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Development of aggregate exposure assessment methodology based on co-use scenario of cosmetic products

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환경보건학과 환경보건학 전공

임 미 영

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지도교수 이 기 영

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환경보건학과 환경보건학 전공
임 미 영

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위 원 장	**최 경 호**	**(인)**
부위원장	**김 성 균**	**(인)**
위 원	**윤 충 식**	**(인)**
위 원	**문 경 환**	**(인)**
위 원	**이 기 영**	**(인)**

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Miyoung Lim

Supervised by Professor Kiyoung Lee

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Data approved by:

Kyungho Choi ______________________

Sungkyoon Kim ______________________

Chung Sik Yoon ______________________

Kyong Whan Moon ______________________

Kiyoung Lee ______________________

Abstract

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Miyoung Lim

Department of Environmental Health Sciences

Graduate School of Public Health

Seoul National University

Traditional chemical exposure assessments were conducted to a single exposure source. For a realistic estimation of chemical exposures to human body, aggregate assessment of a chemical across multiple routes and sources should be considered. The tiered approach for chemical exposure and risk assessment could applied to aggregate exposure assessment. However, the specific application method was not yet developed. The objective of this study were to develop a higher tier aggregate exposure assessment methodology based on co-use scenarios of multiple consumer products and to apply for phthalate aggregate exposure assessment. The target consumer products were cosmetic products, and the target chemicals were three phthalates, that is, di(2-ethylhexyl)phthalate (DEHP), di-n-butyl phthalate (DnBP), and diethyl phthalate (DEP). Exposure factors for 31 cosmetic products were

collected by face-to-face interviews with 1,001 subjects who were selected by national representative sampling of Korean population. The concentrations of phthalates in 214 cosmetic products were analyzed by GC-MS-MS.

The first study aimed to estimate receptor-based aggregate exposures to phthalates through cosmetics and to compare with product-based aggregate exposures. A receptor-based aggregate exposure assessment was conducted according to individuals' exposure factors and simultaneous use patterns including co-use and non-use. A product-based aggregate exposure assessment was conducted by product usage rates of population and users' exposure factors. The average aggregate exposure dose (AED) determined by the receptor-based method for DEHP, DnBP, and DEP were 0.68 ± 0.87, 1.08 ± 5.71, and 2.47 ± 9.05 μg/kg/day, respectively. Based on the receptor-based AED, the most contributing cosmetics were skin care and body care products for DEHP, nail care products for DnBP, and fragrance and hair care products for DEP. The young female group showed the highest exposure. Although average population exposure by product-based aggregate exposure underestimated, 95th percentiles of product-based aggregate exposure for DnBP and DEP were significantly overestimated.

The second study aimed to characterize co-use patterns of cosmetics and to determine the co-use scenarios for gender-age population groups. The co-use patterns of cosmetics should be critical for accurate aggregate exposure assessment. The Korean national representative exposure factor database was used to analyze the co-use patterns of cosmetics. The use or non-use of 31 cosmetics was treated as a categorical variable. Three analytical methods were applied to determine the co-use patterns. Cohen's kappa coefficient was used to analyze the correlation between pairs of cosmetics. This method revealed an influence of gender on the co-use pattern of cosmetics. Hierarchical clustering analysis was performed using the binary linkage distance method. The clusters were divided into one large cluster and small clusters of one or two cosmetics. Frequent pattern mining was performed using the eclat algorithm. The number of used cosmetics and co-use pattern were influenced by gender and age of the population. The co-use patterns exhibited an additive property in that new cosmetics were added to previous combinations with increases in the number of cosmetics. In addition to the three analytical methods, a co-use scenario was proposed using the rank of frequency of occurrence in co-use patterns and percentile values of the distribution of the number of used cosmetics. The 16 co-use scenarios for the 31 cosmetics were determined to the 25, 50, 75, and 95th percentiles of the distribution of four gender-age population groups.

The third study aimed to perform aggregate exposure assessment based on co-use scenarios from the second study and to validate the novel methodology by comparing with the results of receptor-based aggregate exposure assessment. Aggregate exposure assessment considering specific products in co-use scenario was a higher tier approach than product-based aggregate exposure assessment. The aggregate exposures to DEHP, DnBP, and DEP in cosmetics were estimated by co-use scenario based aggregate exposure assessment by probabilistic approaches. The AED values were derived representing 25, 50, 75 and 95th percentiles of four population groups by gender and age. The most contributing cosmetics to co-use scenario based AED were determined by sensitivity analysis. The validation of co-use scenario based aggregate exposure assessment methodology was conducted by comparison with receptor-based AED. The co-use scenario based AEDs were

slightly higher than receptor-based AED below 75th percentiles of population, and slightly lower at 95th percentile. The aggregate exposure assessment methodology using co-use scenarios was closer to the receptor-based AED than product-based AED.

These studies shows that co-use scenario based estimations could be useful to perform aggregate exposure assessment with less resources, rather than investigating each individual's actual product usage patterns each time. It was relatively simple estimation than the receptor-based estimation, nevertheless realistic estimation that considering co-use and non-use rather than all available products, and could be applied easily for integrated risk management of chemicals.

Keywords: aggregate exposure assessment, co-use, consumer exposure, cosmetic, phthalate, receptor-based exposure assessment, product-based exposure assessment, tiered approach

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Contents

List of Tables

List of Figures

Chapter I.

Introduction

1.1. Background

Aggregate exposure assessment

The use of chemicals has increased dramatically. While some chemicals may be beneficial to human health, others may cause a number of adverse health outcomes. Sound management of chemicals is a prerequisite for the protection of human health. Estimating chemical exposure is important keyword for risk-based chemical management. Exposure assessment is a receptor-oriented approach (Ott et al., 2006) that begins with the target itself. The process of exposure assessment is consisted of characterizing, estimating or measuring the magnitude, frequency, and duration of contact with an agent, along with the number and characteristics of the population exposed (IPCS, 2004).

The current exposure and risk assessment paradigm is largely based on considering single chemical substances. Current chemical management is directed towards regulating exposure source on the basis of exposure and risk in a single source. However, people are exposed to chemical via air, water, food, drugs, pharmaceuticals, tobacco, and consumer products. Even if the chemical concentration in all media is below the reference value, the total exposed amount to the human body may have a health risk.

Combined risks need to be estimated from real-life chemical exposure. Combined exposure assessments examine exposure to multiple chemical stressor and/or route and pathway (US EPA, 2003). There are two directions for the combined exposure assessment. Cumulative exposure assessment evaluates combined exposure to multiple chemicals via multiple exposure pathways that affect a single biological target. Aggregate exposure assessment considers combined exposures to a single chemical across multiple exposure sources. An appropriate assessment method for the management of a single chemical is aggregate exposure assessment. Both adding exposures through ingestion, inhalation, and dermal and adding exposures through various foods are area of aggregate exposure assessment.

Consumer aggregate exposure assessment

Consumers are frequently exposed to chemical substances as ingredients, residues, or released from everyday consumer products such as cleaning products, paint, home care products, cosmetics and personal care products. Consumer products are one of a potentially important chemicals exposure pathway of human body, however it is difficult to assess the exposure level via this route. Due to the wide variety of consumer product and consumer heterogeneity, representative exposure data resources are generally not available. Consumer exposures are usually estimated by indirect estimation, such as exposure scenarios or mathematically predict modeling (Delmaar et al., 2006) for chemical substances to which consumer is directly exposed through the use of the product (ECHA, 2016).

The categorical chemical use, functional information, and weight fractions database, Chemical/Product Categories Database (CPCat), was established for used in consumer exposure assessment (Dionisio et al., 2015; Goldsmith et al., 2014). Among many chemical substances, phthalates, bisphenol A, and polybrominated diphenyl ethers were mainly discussed for human health risk through consumer exposure (Li and Suh, 2019). Plasticizers, polymers/monomers, and flame retardants used in food contact products, personal care products, cosmetics, furniture, flooring, and electronics were frequently reported functional use and product application combinations. The literatures show a tendency to focus on the chemicals with known human health risks. There are many chemical substances in consumer products that have not been identified for their toxicity and health effects.

Consumer exposure assessment is appropriate for conducting aggregate exposure assessment. A common ingredient is included in numerous consumer products, and each product is source of aggregate exposure. Previously, many aggregate exposure assessment studies were conducted on fragrances, preservatives and plasticizers contained in consumer products. Table 1-1 shows characteristics of previous consumer aggregate exposure assessment models. There were two major aggregate exposure assessment models for cosmetics and personal care products. Although there were numerous consumer exposure models, mainly for exposure assessment of specific single product. The main subjects of aggregate exposure modeling were food and pesticides.

The Probabilistic Aggregate Consumer Exposure Model (PACEM), had been developed to estimate aggregate exposure of consumers to substances contained in personal care products (Delmaar et al., 2014; Dudzina et al., 2015; Ezendam et al., 2018; Garcia-Hidalgo et al., 2018; Gosens et al., 2014; Karrer et al., 2019; Jongeneel et al., 2018; Nijkamp et al., 2015). The model simulated daily exposure in a population based on product use data collected from a survey among the European population. The aggregation of PACEM model was performed by adding-up of the product exposures based on the exposed person's product use pattern. The PACEM model estimated exposure as probabilistic approach by repeatedly sampling individual product use and person data from the survey database. This estimation method was higher tier assessment due to using realistic product use data.

The Creme RIFM model (Comiskey et al., 2015; 2017, Safford et al., 2015; 2017) were developed to estimate consumer exposure to fragrance materials via dermal, oral, and inhalation routes from the use of products. The first aim of this project was to build a comprehensive database of consumer habits and usage patterns data from consumer surveys, and a database of fragrance levels used in products. The second aim was to develop of a model that can utilize the database, along with body weight/height and surface area data, to calculate consumer exposure of fragrances. This model also used Monte Carlo simulation to combine of full distributions of input data in calculating aggregate exposure to individuals across a population.

