency of leave-on PCPs – such as moisturizer and lotions – were positively associated with paraben concentrations (Vindenes et al., 2021). The same study reported that participants' methyl paraben concentrations increased with the frequency of moisturizer use (Vindenes et al., 2021).

The use of body lotion (Li et al., 2019), creams (Sakhi et al., 2018), day or night cream (Den Hond et al., 2013), sunscreen (Berger et al., 2019; Philippat et al., 2015), and toothpaste (Berger et al., 2019; Stacy et al., 2017) were positively associated with urinary phenol concentrations. One study found an association between the use of Colgate Total® toothpaste and elevated urinary concentrations of triclosan (Berger et al., 2019). Similarly, another study reported that children who used Colgate® toothpaste had greater triclosan concentrations in their urine than those who used different brands of toothpaste (Philippat et al., 2015). Urinary triclosan concentrations in participants aged 6 – 11 years were affected by sunscreen use (Koppen et al., 2019).

Additionally, findings showed that the use of emollient (Overgaard et al., 2017), lotion (Lewis et al., 2013; Runkel et al., 2020), body lotion (Cutanda et al., 2015; Šidlovská et al., 2017), face cream (Sakhi et al., 2017), and sunscreen (Philippat et al., 2015; Runkel et al., 2020) were associated with urinary phthalate concentrations.

Fragrances, Perfumes, and Deodorant

The use of fragrance or perfume (Hong et al., 2021; Huang et al., 2022; Kim et al., 2018; Tkalec et al., 2021) was associated with higher urinary paraben concentrations. More precisely, studies found that perfume and fragrance use was associated with concentrations of ethyl paraben (Huang et al., 2022) and propyl paraben (Hong et al., 2021; Kim et al., 2018), respectively. One study measured higher methyl paraben concentrations in perfume users (Tkalec et al., 2021). Another included study also stated that the risk of exposure to ethyl paraben was enhanced by the use of fragrance (Lim, 2020).

Use of perfume was associated with higher urinary concentrations of triclosan according to one study (Den Hond et al., 2013) and deodorant use was associated with higher urinary concentrations of benzophenone-3 according to another study (Sakhi et al., 2018). One study reported higher concentrations of benzophenone-1 and benzophenone-3 in participants who used fragrances (Tschersich et al., 2021).

Fragrance (Cutanda et al., 2015; Runkel et al., 2020), deodorant (Berger et al., 2019; Runkel et al., 2020), and perfume (Lewis et al., 2013; Sakhi et al., 2017) use was also associated with urinary phthalate concentrations. Indeed, one study has reported that boys had greater phthalate concentrations following the use of perfume or cologne during the 48 hours preceding urine collection (Lewis et al., 2013). The same study found that the use of deodorant was associated with higher monoethyl phthalate concentrations in girls (Lewis et al., 2013). In contrast, spray-on deodorant use had a negative association with mono-ethyl phthalate concentrations in urine (Berger et al., 2019).

Frequently Used Personal Care Products Among Children and Adolescents

Overall, everyday products, such as shower or bath products, soaps, fragrances, and lotions or creams, were most frequently used by children and adolescents. Included studies reported that lotion is a commonly used product among children. One study determined that above 50% of participating parents' children used lotion or baby wipes (Hammel et al., 2019). Among Slovak children, body lotions and creams usage frequency were the highest (Černá et al., 2015). Another study also reported that minors aged 7 – 11 years used more lotion than participants 12 – 17 years (Huang et al., 2022).

Bath and soap products are another category of PCPs that are commonly used by youth. For instance, PCPs with the most frequent usage were liquid soap and toothpaste among young Iranians (Hajizadeh et al., 2020). One study reported that, among Korean preschoolers 3 – 5 years, body cleansers were the most frequently used PCP (Lim, 2020). Furthermore, Californian children of ages 3 – 8 years most frequently used toothpaste, liquid soap, and shampoo (Philippat et al., 2015). In another study, during the 48 hours dedicated to collecting urine, the majority of 5 year-old children had used shampoo and different soaps (Watkins et al., 2014). Another study found that 73% of Taiwanese children and adolescents used body wash daily (Huang et al., 2015). A different study by the same principal author revealed that body wash was the most frequently used product among all age groups (Huang et al., 2022). Among Chinese students aged 19 years and above, shower gels, facial cleansers, and face toner were used quotidianly among 70 – 80% of females (Zhang et al., 2018). For male students, daily use of shower gels and shampoo was practised by 65 to 80% according to this study (Zhang et al., 2018).