Table 1-1. Characteristics of previous consumer aggregate exposure assessment models

	PACEM Model	Creme RIFM Model
Development	- Developed by Netherlands National Institute for Public Health and the Environment (RIVM) and Swiss Federal Institute of Technology Zürich (ETH Zurich) - Implemented in R programming language, shiny available for evaluation/test (prototype in R) - Under development into freely accessible web application (2019/2020)	- Developed by joint project between the Research Institute for Fragrance Materials (RIFM) and Creme Global (www.cremeglobal.com) - Standalone software - Commercially available
Description	- Exposure calculated by sampling individual product uses from the survey database - The concept of exposure fractions for multi-route (dermal, inhalation, ingestion) exposure scenario assessment - Coupled a compound-specific physiologically based pharmacokinetic (PBPK) model to convert external exposure into tissue concentrations - Both systemic human exposure (fixed fraction) and dermal uptake (kinetic approach) to chemicals can be assessed	- For calculate consumer exposure to fragrance materials - Phase 1 model for dermal exposure and phase 2 model for dermal and inhalation exposure - Normally assumes 100% dermal absorption - Inhalation exposure fractions calculated by compartmental RIFM 2-Box model (Petry et al., 2014)

	PACEM Model	Creme RIFM Model
Products	- 38 Personal care products from 7 categories : General hygiene (deodorant cream, deodorant roller, deodorant spray, perfume or eau de toilette, shower gel, bathing foam, bathing oil, toothpaste), shaving products (shaving foam, shaving gel, shaving oil, aftershave lotion/balm/gel, aftershave spray), hair care (shampoo, conditioner, hair foam, hair gel, hair lotion, hair wax), skin care (body lotion, hand cream, day cream, night cream, facial cleaning lotion or tonic), cosmetics (foundation, make-up remover, powder or rouge, mascara, eye pencil, eyebrow pencil, lip pencil, lipstick or lip gloss, lip balm), nail care (nail polish, nail polish remover), tanning products (bronzers, sunscreen, after sun) - 9 Household cleaning products : all-purpose cleaner liquid/spray/wipes, bleach, hand-dishwashing detergent, kitchen cleaner liquid/spray, bathroom cleaner liquid/spray, toilet cleaner, glass cleaner, carpet cleaner, fungicide spray	- 25 Products from 9 categories : Body lotion (body lotion (mass market), body lotion (prestige), body lotion (other)), deodorant (deodorant spray, deodorant roll-on, body spray), oral care (toothpaste, mouthwash), cosmetic styling (lipstick, liquid makeup foundation, hair styling, hair spray), hydro-alcoholics (eau de toilette, eau de parfum, after shave), shower products (shower gel, shampoo, rinse-off conditioner), moisturisers (face moisturizer, hand cream), soaps (bar soap, liquid hand soap), air care products (aerosol air freshener, plug-in air freshener, scented candle)

	PACEM Model	Creme RIFM Model
Tested chemicals	Gosens et al. (2014) : Parabens (methyl-, ethyl-, propyl- and butylparaben) Delmaar et al. (2014) : Diethyl phthalate (DEP) Dudzina et al., (2015) : Decamethylcyclopentasiloxane (D5) Nijkamp et al. (2015), Jongeneel et al. (2018) : Geraniol Garcia-Hidalgo et al. (2018) : Benzisothiazolinone (BIT) Ezendam et al. (2018) : Methylisothiazolinone (MIT) Karrer et al. (2019) : Bisphenols (BPA, BPS, BPF, and BPAF)	Safford et al. (2015) : 2-Phenylethanol (PEA) Safford et al. (2017) : 4-Hydroxy-3-methoxybenzaldehyde Sweet basil leaf oil Benzaldehyde p-tert-Butyl-alpha-methylhydrocinnamic aldehyde Juniperus virginiana oil Eugenia caryophyllus oil 2-Methoxy-4-(prop-1-en-1-yl)phenol Cymbopogon schoenanthus oil

	PACEM Model	Creme RIFM Model
Concentration data	- Weight fractions ere determined based on the empirical data available from literatures - Depending on data availability, represented either by point values or parametric probability distributions (uniform or triangular)	- Supplied by industry (collated from 33 fragrance houses and 10 manufacturers)
Exposure factor survey population	- Dutch survey for personal care products (Biesterbos et al., 2013) : 516 persons, 18 to 71 years of age - Swiss survey for personal care and household cleaning products (Garcia-Hidalgo et al., 2017) : 759 persons, 0 to 91 years of age - Mixed European Colipa survey (Hall et al., 2007; 2011) : Several investigations carried out in Denmark, France, Germany, Great Britain and Spain	- SUPERB survey (Moran et al., 2012) : 612 California residents - Kantar Worldpanel survey (Comiskey et al., 2015; 2017) : 36,446 subjects from the US and EU (including France, Germany, Great Britain and Spain) over 18 years' old - BodyCare survey (Tozer et al., 2015) : 448 US subjects ages 18-64

	PACEM Model	Creme RIFM Model
Exposure algorithm	$D_{ext} = \frac{wf \times A_{prod} \times F \times Rf}{W_{body}}$ $D_{int} = \frac{wf \times A_{prod} \times F \times Rf \times F_{dermal}}{W_{body}}$ D_{ext}: external dose after the dermal and oral route (mg/kg /day) D_{int}: internal dose after the dermal route (mg/kg/day) wf: weight fraction of the compound in the product (mg/kg) A_{prod}: amount of product applied (kg) F: frequency of use (events/day) Rf: retention factor (-) W_{body}: body weight (kg) F_{dermal}: dermal absorption fraction (-)	$DE_{BW} = \frac{F \times A \times R \times C \times P}{BW}$ $DE_{SA} = \frac{F \times A \times R \times C \times P}{SA}$ DE_{BW}: daily exposure per unit (μg/kg/day) DE_{SA}: daily exposure per unit (μg/cm^2/day) F: frequency of product use per day (use/day) A: amount of product used per occasion (g/use) R: product retention (-) C: concentration of ingredient in a product (μg/g) P: dermal penetration (or absorption) factor (-) BW: body weight (kg) SA: surface area (cm^2)
Aggregation method	- Receptor-based aggregation : Person-oriented estimation, probabilistic estimation using 1000 model population conducted by repeated sampling from the survey data	- Product based aggregation : Adding up the exposures from each all product

Tiered aggregate exposure assessment

The tiered approach, which begins with a rough exposure estimation to a more complex realistic estimation, is recommended for efficient exposure assessment. The aim of the low tier or screening-level assessment is screen chemicals of no immediate concern (ECETOC, 2004). Low tier exposure assessments typically use readily available data and conservative assumptions to estimate a high-end exposure. Chemicals which are not screened out at low tier are evaluated in the high tier or refined assessment. The higher-tiered exposure assessments require specific exposure assumptions and more resources to estimate realistic exposures.

Screening-level assessments usually use a deterministic approach, which apply single values as inputs to exposure algorithm. Deterministic assessments are simple to produce a point estimation either screening-level or higher-tier assessment. Probabilistic assessments use distributions as inputs to key parameters of exposure algorithm. The results of probabilistic exposure estimation are presented by distributions, and greater ability to characterize variability and uncertainty (US EPA, 1992). An appropriate approach is selected depending on the purpose and scope of the exposure assessment.

The tiered approach is also recommended to aggregate exposure assessment (Meek et al., 2011). However, there are no standard methods recognized for aggregate exposure assessment. ECETOC (2016) presented case studies conducted aggregate exposure assessment at tier 0, 1, and 2. The tier 0 was qualitative exposure assessment to provide a preliminary overview of all possible exposure sources. The tier 1 was worst-case scenario exposure assessment to determine a realistic upper bound of the aggregate consumer exposure to the chemical in a population. The tier 2 was probabilistic assessment to determine more realistic estimates of aggregate consumer exposure to the chemical, by increased use of measured data, using probabilistic techniques.

Consumer exposure assessments are also directed towards realistic and refined aggregate estimations as tiered approach. The most accurate estimation was to use the actual each exposure factor and chemical concentration of all products used by the individual. This method required a lot of big databases through large scale survey, chemical analysis or literature analysis. This high tier estimation method is called receptor- or subject-based approach. On the other hand, product-based approach is low tier estimation method that estimates exposure conservatively by adding all product exposures. The Creme RIFM model was product-based approach that summed the exposures from each all product. The PACEM model was receptor-based approach, however estimated exposure differed from the individual's actual exposure. The receptor of PACEM model was a model population conducted by repeated sampling from the survey population.

High tier consumer aggregate exposure assessment would be considered co-use and non-use of products for more accurate and realistic estimation. Current studies focused knowing one individual's product co-use combination. It was difficult to accurately investigate the usage patterns and exposure factors by every individual. The combination of co-used products was a kind of exposure scenario for aggregate exposure assessment. By estimating the aggregate exposure from only the products included in the co-used products combination, it was possible to evaluate with less exposure factors than receptor-based approach. Also, it was a higher tier assessment rather than a product-based approach in that considering specific products rather than all products. Figure 1-2 shows the concept of tiered aggregate exposure assessment; product-based, co-use based, and receptor-based approaches. A new aggregate exposure assessment method could be proposed as middle tier using co-used products as exposure scenario.

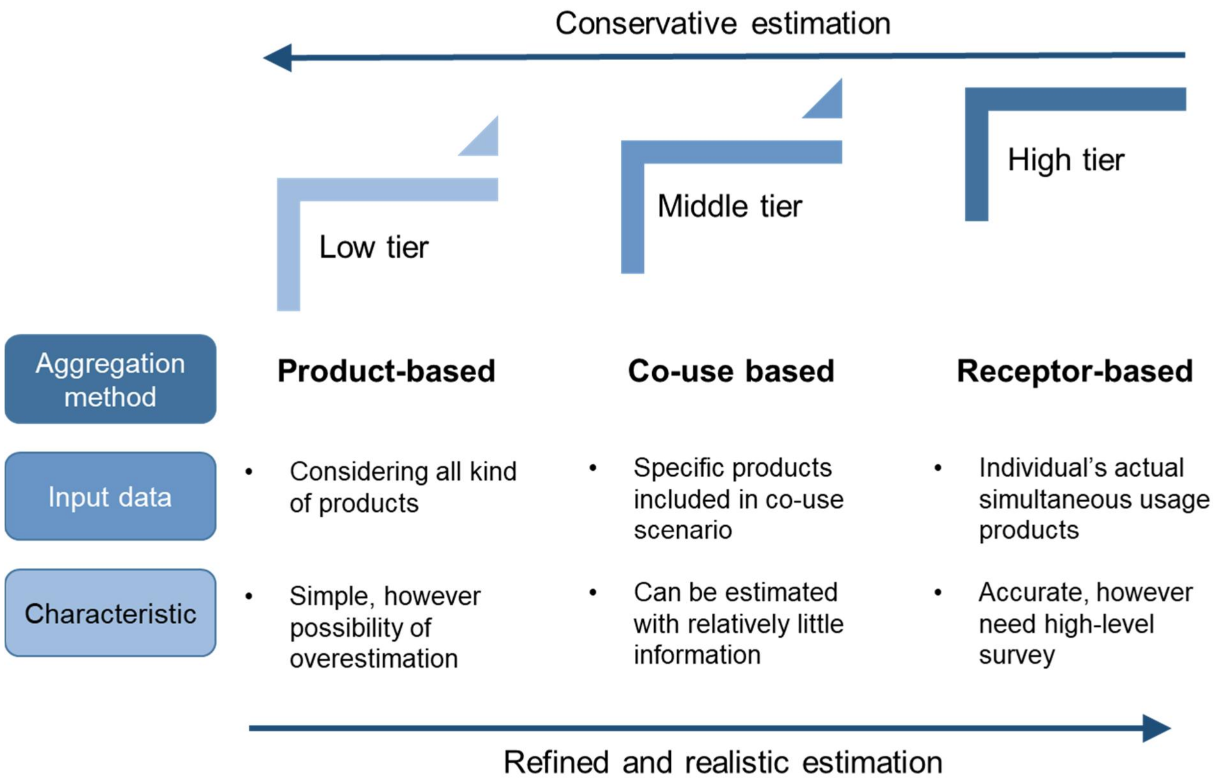

Figure 1-1. The concept of tiered aggregate exposure assessment.

1.2. Objectives

The overall objective of this study was to development of a novel aggregate exposure assessment methodology based on co-use scenarios of multiple consumer products. The target consumer products were cosmetics, and the target chemicals were three phthalates, that is, di(2-ethylhexyl)phthalate (DEHP), di-n-butyl phthalate (DnBP) and diethyl phthalate (DEP). The Korean national representative exposure factor database to 31 cosmetics were used for determination of co-use scenarios and aggregate exposure assessment.

The specific objectives of three studies were as follows:

1) To estimate receptor-based aggregate exposures of phthalates for cosmetics and to compare the results with product-based aggregate exposures.

2) To characterize co-use patterns of cosmetics and to determine the co-use scenarios for gender-age population groups.

3) To perform aggregate exposure assessment based on co-use scenarios and to validate a novel methodology by comparing receptor-based aggregate exposures.

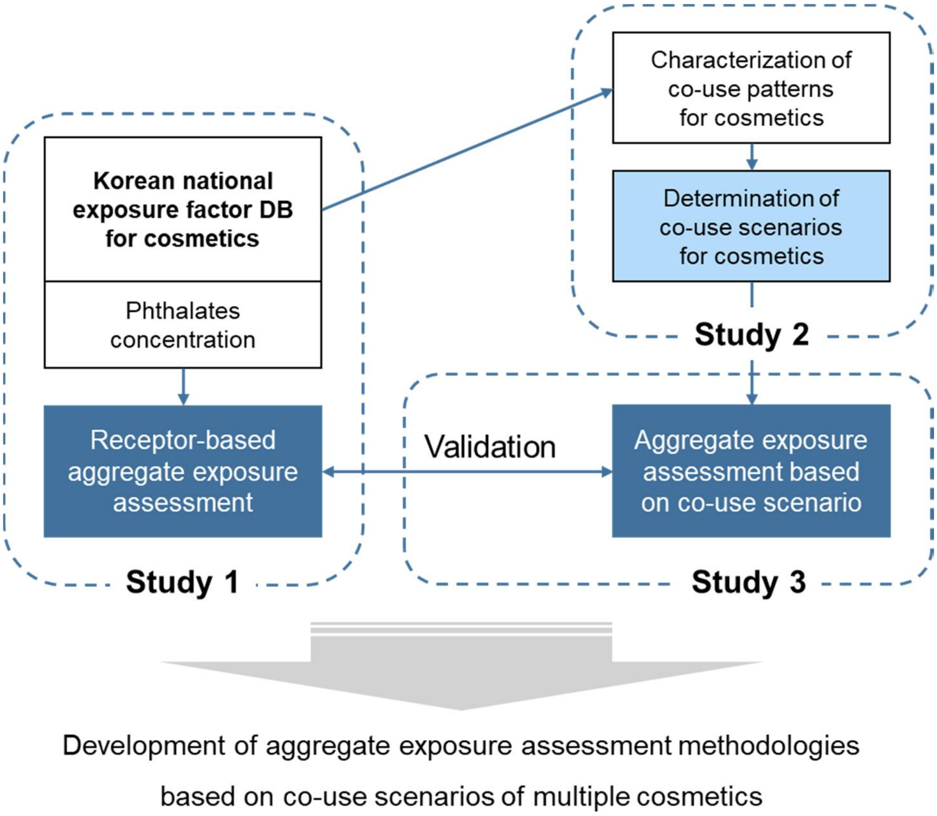

Figure 1-2. The overall outline of the study.

Outline of the study is shown in Figure 1-2. Firstly, receptor-based aggregate exposure was estimated from individuals' exposure factors considering multiple cosmetics and actual phthalate concentrations. The receptor-based aggregate exposure assessment was realistic and accurate assessment as highest tier. Secondly, cosmetic co-use patterns were analyzed by using correlation coefficient, hierarchical clustering and frequent pattern mining analysis method. The co-use scenario proposed through comparative analysis of the three methods. Thirdly, aggregate exposure assessment of three phthalates in cosmetics based on co-use scenarios were performed in deterministic and probabilistic approaches. The aggregate exposures estimated from the co-use scenarios were compared with the receptor-based exposures of the four gender-age populations.

Chapter II.

Receptor-based aggregate exposure assessment of phthalates using individual's simultaneous use of multiple cosmetic products

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2.1. Introduction

Individuals are exposed to chemical pollutants during their daily lives through multiple sources and routes. Consumer products such as cosmetics, personal care products, and home care products can make our lives more convenient; however, they are the main sources of chemical exposure (Ginsberg and Balk, 2016; Glegg and Richards, 2007). The use of consumer products has been associated with adverse health effects, such as the effect of fragrance products on asthma (Steinemann, 2018), allergic contact dermatitis (Cheng and Zug, 2014) and mucosal symptoms (Elberling et al., 2005). To respond to and manage the potential risk of chemical exposure, the importance of an accurate exposure assessment is growing.

For a realistic exposure assessment of chemicals, combined assessment of multiple sources and routes is needed. This differs from traditional exposure assessments, which are often limited to a single compound with a single exposure pathway. Aggregate exposure is the combined exposure to a single chemical across multiple routes and sources, and cumulative exposure is the combined exposure of a single biological target to multiple chemicals via multiple routes (US EPA, 2003). As concerns about combined exposures to chemicals have increased, the framework for aggregate/cumulative risk assessments of chemical mixtures have been proposed by various organizations (Meek et al., 2011; Pose-Juan et al., 2016).

With regard to the multiple sources and pathways of chemical exposure, aggregate exposure assessment tools for cosmetics and personal care products have recently been developed in Europe (Dudzina et al., 2015; McNamara et al., 2007). Aggregate exposure assessment can be divided into two approaches: product based and receptor based. The product-based approach, also called the population exposure method, estimates the aggregate exposure dose (AED) as a product exposure dose by considering the use rates of the population and the exposure dose of product users (Hall et al., 2007). Some case studies on fragrance ingredients (Safford et al., 2015; Safford et al., 2017) have integrated databases to expand the target population for aggregate exposure estimation (Comiskey et al., 2015; Comiskey et al., 2017). The receptor-based approach is similar to individual exposure scenarios (Delmaar and van Engelen, 2006), and case studies have been conducted on parabens (Gosens et al., 2014), UV filter substance (Manova et al., 2015), and cyclic siloxane substance (Dudzina et al., 2015) in consumer products.

The receptor-based aggregate exposure of a chemical should include only the products that the individual actually uses. The individual's simultaneous use patterns, exposure factors to each product, and the target chemical concentration of each product are needed for receptor-based aggregate exposure assessment. Previous receptor-based studies have used a model population through repeated sampling from a small survey population, which cannot represent the entire national population (Gosens et al., 2014). When exposure factors are obtained from a representative population sample of sufficient size, the aggregate exposure distribution of the total population can be determined. Furthermore, many aggregate exposure studies have conduct assessments using chemical concentrations reported in the literature (Delmaar et al., 2015; Dudzina et al., 2015) or other limited sources (Safford et al., 2015; Safford et al., 2017). The actual concentrations of target chemicals in the target products must be known for an accurate aggregate exposure assessment.

Among the chemicals mainly used in consumer products, plasticizers, preservatives, waterproofing agents, and flame retardants are known to be endocrine-disrupting chemicals (EDCs) and there is increasing concern about their adverse human health effects. Phthalates are well-known EDCs that are widely used in consumer products as additives and as plasticizers in plastics. Numerous studies have examined the health effects of phthalate exposure on the human body, including male reproductive effects; breast cancer; weight gain and obesity; development of allergies and asthma; and epigenetic modulation (Benjamin et al., 2017; Lottrup et al., 2006; Radke et al., 2018; WHO/UNEP, 2013; Zuccarello et al., 2018). The major exposure route of low-molecular-weight phthalates, for example di-n-butyl phthalate (DnBP) and diethyl phthalate (DEP), is non-dietary sources such as cosmetics and personal care products (Giovanoulis et al., 2018; Koch et al., 2013).

The aims of this study were to estimate the AED of phthalates through a receptor-based aggregate exposure assessment for cosmetic products and to compare the results with those of a product-based aggregate exposure assessment. Three phthalates, namely di(2-ethylhexyl)phthalate (DEHP), DnBP, and DEP, were selected as target chemicals. The receptor-based aggregate exposure was estimated from individuals' exposure factors considering multiple cosmetics and actual phthalate concentrations. In addition, the contribution of each product category to the receptor-based AED (AED_r) was determined.

2.2. Methods

Collection of exposure factors

A total of 1,001 subjects over 19 years old from 17 metropolitan areas and provinces in Korea participated in the exposure factor survey from June to August 2017. The number of subjects was determined by proportionate quota sampling based on the total population composition ratio considering sex, age, and regional distribution. Field survey staff visited homes and collected product use information through face-to-face interviews using a structured questionnaire. The home-visit survey was approved by the Institutional Review Board of the Seoul National University (SNU IRB No. 1608/001-020).

The exposure factors of 31 cosmetic products from nine categories (4 skin care, 3 hair care, 4 body care, 3 cleansing, 3 base makeup, 4 eye makeup, 4 lip makeup, 4 nail care, and 2 fragrance products) were collected. The questionnaire was designed to investigate the use pattern of cosmetic products. Cosmetic products were divided into 69 subtypes by considering the various product types, such as liquid, trigger spray, cream and solid, that exist in the market for each product. The questionnaire was structured to assess the use of each subtype within the past year, and only users of the subtype replied to questions regarding the use frequency, use amount, and brand name of products used. Where several products could be used at the same time for cosmetic purposes, such as face creams, the questionnaire was designed to assess each product individually.

To estimate the single use amount of the product, different types of questions for each subtype were presented. For the most representative liquid, lotion, cream, and foam-type products, five cards showing different product sizes (Park et al., 2015) was provided. Survey participants answered the most similar size of example card for cream-type products, the number of pumps for trigger-type products, the duration of spraying or rubbing for spray- and solid-type products, and the number of tissues used at one time for tissue-type products. In the laboratory, the mass of each unit was measured according to the response patterns. For some colored cosmetic products, such as mascara and lipstick, it was difficult to quantitatively measure the amount used. In these cases, the value published by the Korea Ministry of Food and Drug Safety was used, i.e., the difference between the product's mass before and that after use for 2 weeks (MFDS, 2016)

Chemical analysis

A total of 214 products were purchased from a market, with at least 3 products in each of the 69 product subtypes. Products were selected in two stages. First, cosmetic brands were selected based on survey results for each product subtype. Second, specific products were selected based on the sales ranking of a Korean online shopping intermediary site. The DEHP, DnBP, and DEP concentrations in 214 products representing 31 cosmetic types was measured.