Among older youth, popular products were fragrance, perfume, makeup, and nail polish. Indeed, participants who were 18 and 19 years of age (categorized as adults) were reported to have higher perfume and nail polish use compared to children (Huang et al., 2022). In Korean adolescents aged 12 – 17 years, fragrance and makeup were among the most commonly used PCPs (Lim, 2020). This being said, for female participants in general, use of nail polish was high, and for female adolescents, all types of PCPs were used more substantially (Lim, 2020).

4. Discussion

Through our review, we provided an overview of childhood and adolescent exposure to chemicals found in PCPs through the synthesis of findings reported by 37 studies, allowing us to gain insight on this fairly novel topic. We documented relevant information and key findings relative to the use of PCPs and chemical concentrations. To our knowledge, this is the first scoping review on the emerging subject of childhood and adolescent exposure to chemicals found in PCPs. Findings of the studies included in our review have shown that PCP use among children and adolescents Information on the limitations of this scoping review and knowledge gaps arising from this review are presented below.

Concentrations of chemicals resulting from chemical exposure may be influenced by multiple factors. Human biomonitoring data represents chemical exposure from all sources of exposure and not only from PCP use. For instance, occupational exposure to bisphenol A among cashiers through contact with thermal paper receipts – a source of bisphenol A – may result in higher concentrations of this chemical among these workers (Lv et al., 2017; Ndaw et al., 2016). This type of exposure will be captured by human biomonitoring. Chemical exposure may also occur through a primary or secondary source. A product and the ingredients it contains, including chemical compounds, is considered as a primary source. The product's packaging can be a secondary source, as chemicals found in the package may leach into the main product. For instance, bisphenols may be found in PCPs due to contamination from the plastic packaging of the product (Vandenberg et al., 2007). Therefore, there is a possibility that some reported chemical exposures may originate from a secondary source. There is a difficulty in differentiating chemical exposure sources. Indeed, sources of chemical exposures are various and may also be foods (Błędzka et al., 2014; Soni et al., 2001), clothes (Rodgers et al., 2022), pharmaceuticals (Soni et al., 2001), or items in people's surrounding environment (*e.g.,* carpets, furniture) (Rodgers et al., 2022; Wu et al., 2020). Thus, the included studies cannot unequivocally determine the precise source of a chemical exposure. Together, these elements may act as confounding factors that influence the association between PCP use and measured chemical concentrations. Furthermore, it is difficult to assess the duration of the exposure to a chemical, which is variable from an individual to another. Thus, duration of exposure is a factor that influences chemical concentrations.

Most of the chemical classes investigated in the retained studies are recognized to have short half-lives. Parabens, phenols, and phthalates have half-lives of less than 24 hours in the human body (Leppert et al., 2020; Sandborgh-Englund et al., 2006; Y. Wang et al., 2019). Short half-lives imply that measured biological concentrations of chemicals reflect recent exposure only, due to the chemical's rapid metabolism. Moreover, most of the studies that have used urine as a biological matrix only included a single sample of spot urine, which may lead to exposure misclassification due to the short half-lives of the studied non-persistent chemicals. The collection of several spot urine samples in the same day may decrease exposure misclassification (Bastiaensen et al., 2021). In contrast to non-persistent chemicals, PFAS have longer half-lives that are in the range of 2 to 4 years (Y. Li et al., 2018). Despite their long half-lives and their presence in PCPs, we have retrieved only one study that measured the serum concentrations of PFAS in relation with PCP use.

Most studies in this scoping review were cross-sectional. First, cross-sectional studies do not allow to infer causal relations. In fact, the temporal link between outcome and exposure cannot be determined precisely since both elements are studied concurrently. Furthermore, cross-sectional studies do not allow to track changes over time, as they are designed to analyze collected data at a designated point in time.

In this scoping review, a heterogeneity in the results provided by the retained studies was noticed. First, different questionnaires were used to collect participants' self-reported responses on PCP, which made it unfeasible to compare findings between studies and may have contributed to the heterogeneity of the results. Second, the different populations studied in each study and their different patterns of PCP use may also explain this heterogeneity in the results. Third, sources of exposure other than PCP use may be another explanation for heterogeneous results. Last, differences in regulations on chemical use in PCPs between countries may contribute to this heterogeneity in findings. Such regulations may also vary within a country. For example, there is no regulation at the national level regarding PFAS use in PCPs in the United States, but the state of California banned the use of 13 PFAS in PCPs – including PFOA and PFOS – through the Toxic-Free Cosmetic Act in 2020 and the act will be effective from January 1, 2025 (California Legislative Information, 2020; Little, 2020). The Toxic-Free Cosmetic Act also bans the use of dibutyl phthalate, di-(2-ethylhexyl) phthalate, isobutyl paraben, and isopropyl paraben (California Legislative Information, 2020). Another example is the state of Maryland which also passed a similar bill prohibiting the use of 24 ingredients, including certain PFAS, in PCPs (Backhaus, 2021; Myers, 2021).