Sample preparation

Three phthalates (DEP, DnBP, and DEHP) were purchased from AccuStandard (New Haven, CT, USA), and their corresponding deuterated (d4) internal standards were prepared following a method described elsewhere, with minor modifications (Guo and Kannan, 2013; Guo et al., 2014). After spiking 500 ng of d4-DEP, d4-

DnBP, and d4-DEHP to cosmetic samples (~0.03 g), 2 mL of Mili-Q water was added, and the mixtures were equilibrated overnight at room temperature. Samples were then extracted twice with 4-mL aliquots of methyl tert-butyl ether (MTBE) by shaking on a horizontal shaker for 30 min and then centrifuged at 4,500 g for 10 min. The supernatants were combined, transferred to 15-mL polypropylene tubes, and concentrated to near dryness under a gentle nitrogen stream. The extract was reconstituted with 1 mL of hexane, vortex mixed, and placed in a vial for instrumental analysis.

Instrumental analysis

For the identification and quantification of phthalates, gas chromatography (Agilent Technologies 7890B) coupled to a tandem mass spectrometer (Agilent Technologies 7000C) was used. A fused-silica capillary column (DB-5; 30 m length, 0.25 mm internal diameter, 0.25 μm film thickness) was used for the separation of phthalates. The oven temperature was programmed from 50℃ (held for 3.0 min) to 230℃ at 10℃/min and 230℃ to 300℃ at 5℃/min. The multiple reaction monitoring (MRM) mode was used; MRM transitions are presented in Table S-1. The instrumental limits of quantification (iLOQ) for DEP, DnBP, and DEHP were 5.2, 6.4, and 41.6 ng/g, respectively. The iLOQ was calculated as 10 times the standard deviation of the lowest calibration point. The sample was diluted and reanalyzed when concentrations exceeded the instrument's calibration range.

Quality assurance/quality control

For each bath of samples analyzed, two procedural blanks and solvent (hexane) were injected to check the procedural contamination and carryover between samples. Relatively low concentrations of phthalates, i.e., 3.6, 4.5, and 116 ng/g for DEP, DnBP, and DEHP, respectively, were detected in blank samples. The concentrations detected in procedural blanks were subtracted from the concentrations in samples. The mean recoveries of deuterated phthalates used as internal standards ranged from 86 to 110%. Known amounts of native and internal standards (ng/mL) were injected for every two batches to check instrumental stability; results showed that the relative standard variation (RSD) ranged from 3.07 to 13.6%.

Receptor-based aggregate exposure assessment

The AED_r (μg/kg/day) values for 1,001 participants were calculated from the information on each individual's cosmetic use. Individual AED values were calculated using following equation:

$$\mathrm{AED}(\mu g/kg/day) = \sum_{i=1}^{n} \frac{C_i(\mu g/g) \times f_i(use/day) \times q_i(g/use) \times RF_i}{BW\ (kg)}$$

where n is the number of products used by an individual, C_i is the phthalate concentration in these cosmetic products (μg/g), f_i is the frequency of cosmetic use (use/day), q_i is the amount of cosmetic use (g/use), RF_i is the retention factor on the skin (unitless), and BW is the body weight (kg).

The types and numbers of cosmetic products used by individuals and the use frequency (f_i) and use amount (q_i) of each product were obtained from the survey results. The values of C_i used for DEHP, DnBP, and DEP were the maximum value for each cosmetic product. The value of RF was 1 for leave-on cosmetic products and 0.01 for wash-off cosmetic products (SCCS, 2015). Only cleansing products such as hand washes, face cleansers, and shaving foam were classified as wash-off products. The BW value used in the calculation was taken from the participant's actual questionnaire answer.

Comparison of product-based AED (AED_p) and receptor-based AED (AED_r)

The receptor-based and product based AEDs were compared (Figure 2-1). The AED_p of cosmetic products was calculated as the sum of each product's exposure dose by product users considering the population product use rate. Each percentile value of the AED_p was estimated as the sum of each percentile value multiplied by the use rate for 31 cosmetic products. Because the sample size was sufficiently large (1,001), the distribution of AEDs was estimated by the deterministic method in percentile units.

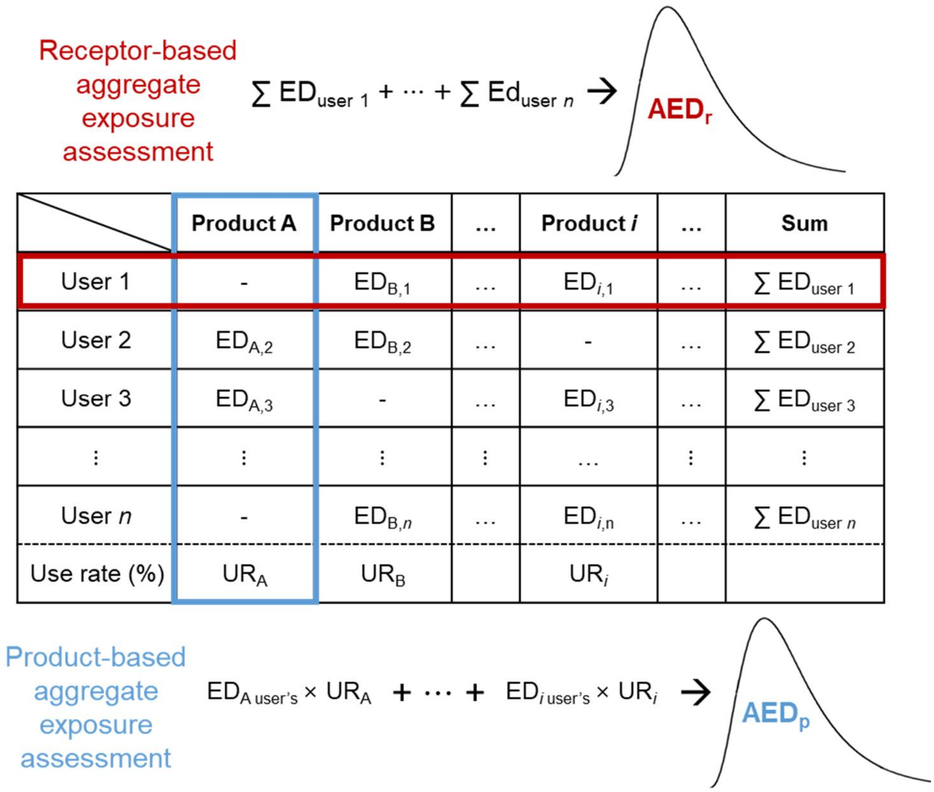


Figure 2-1. The concepts of receptor-based and product-based aggregate exposure assessment. $ED_{i,1}$ is exposure dose of product i for user 1. $ED_{\text{A user's}}$ is exposure dose of product A users and UR_A is use rate of product A in entire population.

Data analysis

Chi-square tests were used to analyze the use rates by gender and age group. One-way ANOVA was used to analyze use frequency, use amount, and daily mass of product per use by product type and population group. Two-way ANOVA was used to analyze the AED of the three phthalates by gender and age group. All calculations and statistical analyses were conducted using SPSS ver. 23 (IBM Corporation, Armonk, NY, USA).

The contributions of the nine cosmetic product categories to the AED were calculated by population group. The population was divided into 10 groups, i.e., two gender groups (female and male) by five age groups (19–29, 30–39, 40–49, 50–59, and ≥60 years). The product contributions were estimated from the ratio of the sum of individual AEDs in the population group to the sum of exposure doses in each product category.

2.3. Results

Demographic characteristics of the study population

The demographic characteristics of the 1,001 study population are summarized in Table 2-1. The participants were 50.8% male and 49.2% female. The participants were divided into five age groups: 19–29, 30–39, 40–49, 50–59, and ≥60 years; they were evenly distributed. The most common household income level was between 2,000 and 4,000 US dollars per month, and the most common education group comprised those with college education or beyond. The proportions of individuals in each household income, education, and marital category were significantly different by gender ($p < 0.01$). The average participant body weight was 56.9 ± 6.5 kg in females and 71.4 ± 9.5 kg in males.

Table 2-1. Demographic characteristics of the study population (n, %)

	Female		Male		Total	
Total number	492	49.2	509	50.8	1,001	
Age (years)						
19–29	93	18.9	102	20.0	195	19.5
30–39	98	19.9	103	20.2	201	20.1
40–49	115	23.4	118	23.2	233	23.3
50–59	112	22.8	114	22.4	226	22.6
60+	74	15.0	72	14.1	146	14.6
Household monthly income						
<$2,000	32	6.5	30	5.9	62	6.2
$2,000–4,000	154	31.3	212	41.7	366	36.8
$4,000–6,000	228	46.3	187	36.7	415	41.8
>$6,000	77	15.7	74	14.5	151	15.2
Education						
< Middle school	28	5.7	22	4.3	50	5.0
High school	247	50.2	212	41.7	459	45.9
> College	210	42.7	259	50.9	491	49.1
Marital status						
Single	111	22.6	171	33.6	282	28.2
Married	369	75.0	325	63.9	694	69.3
Divorced/Separated	12	2.4	13	2.6	25	2.5
Body weight (kg, mean ± SD)	56.86 ± 6.45		71.39 ± 9.48		64.25 ± 10.91	

Exposure factors

Use rates of cosmetic products

The classification of the cosmetic products (9 categories; 31 products; 69 subtypes) and the number of respondents who used each cosmetic product at least once in the last year are summarized in Table 2-2. The categories were classified according to body part (face, hair, body, eye, lip, and nail) and purpose (care, cleansing, and makeup). Skin care products had the greatest number of users (959 of 1,001) among the nine categories. The cleanser, body care, and hair care categories were used by more than 50% of respondents.

The use rates of the 31 cosmetic products ranged from 2.7 to 90.6%. Skin toner had the highest use rate (90.6%), followed by face lotion (90.2%), face cleanser (86.6%), facial sunscreen (59.5%), and body lotion (53.7%), whereas nail strengthener and gel nail polish had the lowest use rates, 2.7 and 3.7% respectively. For the skincare products, 31 of 491 users of skin toner, 123 of 501 users of face lotion, and 43 of 457 users of face cream used more than one product from the same subtype. Face cleanser had the greatest diversity of sub-products (foam, bubble, oil, water, cream, lip- and eye-makeup remover, tissue, soap, and powder).

The use rates of cosmetic products differed by gender and age groups (see Table S-2). Makeup products, such as base, eye, and lip makeup and nail care categories were mainly used by females. In the case of lip makeup products, the product preference changed by age group, with the young group using lip tint more frequently and the senior group using lipstick more frequently. The use rates differed significantly among the 10 population groups by both gender and age ($p < 0.001$) for all 31 cosmetic products.

Table 2-2. Classification of cosmetic products and the number of respondents who used the products (n = 1,001)

Category (number of respondents)	Cosmetic products (number of respondents)	Sub product types (number of respondents)
Skincare (959)	Skin toner (907)	Liquid type (491), second liquid type product (31), third liquid type product (1), gel type (41), aerosol spray type (23), pump spray type (36), skin toner for men (399)*, aftershave (2)
	Face lotion (903)	Lotion type (501), second lotion type product (123), third lotion type product (5), lotion for men (405)*
	Face cream (473)	Cream type (457), second cream type product (43), third cream type product (4), eye cream (161)
	Facial sunscreen (596)	Lotion type (391), cream type (191), balm/solid type (9)
Hair care (564)	Hair dye (171)	Bubble type (32), cream type (135), powder type (7)
	Hair treatment (362)	Lotion type (339), pump spray type (25)
	Hair styling (195)	Gel type (78), wax type (80), aerosol spray type (43)
Body care (680)	Body lotion (538)	Lotion type (493), oil type (47)
	Hand cream (490)	-
	Deodorant (69)	Roll-on type (21), stick type (27), aerosol spray type (24)
	Body sunscreen (121)	Cream type (78), roll-on/stick type (22), aerosol spray type (20), pump spray type (1)
Cleanser (903)	Hand wash (180)	Bubble type (124), gel type (28), soap type (31)
	Face cleanser (867)	Foam type (556), bubble type (44), oil type (101), water type (33), cream type (50), lip-and-eye remover type (25), tissue type (50), soap type (39), powder type (3)
	Shaving cream (97)	-
Base makeup	Foundation (415)	BB/CC cream (197), liquid foundation

Category (number of respondents)	Cosmetic products (number of respondents)	Sub product types (number of respondents)
(459)		type (125), cushion foundation type (244)
	Makeup base/primer (46)	-
	Pact/powder (167)	-
Eye makeup (344)	Eyeliner (146)	-
	Eyeshadow (236)	-
	Mascara (162)	-
	Eyebrow (215)	-
Lip makeup (488)	Lip balm (82)	-
	Lip Tint (74)	-
	Lip gloss (88)	-
	Lipstick (415)	Stick type (414), pencil type (12)
Nail care (102)	Nail polish (105)	
	Gel nail polish (37)	-
	Nail strengthener (27)	-
	Nail remover (112)	-
Fragrance (313)	Shower cologne (66)	Body mist type (34), cologne type (37)
	Perfume (277)	Perfume for women (224), Perfume for men (55)

* Men's products were classified separate subtypes

Daily mass of cosmetic products

The daily mass (g/day) was calculated for the 31 cosmetic products by multiplying the use frequency (use/day) by the use amount (g/use). The statistical values of the exposure factors for the 69 product subtypes are presented in Table S-3. Shaving cream and face cleanser were the products with the highest average daily mass. Skin care products, such as skin toner, face lotion, and face cream, were usually applied twice a day, and the daily mass used was high. Although lip makeup products were used more than twice a day, the daily mass was low because the amount applied was very small. Large variation was observed in the daily mass of body care products that were used over a wide area of the body. There was no gender difference ($p > 0.05$) in the daily mass of skin care, hair care, and body care products applied among product users.

Phthalate concentrations in cosmetic products

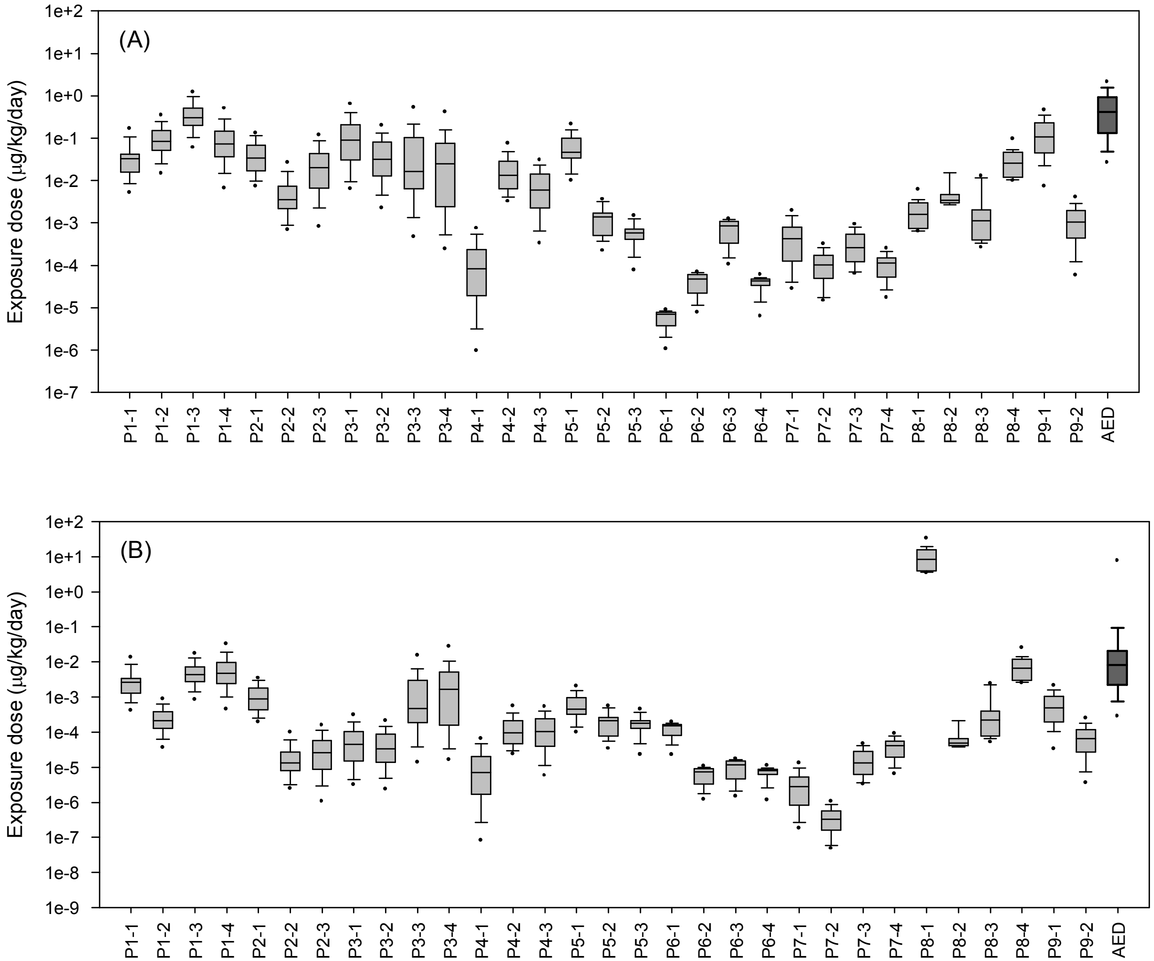
The detection frequency and concentrations of three phthalates in 31 cosmetic products are shown in Table S-4. DEHP was the most frequently detected (66.8%) phthalate in the 214 samples analyzed, followed by DnBP (45.3%), and DEP (19.2%). Among the nine categories of cosmetic products, DEHP was found frequently in lip makeup products (16 of 16) and fragrance products (12 of 13). In the other five categories, except base makeup products, the detection frequency was more than 50%. Di-n-butyl phthalate was detected most frequently in nail care products (27 of 31) and had a detection frequency of more than 50% in eye makeup, base makeup, and cleansing products. Diethyl phthalate was mainly detected in hair care products (15 of 15) and fragrance products (11 of 13).

The maximum DEHP concentration (75.24 μg/g) was detected in face cleanser within the cleansing products category. The maximum DEHP concentration in the five categories (nail care, skin care, body care, fragrance, and base makeup products) exceeded 10 μg/g. For DnBP, the maximum concentration (46.34 mg/g) was found in nail polish in the nail care products category. For DEP, the maximum concentration (1.58 mg/g) was found in shower cologne within the fragrance products category, and the median value was highest in hair care products. In the other categories, both the detection frequency and maximum DEP concentration were low.

Receptor-based aggregate exposure assessment

Figure 2-2 shows the distribution of the exposure dose (μg/kg/day) of the three phthalates for 31 cosmetic products and aggregate exposure dose determined using the receptor-based approach with the maximum phthalate concentrations, daily mass, and body weight of the product users. The Distribution of receptor-based aggregate exposure dose by gender and age groups are shown in Figure S-1. The average receptor-based aggregate exposures of the Korean population to phthalates in cosmetic products were 0.68 ± 0.87, 1.08 ± 5.71, and 2.47 ± 9.05 μg/kg/day for DEHP, DnBP, and DEP, respectively. The 95th percentiles (P95) of the AED were 2.06, 7.67, and 11.04 μg/kg/day for DEHP, DnBP, and DEP, respectively.

For DEHP, face cream had the highest average exposure dose (0.44 ± 0.43 μg/kg/day), followed by body lotion (0.18 ± 0.26 μg/kg/day) and shower cologne (0.16 ± 0.17 μg/kg/day). Overall, the exposure dose was higher for the products applied to a large surface area of the body, such as the whole face, hair, and body, than for eye and lip makeup products that were applied to a smaller surface area. For DnBP, nail polish had the highest average exposure dose (12.29 ± 15.45 μg/kg/day), followed by facial sunscreen (0.01 ± 0.03 μg/kg/day) and nail polish remover (0.01 ± 0.01 μg/kg/day). For DEP, shower cologne had the highest average exposure dose (20.73 ± 21.3 μg/kg/day), followed by hair styling products (2.71 ± 5.52 μg/kg/day) and perfume (0.96 ± 0.96 μg/kg/day).



(A)
Exposure dose (μg/kg/day)
1e+2
1e+1
1e+0
1e-1
1e-2
1e-3
1e-4
1e-5
1e-6
1e-7
P1-1 P1-2 P1-3 P1-4 P2-1 P2-2 P2-3 P3-1 P3-2 P3-3 P3-4 P4-1 P4-2 P4-3 P5-1 P5-2 P5-3 P6-1 P6-2 P6-3 P6-4 P7-1 P7-2 P7-3 P7-4 P8-1 P8-2 P8-3 P8-4 P9-1 P9-2 AED
(B)
Exposure dose (μg/kg/day)
1e+2
1e+1
1e+0
1e-1
1e-2
1e-3
1e-4
1e-5
1e-6
1e-7
1e-8
1e-9
P1-1 P1-2 P1-3 P1-4 P2-1 P2-2 P2-3 P3-1 P3-2 P3-3 P3-4 P4-1 P4-2 P4-3 P5-1 P5-2 P5-3 P6-1 P6-2 P6-3 P6-4 P7-1 P7-2 P7-3 P7-4 P8-1 P8-2 P8-3 P8-4 P9-1 P9-2 AED