Strengths and Limitations of This Scoping Review

For the present review, we followed a methodology based on a detailed framework proposed specifically for scoping reviews. A rigorous search strategy combining subject headings and keywords was employed to retrieve pertinent publications. Moreover, restrictions were not applied to publication language and date, allowing us to retrieve one French-language study (Fillol et al., 2020). The retained studies were carried out in various countries which allowed to provide an overview that also includes findings from regions outside of the North-American continent.

Information found in the grey literature was not assessed for this scoping review as only original research articles were considered. This limits our findings only to evidence reported by publications of scientific journals. Additionally, a scoping review is helpful in providing knowledge on emergent subjects. Although, it is an exploratory type of review that provides only a summary of a subject.

5. Conclusion

This scoping review is the first to synthesize findings from existing scientific publications on children and adolescents' exposure to chemicals found in PCPs. Our review has shown that the study of PCP use in relation with chemical exposure is recent, as studies were published only 10 years ago. The compilation of findings indicates that PCP use was associated with higher concentrations of parabens, phenols, and phthalates. On the other hand, use of soaps and other hygiene products was associated with lower urinary levels of these chemicals. Methods to assess PCP use and the products used were heterogenous, which contributed to complicating the comparison of findings between individual studies. Our review indicates that further studies are necessary to better assess PFAS exposure in relation with PCP use, since only one study investigating this class of chemicals was found, despite their presence in PCPs. Finally, more studies on this topic are needed to further document the relative importance of personal care product use to total chemical exposure.

Supplementary Material

Table S1. Search strategy and criteria for MEDLINE database

1	adolescent/ or exp child/
2	exp Environmental Exposure/
3	exp Cosmetics/
4	Parabens/
5	exp Phenols/
6	exp Phthalic Acids/
7	exp Plasticizers/
8	Biological Monitoring/
9	Biomarkers/
10	(kid* or child or children or preschool child or school child or boy or girl or adolescen* or teenager* or teens or youth or young adult).ab,kf,ti.
11	"expos*".ab,kf,ti.
12	(personal care product* or cosmetic* or skin care or skin-care or make up or make-up or beauty products or self care products or self-care products or fragrances or cosmeceutical*).ab,kf,ti.
13	(chemical* or parabens or 4 hydroxybenzoic acids or 4-hydroxybenzoic acids or 4 hydroxybenzoic acid esters or 4-hydroxybenzoic acid esters or para hydroxybenzoic acids or para-hydroxybenzoic acids or phthalates or phthalic acids or plasticizer* or phenols or perfluoroalkyl substances or polyfluoroalkyl substances or PFAS or PFASs).ab,kf,ti.
14	(((bio or biologic*) adj1 (monitoring or marker)) or bio-monitoring or bio-marker or exposure biomarker or blood or urin*).ab,kf,ti.
15	1 or 10
16	2 or 11
17	3 or 12
18	4 or 5 or 6 or 7
19	13 or 18
20	8 or 9
21	14 or 20
22	15 and 16 and 17 and 19 and 21

The search was executed on September 19^{th}, 2022, on Ovid MEDLINE (1946 to September 19, 2022).

Table S2. Search strategy and criteria for Embase database

1	child/ or juvenile/ or boy/ or girl/ or preschool child/ or school child/
2	exposure/ or environmental exposure/ or exp exposure science/
3	exp cosmetic/
4	exp 4 hydroxybenzoic acid ester/
5	phenol derivative/
6	phthalic acid/
7	perfluorooctanesulfonic acid/ or perfluorooctanoic acid/
8	biological marker/
9	biological monitoring/
10	(kid* or child or children or preschool child or school child or boy or girl or adolescen* or teenager* or teens or youth or young adult).ab,kf,ti.
11	"expos*".ab,kf,ti.
12	(personal care product* or cosmetic* or skin care or skin-care or make up or make-up or beauty products or self care products or self-care products or fragrances or cosmeceutical*).ab,kf,ti.
13	(chemical* or parabens or 4 hydroxybenzoic acids or 4-hydroxybenzoic acids or 4 hydroxybenzoic acid esters or 4-hydroxybenzoic acid esters or para hydroxybenzoic acids or para-hydroxybenzoic acids or phthalates or phthalic acids or plasticizer* or phenols or perfluoroalkyl substances or polyfluoroalkyl substances or PFAS or PFASs).ab,kf,ti.
14	(((bio or biologic*) adj1 (monitoring or marker)) or bio-monitoring or bio-marker or exposure biomarker or blood or urin*).ab,kf,ti.
15	1 or 10
16	2 or 11
17	3 or 12
18	4 or 5 or 6 or 7
19	13 or 18
20	8 or 9
21	14 or 20
22	15 and 16 and 17 and 19 and 21

The search was executed on September 19th, 2022, on Embase (1974 to 2022 September 19).