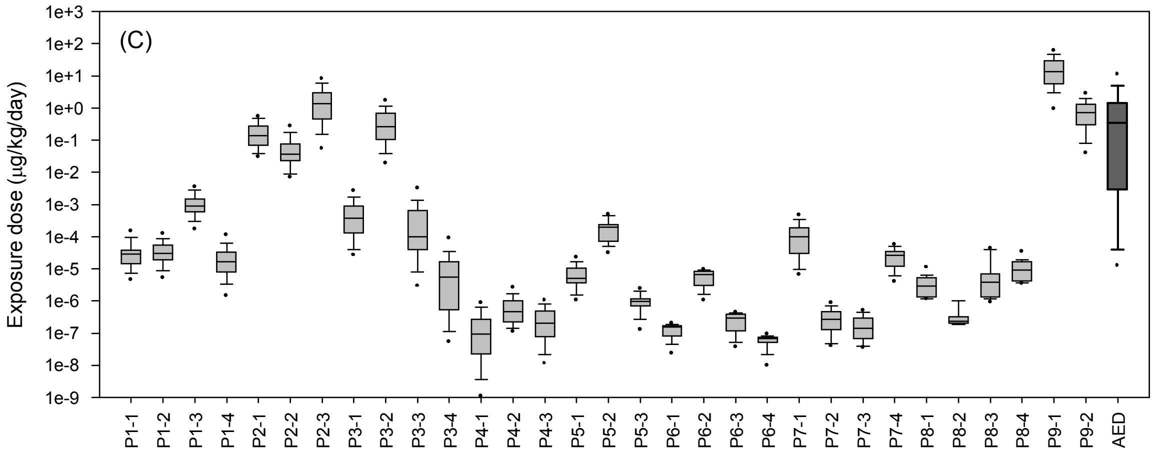


Figure 2-2. Exposure dose (μg/kg/day) from the use of cosmetic products to (a) di(2-ethylhexyl)phthalate (DEHP), (b) di-n-butyl phthalate (DnBP), and (c) diethyl phthalate (DEP). Each grey box represents one cosmetic product (P1-1: skin toner, P1-2: face lotion, P1-3: face cream, P1-4: face sunscreen, P2-1: hair dye, P2-2: hair treatment, P2-3: hair styling, P3-1: body lotion, P3-2: hand cream P3-3: deodorant, P3-4: body sunscreen, P4-1: hand wash, P4-2: face cleanser, P4-3: shaving cream, P5-1: foundation, P5-2: makeup base/primer, P5-3: pact/powder, P6-1: eyeliner, P6-2: eyeshadow, P6-3: mascara, P6-4: eyebrow, P7-1: lip balm, P7-2: lip tint, P7-3: lip gloss, P7-4: lipstick, P8-1: nail polish, P8-2: gel nail polish, P8-3: nail strengthener, P8-4: nail remover, P9-1: shower cologne, P9-2: perfume), with the dark grey box indicating the aggregate exposure dose (AED) based on individual cosmetic product use and exposure factors. The horizontal lines show the median, the boxes show the quartiles, the whisker caps show the 10th and 90th percentile values, with the 5th and 95th percentiles plotted as dots.

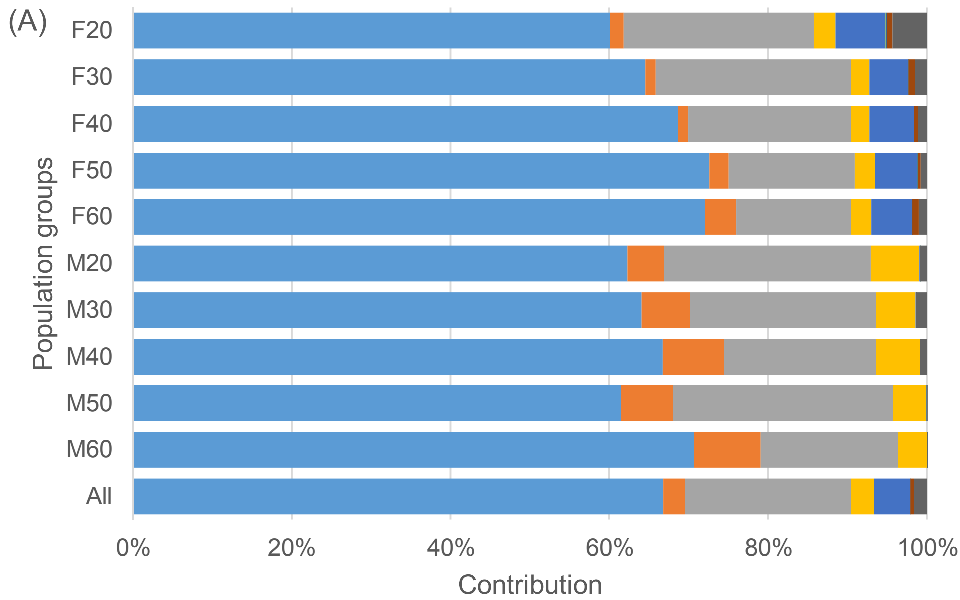
Table 2-3 shows the number of cosmetics used and the AED for the 10 gender–age population groups. The highest AEDs were found for the female and young groups. The difference by gender was significant for DEHP, DnBP, and DEP ($p < 0.001$); however, the difference by age was significant only for DEP. The 19–29-year-old female group had the highest average AEDs for DEHP and DEP and the second highest AED for DnBP among the 10 gender-age groups, likely because they used the largest number of cosmetic products.

Table 2-3. Number of cosmetic products used and aggregate exposure dose (AED, μg/kg/day) by gender–age population group (mean ± SD).

	Age group	Number of products used	AED (μg/kg/day)		
			DEHP	DnBP	DEP
Female					
	19–29	14.5 ± 3.9	1.23 ± 1.36	2.68 ± 7.15	8.73 ± 24.33
	30–39	13.0 ± 3.9	1.16 ± 1.09	2.74 ± 6.06	3.61 ± 8.08
	40–49	12.7 ± 3.3	1.22 ± 1.07	1.92 ± 5.93	3.00 ± 7.11
	50–59	11.9 ± 2.8	1.11 ± 0.77	1.56 ± 5.03	2.22 ± 5.44
	60+	11.1 ± 2.6	0.90 ± 0.52	2.26 ± 14.90	2.11 ± 5.37
	Total	12.7 ± 3.5	1.14 ± 1.02	2.20 ± 8.00	3.89 ± 12.34
Male					
	19–29	5.0 ± 1.4	0.31 ± 0.41	0.01 ± 0.01	1.55 ± 3.77
	30–39	5.2 ± 2.4	0.28 ± 0.30	0.03 ± 0.24	1.84 ± 4.53
	40–49	4.3 ± 2.0	0.19 ± 0.20	0.00 ± 0.01	1.06 ± 2.94
	50–59	4.0 ± 2.1	0.22 ± 0.36	0.00 ± 0.01	0.57 ± 1.77
	60+	3.8 ± 1.6	0.19 ± 0.23	0.00 ± 0.01	0.22 ± 0.49
	Total	4.5 ± 2.2	0.24 ± 0.32	0.01 ± 0.11	1.09 ± 3.16
Total					
	19–29	9.5 ± 5.8	0.75 ± 1.08	1.28 ± 5.10	4.97 ± 17.35
	30–39	9.0 ± 5.1	0.71 ± 0.90	1.35 ± 4.44	2.70 ± 6.55
	40–49	8.4 ± 5.0	0.70 ± 0.92	0.95 ± 4.27	2.02 ± 5.49
	50–59	7.9 ± 4.7	0.66 ± 0.75	0.77 ± 3.61	1.39 ± 4.10
	60+	7.5 ± 4.3	0.55 ± 0.53	1.15 ± 10.64	1.18 ± 3.94
	Total	8.5 ± 5.1	0.68 ± 0.87	1.08 ± 5.71	2.47 ± 9.05

Product contribution for the AED_r

The contributions of cosmetic products to AED differed among phthalates. Figure 2-3 shows the pattern of product contributions by population group. For the DEHP exposure of the entire population, skin care products, body care products, and cleanser products contributed 66.8, 20.9, and 4.5%, respectively. As age increased, the contribution to DEHP exposure from skin care and hair care products increased, while that of body care products decreased. For the DnBP exposure of the entire population, nail care products contributed 98.6%, and skin care products contributed 1.2%. The contribution to DnBP exposure from nail care products was consistent. For the DEP exposure of the entire population, fragrance products, hair care products, and body care products contributed 66.3, 23.3, and 10.3%, respectively. The contribution to DEP exposure from hair care products increased with age. The contribution to DEP exposure from fragrance products was higher in the female group than in the male group.


(A)
F20
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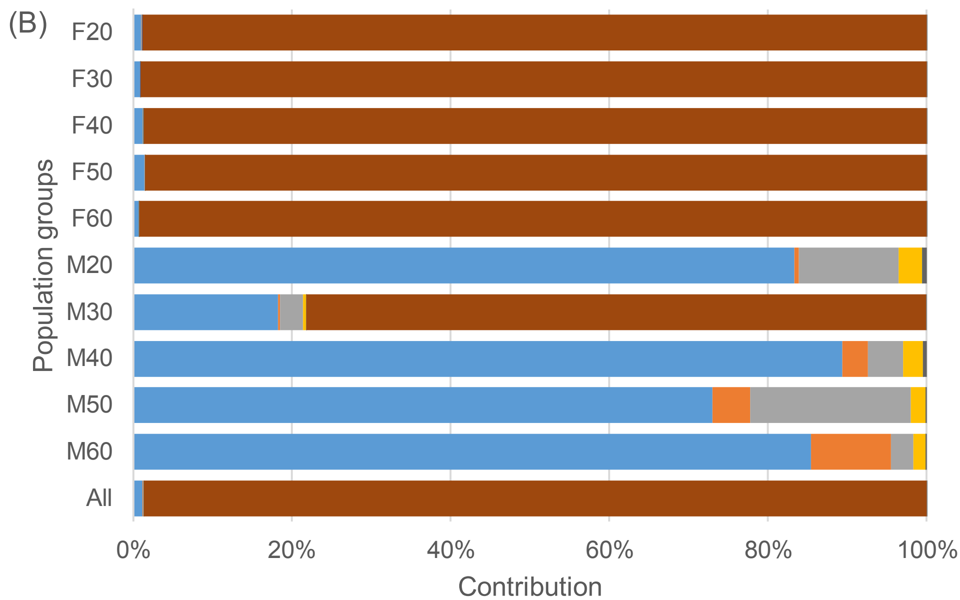
All
Population groups
0%
20%
40%
60%
80%
100%
Contribution


(B)
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Population groups
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60%
80%
100%
Contribution