Table S3. Search strategy and criteria for Global Health database

1	(kid* or child or children or preschool child or school child or boy or girl or adolescen* or teenager* or teens or youth or young adult).ab,hw,ti.
2	"expos*".ab,hw,ti.
3	(personal care product* or cosmetic* or skin care or skin-care or make up or make-up or beauty products or self care products or self-care products or fragrances or cosmeceutical*).ab,hw,ti.
4	(chemical* or parabens or 4 hydroxybenzoic acids or 4-hydroxybenzoic acids or 4 hydroxybenzoic acid esters or 4-hydroxybenzoic acid esters or para hydroxybenzoic acids or para-hydroxybenzoic acids or phthalates or phthalic acids or plasticizer* or phenols or perfluoroalkyl substances or polyfluoroalkyl substances or PFAS or PFASs).ab,hw,ti.
5	(((bio or biologic*) adj1 (monitoring or marker)) or bio-monitoring or bio-marker or exposure biomarker or blood or urin*).ab,hw,ti.
6	children/ or boys/ or girls/ or preschool children/ or school children/
7	exposure/
8	cosmetics/
9	exp parabens/
10	exp phenols/
11	exp phthalates/
12	biological markers/
13	1 or 6
14	2 or 7
15	3 or 8
16	9 or 10 or 11
17	4 or 16
18	5 or 12
19	13 and 14 and 15 and 17 and 18

The search was executed on September 19th, 2022, on Global Health (1910 to 2022 Week 37).

Authors' Contribution

Nahiyan S. Khan

- Executed the scoping review;
- Drafted the manuscript;
- Edited the manuscript according to the corrections deemed necessary by their supervisors.

Jillian Ashley-Martin:

- Developed the research question;
- Edited the manuscript;
- Supervised the drafting of the manuscript.

Maryse F. Bouchard:

- Developed the research question;
- Edited the manuscript;
- Supervised the drafting of the manuscript.

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VI
General Discussion

For this thesis, the conducted scoping review aimed to synthesize findings of available scientific literature on childhood and adolescent exposure to four primary chemical families – parabens, phenols, phthalates, and PFAS – found in PCPs. The biomonitoring results associated with the use of PCPs among youth with an age ranging from 5 – 19 years old were compiled and presented. In this chapter, the findings from our scoping review are rapidly revisited. The regulation of PCPs and implications of our scoping study are also discussed.

6.1 General Summary of Findings

The findings of the studies included in our scoping review frequently reported positive associations between PCP use and chemical concentrations in participants. For instance, nail polish use was associated with higher phthalate concentrations (Chen et al., 2017; Runkel et al., 2020; Šidlovská et al., 2017; Stuchlík Fišerová et al., 2022). Other products such as lotion (Hajizadeh et al., 2020; Huang et al., 2022; Levasseur et al., 2021; Murawski et al., 2021), fragrance and perfume (Hong et al., 2021; Huang et al., 2022; Kim et al., 2018; Tkalec et al., 2021) were associated with higher paraben concentrations. Sunscreen (Berger et al., 2019; Philippat et al., 2015) and toothpaste (Berger et al., 2019; Stacy et al., 2017) were associated with higher phenol concentrations. Interestingly, inverse associations between body wash (Huang et al., 2022) and bar soap (Philippat et al., 2015) use, and paraben concentrations have been reported. For instance, hand soap use was associated with lower di-(2-ethyl-5-hexyl) phthalate concentrations in urine Sakhi et al. (2017). Likewise, regular handwashing was associated with lower concentrations of urinary mono-n-butyl phthalate Chen et al. (2015). Some studies did not report any association between PCPs and chemical concentrations. Nevertheless, PCPs as a source of exposure should not be omitted because of such findings, as they are products typically used on a daily basis by youth.

6.2 Use of Personal Care Products: Why Regulation Matters

As reported in our scoping review, children and adolescents use various PCPs, many of which are commonly used on a daily basis, such as body wash, lotion, soap, shampoo, or toothpaste. Since each product contains its own set of ingredients, it is essential to understand that using several PCPs simultaneously exposes the consumer to a wide range of chemicals. Furthermore, certain PCPs such as toothpaste may be used several times daily. In such cases, exposure to chemicals can occur repeatedly. The use of numerous PCPs and repeated use of certain products may cause cumulative exposure to different chemicals. Many of the chemicals contained in PCPs are suspected to have endocrine-disrupting properties and have been linked to health issues such as behavioural problems, fertility problems, and cancer among several others. The health risks posed by these chemical exposures are concerning for youth because of their greater vulnerability to potential adverse effects. Thus, the regulation of PCPs and chemicals used as ingredients in these products is important for reducing chemical exposure.

To help improve existing regulations targeting PCPs, it is necessary to expand our knowledge on children and adolescents' exposure to chemicals found in PCPs by continuing to investigate these chemical exposures. Furthermore, it is important for future studies to address the exposure to PFAS relative to PCP use among youth; which is a gap in knowledge identified in our review. These studies could also encourage countries and regions lacking regulations targeting PCPs to create effective regulations concerning the use of chemicals that are potentially harmful to children and adolescents' health.

6.3 Alternatives to Regulation

While policies and regulations are being improved or created, companies manufacturing PCPs can reduce consumers' exposure to potentially toxic chemicals by reducing or removing them from their products. Some major companies have already stopped incorporating certain chemicals in their products. In 2012, Johnson & Johnson eliminated parabens, triclosan, and phthalates from their baby products, and eliminated triclosan and phthalates from their adult products (Cheadle, 2013; Kay, 2013). In 2014, another PCP manufacturing company, Proctor and Gamble, stopped incorporating triclosan and phthalates in their PCPs (Cheadle, 2013). Such initiatives help consumers lower unwanted chemical exposure.

Since it is not feasible to stop using PCPs, consumers can follow advice shared by non-profit or advocacy organizations that advocate for stricter guidelines for chemicals found in PCPs. Two Canadian organizations, the David Suzuki Foundation and Environmental Defence, have websites that list chemicals found in cosmetics (David Suzuki Foundation, n.d.) or skincare (Environmental Defence, n.d.) products, and also provide information on suspected adverse health effects. In the United States, the Environmental Working Group also offers a short list of twelve potentially harmful chemicals and contaminants that are commonly found in cosmetics (Faber, 2020). Hence, consumers can be informed about which chemicals to avoid in the ingredient list when choosing their PCPs. These organizations also provide information on safer PCP alternatives.

6.4 Implications for Future Research

Presented in this thesis is an original scoping study that is the first to synthesize knowledge on childhood and adolescent exposure to four major classes of chemicals found in PCPs. To the best of our knowledge, this type of study has not been conducted in adults either. Our review showed a lack of Canadian studies assessing chemical exposure through PCP use among youth. It also highlights the absence of studies investigating exposure to persistent chemicals, such as PFAS, in youth. In Canada, currently available studies investigating chemical exposure did not consider the exposure among youth. An example of such study is the Plastics and personal care product use in pregnancy study conducted in 2009-2010 among 80 pregnant women (Arbuckle et al., 2016; Government of Canada, 2009). Bisphenol A, phthalates, triclosan, and triclocarban were the chemicals of interest in this study (Government of Canada, 2009). The exposure to persistent chemicals was not studied.

Our literature search yielded only one study investigating PFAS exposure. Thus, our review may encourage researchers to conduct further studies on the contribution of PCP use to PFAS exposure among youth and the sources of this exposure, to address this gap in knowledge.

Further research on childhood and adolescent exposure to chemicals found in PCPs may prove important for scientific knowledge and policy. Indeed, data from such studies may progressively contribute to the knowledge on the sources of chemical exposure that may result in adverse health effects among youth.

VII
Conclusion

The scoping review conducted in the context of the present thesis aimed to grasp the scope of the available scientific literature and deliver a synthesis of children and adolescents' exposure to parabens, phenols, phthalates, and PFAS following PCP use. Our review has shown that interest in this topic is quite recent, as the first studies were published about 10 years ago. Most of the included studies revealed that PCP use appears to increase the concentrations of parabens, phenols, and phthalates. The findings reported by the studies were heterogeneous; therefore, comparing studies was difficult. Moreover, the retained studies mostly had a cross-sectional design, thus not allowing to determine if a causal relationship exists between PCP use and urinary chemical concentrations. Furthermore, only one study investigated PCPs in relation to PFAS exposure. Given that PFAS were found in PCPs (Whitehead et al., 2021), future studies could address youth exposure to this class of chemicals, especially since they tend to persist longer in the body and youth are more susceptible to the potential adverse effects of chemical exposures. To conclude, further studies on this topic are needed to document the relative importance of personal care product use to the total exposure to chemicals.

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