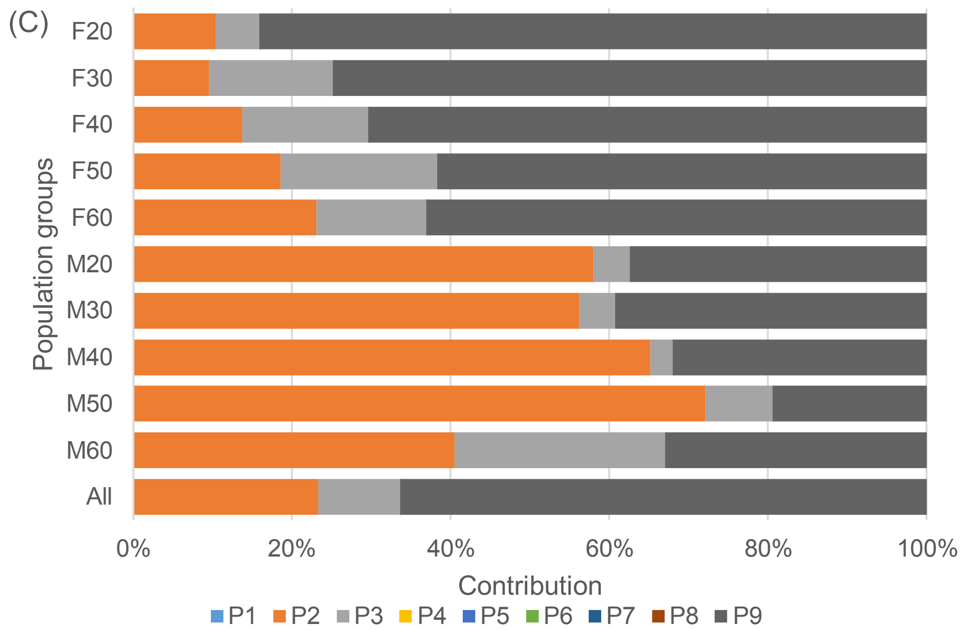
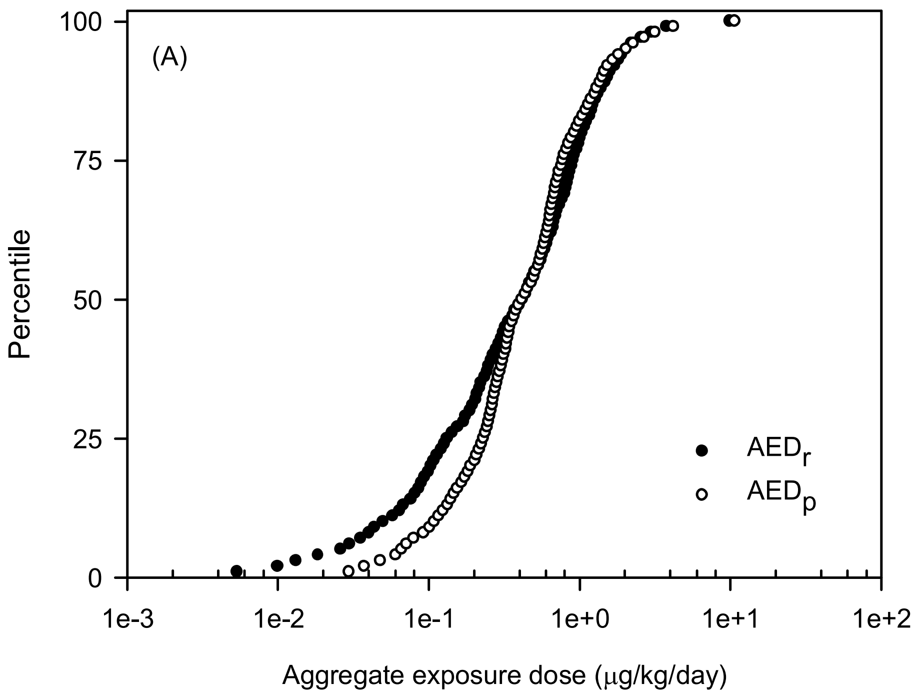


Figure 2-3. The contribution of different products to the receptor-based aggregate exposure dose (AED) of (a) di(2-ethylhexyl)phthalate (DEHP), (b) di-n-butyl phthalate (DnBP), and (c) diethyl phthalate (DEP) by population group. Each colored bar represents one cosmetic category (P1: skin care products; P2: hair care products; P3: body care products; P4: cleanser products; P5: base makeup products; P6: eye makeup products; P7: lip makeup products; P8: nail care products; P9: fragrance products).

Comparison of AED_r and AED_p

Figure 2-4 compares AED values determined by the receptor-based exposure method (AED_r) and by the product-based exposure method (AED_p). For all three phthalates, the increase in AED_p was steeper than that in AED_r. The AED_r was lower than the AED_p at low percentiles, but was similar or higher than the AED_p at high percentiles. At P1, i.e., the lowest value, AED_r values were one order of magnitude lower than those of AED_p for DEHP, and four orders of magnitude lower for DnBP and DEP. At P50, i.e., the median value, DEHP had similar AED_r and AED_p values, and AED_r was slightly higher than AED_p in the percentile range of P56 to P95. However, AED_r values at P50 were lower than AED_p values by two orders of magnitude for DnBP and by one order of magnitude for DEP. DnBP and DEP had a higher AED_r than AED_p above P91 and P90. At P100, i.e., the highest value, DEHP had a slightly lower AED_r than AED_p, whereas AED_r values were one order of magnitude higher than AED_p values for DnBP and DEP.


(A)
Percentile
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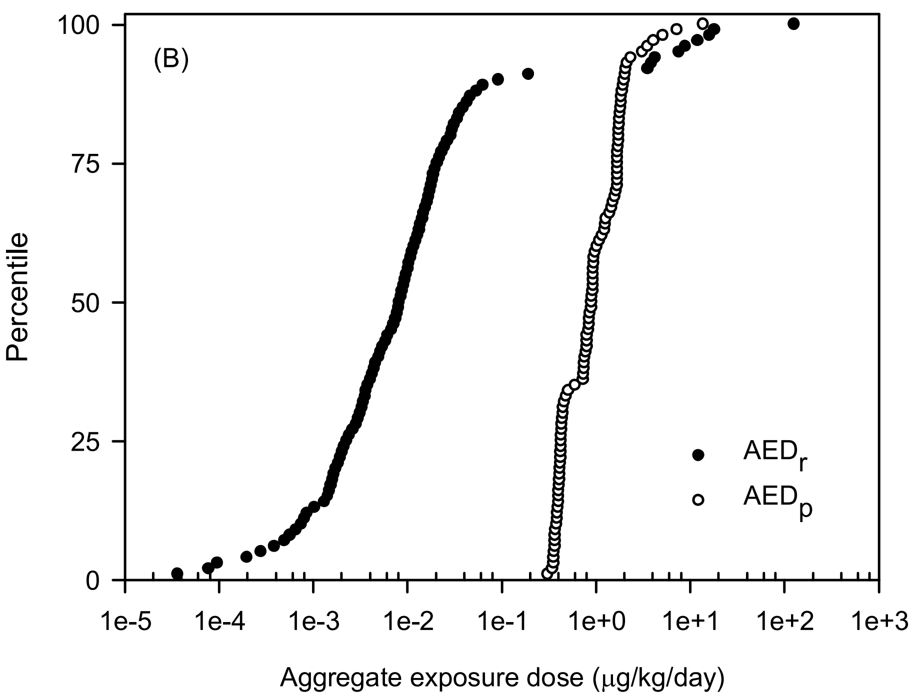
1e+0
1e+1
1e+2
Aggregate exposure dose (μg/kg/day)
AED$_r$
AED$_p$


(B)
Percentile
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1e+3
Aggregate exposure dose (μg/kg/day)
AED$_r$
AED$_p$

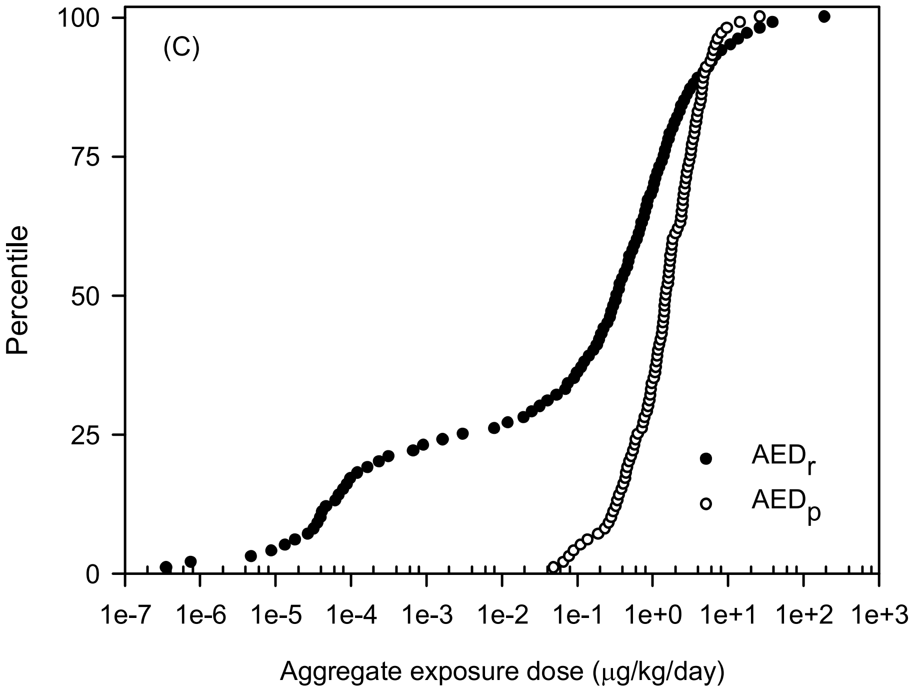


Figure 2-4. Comparison of the aggregate exposure dose (AED) estimated by the receptor-based exposure method (AED_r) and product-based exposure method (AED_p) for (a) di(2-ethylhexyl)phthalate (DEHP), (b) di-n-butyl phthalate (DnBP), and (c) diethyl phthalate (DEP). Each black dot represents 1 percentile of the AED based on individuals' actual use of a product and the exposure factor. Each white dot represents a 1 percentile value of AED based on the exposure dose of each product consumed and the use rate of the population.

2.4. Discussion

Exposure factors

Korean national exposure factors for multiple cosmetic products were collected in this study. As concern over chemical exposure through cosmetic products has increased, several large-scale exposure factor surveys have been conducted in the Netherlands (Biesterbos et al., 2013), France (Dornic et al., 2017; Ficheux et al., 2016; Ficheux et al., 2015) and the United States (Loretz et al., 2006; Loretz et al., 2008; Loretz et al., 2005; Wu et al., 2010). The consumption patterns of cosmetics can be strongly influenced by national, ethnic, and cultural backgrounds. Therefore, it is not appropriate to apply European and American exposure factors the estimate the exposure of the Korean population.

This study derived nationally representative exposure factors for Korea. The subjects were adults (over 19 years old) and were sampled considering gender, age, and regional distribution. The use rates and exposure factors of 31 cosmetic products sorted into nine categories were derived from a face-to-face survey. Most of the exposure factors used in recent Korean studies (Jung et al., 2018; Park et al., 2018) were obtained through online questionnaire surveys. Although online surveys are simple and they make it easy to obtain a large number of responses, the sample can be biased and less representative. The advantages of a face-to-face interview include the selection of an unbiased representative sample of subjects and enhanced accuracy of questionnaire responses. Subjects in this study had a similar use frequency to Americans and Europeans, but used lesser amounts of cosmetic products, overall.

The exposure factors of many cosmetic products were the same. For many non-makeup products, e.g., skin care products, the use frequency was similar at the median, 75th percentile, and 95th percentile. Variations in the amount of product used were also very small. When the daily mass of products was derived from the use frequency and amount, the variation in the daily mass of non-makeup products was found to be very small. Therefore, the daily mass of many non-makeup products did not differ significantly with demographic factors. Makeup cosmetics are mainly used by females. The daily mass of makeup cosmetics differed significantly between females and males, as males do not tend to use these products. However, the variation in the daily mass of non-makeup products used by females was also very small.

The exposure factor database included users and non-users of multiple representative cosmetic products. Exposure factors for the simultaneous use of multiple products are critical for receptor-based aggregate exposure assessments. Aggregate exposure was therefore based on the actual use of cosmetic products. The use pattern of cosmetic products was very different for specific populations. For example, makeup cosmetics were mainly used by females. Because the exposure factor survey collected use patterns and exposure factors of products used at the same time, the data could be applied to receptor-based aggregate exposure assessments.

Chemical concentrations

Phthalates in cosmetic products are used as additives, stabilizers, and fixing agents. DEHP is used for plasticizing or softening other ingredients. DnBP is used as a coating agent to reduce cracks in cosmetic products such as nail polish. DEP is used as a solvent and fixative in fragrances (US FDA, 2018). Due to their widespread use, phthalates in cosmetic products have been reported in Korea (Koo and Lee, 2004), Canada (Koniecki et al., 2011), the United States (Guo and Kannan, 2013), China (Guo et al., 2014) and Saudi Arabia (Al-Saleh and Elkhatib, 2016).

This study found a high frequency of DnBP at high concentrations in coating products, such as nail care products. Although DEP was frequently detected in fragrance products (8 of 10 products) at high concentrations, the overall detection rate (41 of 214 products, 19.2%) was the lowest of the three phthalates. DEHP was the most frequently detected (143 of 214 products, 66.8%) phthalate in the cosmetic products investigated in this study. This differed from previous studies in which DEP was detected at the highest frequency (Guo and Kannan, 2013; Koniecki et al., 2011). However, the maximum DEHP concentration in cosmetic products was relatively low compared to the maximum DnBP and DEP concentrations.

Aggregate exposure assessment

Initially, estimates of the aggregate exposure to chemicals in consumer products were made by measuring the annual volume of chemicals used over a specific geographic area. This approach provides a crude estimate. The aggregate consumer exposure from each product, represented by the product-based method in this study, is a more realistic estimation method than is determining environmental exposure (Cadby et al., 2002). Measurement of product-based aggregation requires data on the use rate of each product, the product exposure factor, and the concentration of its chemical ingredients. However, the product-based aggregate exposure approach can provide an inaccurate estimate. When the use rate of a single product is employed, the population that rarely uses products or that uses many kinds of products cannot be included in the product-based aggregate exposure distribution.

The receptor-based aggregate exposure method used in this study can provide a more accurate measure because it uses simultaneous information on use in nationally representative samples. In this study, the simultaneous use patterns for 31 cosmetic products included actual co-use and non-use information. The daily mass amount derived from the exposure factors clearly differed according to use or non-use. Nationally representative study samples that considered gender, age, and regional distribution provided an accurate estimate of exposure among the Korean population. Exposure factors for multiple cosmetic products were collected simultaneously with use patterns. The database used in the study had a critical impact on the receptor-based aggregate exposure estimation of common ingredients in cosmetics and on product contribution to the AED.

The distributions of AED_p and AED_r clearly differed for DnBP and DEP, whereas the AED_p and AED_r distributions for DEHP were similar. The population averages of the AED_r values for DnBP and DEP were lower than those obtained using the product-based method. Cowan-Ellsberry and Robison (2009) suggested an aggregate exposure estimation method using a female exposure group based on the use and non-use of nine consumer products. Their refined model partially considered co-use patterns and estimated 36–56% lower aggregate exposure than did a simple product exposure addition method. However, the 95th percentile of the

AED_r was higher than the AED_p for DnBP and DEP.

The AED_p for the three phthalates in cosmetic products displayed less variation than did the AED_r. In the AED_p, the use rate of each product was applied. However, aggregate exposure is associated with the simultaneous use of multiple products. This method did not consider those who rarely use products or those who use many kinds of products. In addition, the exposure factors of cosmetic products had a narrow distribution of values, with a small range. The smaller range of the AED_p for cosmetic products might be related to the aggregate exposure's being derived from such narrow distributions of exposure factors.

The population for which AED_r was higher than AED_p comprised mostly female and younger subjects. The contact points of the AED_r and AED_p distributions were the 91^{st} percentile for DnBP and the 90^{th} percentile for DEP. Of the 90 subjects above the 91^{st} percentile for the DnBP AED_r, 89 were females and 53 were aged 19–39. Of the 100 subjects above the 90^{th} percentile of the DEP AED_r, 71 were females and 58 were aged 19–39. The difference between the AED_r and AED_p ratios among the young female group were larger than those for the senior male group for all three phthalates (See Table S-5).

The receptor-based aggregate exposure was previously calculated for Europeans using a person-oriented exposure model. The probabilistic aggregate consumer exposure model (PACEM) is based on exposure factors for 32 personal care and cosmetic products obtained from a survey of 512 Dutch adults (Delmaar et al., 2015). The PACEM model includes personal care products that were not considered in this study, such as shower gel, shampoo, conditioner, and toothpaste. The PACEM model used a DEP concentration from the available literature. The dermal absorption factor for the different products (range from 0.02 to 1) was used in the exposure dose calculation. Although the target products and estimation method were not identical for the different studies, the AED trend by gender was similar in Korean and European populations. The 95th percentile aggregate DEP dose for the Korean population was 3.46 times higher in females than in males. The 95th percentile aggregate DEP dose for the European population was 1.12 times higher for females than males.

The highest exposure group estimated by the receptor-based approach was the 19–29-year-old female group. This group was exposed to 6.4 times, 660.5 times, and 39.7 times higher concentrations of DEHP, DnBP, and DEP, respectively, than was the male group aged 60+ years, which had the lowest exposure. The number of cosmetic products used by the 19–29-year-old female group was 3.9 times greater that used by the 60+ male group. The population that co-used many different products was also the high exposure population. Although current regulations are based on exposure from a single product, aggregate exposure should be considered in the future. If the aggregate exposure is applied for the regulation of cosmetics, particular attention should be given to the exposure status and patterns of the young female group.

Product contribution

The cosmetic products that made the largest contributions to the total exposure differed among the three phthalates. Aggregate DEHP doses were influenced by relatively more cosmetic products than were aggregate DnBP and DEP doses. DEHP was present in low concentrations in most cosmetic product categories. All product categories contributed to the aggregate DEHP doses. Nail care products were the major contributor to the aggregate DnBP doses. Fragrance products, hair care products, and body care products were the major contributors to aggregate DEP doses.

The products contributing the majority of DnBP among the 29–39-year-old male group were different from those responsible for exposure in male groups of other ages. Of the 509 male subjects, only one person answered that he used both nail polish and nail strengthener. As a result, nail care products contributed 78.0% of the DnBP AED for the 29–39-year-old male group. Excluding this respondent, the contribution of skin care products increased from 18.3 to 83.1%, and the contribution of body care products increased from 2.9 to 13.4%, similar to the contributions for the other male groups. The DnBP concentration in the nail care products investigated in this study was overwhelmingly high, with a maximum concentration of 46,337.68 μg/g), and the second (1.88 μg/g) and third (1.53 μg/g) highest DnBP concentrations were also detected in nail care products. Therefore, there would be a similarly high contribution from nail care products to the DnBP AED nail care product users regardless of the nail care product's DnBP concentration. The distribution of DnBP AED was determined by nail care product use. Specific product management is required when certain cosmetics contain particularly high levels of certain chemicals.

Cosmetics were usually used at a regular frequency, typically once or twice a day. The variation among product users in daily mass used was small. Demographic factors had no effect on the exposure dose of the product. The number of cosmetics used and the use of specific cosmetic products containing high concentrations of phthalates were one of the main characteristics of the high exposure group. To obtain an accurate receptor-based aggregate exposure assessment of cosmetic products, it is important to know which cosmetic products are used simultaneously. Furthermore, it is necessary to develop a cosmetics co-use exposure scenario by population group.

Limitations

This study estimated the aggregate exposure to three phthalates from the use of 31 cosmetic products. The exposure factors of this study might have potential error because all the survey responses were considered true. The three phthalates may also be included in other consumer products. In particular, personal care products such as shampoo, toothpaste, and body cleanser were not considered in this study. The diet sources had larger contribution than non-diet sources to phthalate exposure (Giovanoulis et al., 2018; Martínez et al., 2018; Romano et al., 2019). Therefore, the results could have underestimated the aggregate exposure of the three phthalates in the Korean population. For the more accurate receptor-based aggregate exposure assessment, diet and non-diet sources should be considered.

The AED of cosmetic products might have been overestimated because the maximum concentration in the cosmetic product categories was used for aggregate exposure estimation. The maximum concentrations used for each product in this study may have been over-estimated. The phthalate concentrations in various products would likely be lower than the maximum values used in this study. For more accurate assessment, the actual concentrations in the particular cosmetics used should be applied. However, the 214 products analyzed did not include all of the products that survey respondents actually used.

The AED of cosmetic products might be overestimated because this study assumed a skin absorption rate of 100% for all three phthalates. Although there have been experimental studies at the cellular level regarding the rate of skin absorption of single phthalates (Koo and Lee, 2004), the absorption of the substances contained in actual products has not yet been assessed. Although hair follicles are the main location of DEHP absorption, and they have been the focus of previous studies (Pan et al., 2014), it is possible that the absorption rate via other body parts could also be significant. Due to the lack of specific skin absorption rate information by product and body part, a conservative skin absorption rate was used in this study.

2.5. Conclusions

The DEHP, DnBP, and DEP AED values for 31 cosmetic products were estimated for the Korean population. The receptor-based aggregate exposure assessment method would be used to determine high exposure groups. The product-based aggregate exposure assessment method underestimated the high exposure group but overestimated the average exposure for DnBP and DEP. Further studies needed to be confirm whether a similar phenomenon occurred for other chemicals. The AED_r was significantly different by age and gender. The high exposure group for phthalates in cosmetics was young females because they used a large number of cosmetic products. The receptor-based AED for DEHP, DnBP, and DEP could identify the contribution of cosmetic products.

Chapter III.

Characteristics of cosmetics co-use pattern and determination of co-use scenarios for aggregate exposure assessment

3.1. Introduction

The human body is exposed to chemicals through multiple sources and routes. Consumer products are one major source of chemical exposure. Aggregate exposure refers to the risks over time from multiple sources, pathways, and routes for a single chemical (US EPA, 2003; WHO, 2004). Because the human body can be exposed to certain chemicals through multiple consumer products, understanding how multiple products are co-used is critical for realistic exposure estimation as receptor-oriented approach. Aggregate exposure assessment that consider the co-use and non-use of products was more accurate and realistic estimation (Cowan-Ellsberry and Robison, 2009). Therefore, for aggregate exposure assessments of common chemical substances, it is necessary to identify which products are co-used more frequently.

Among consumer products, cosmetics and personal care products were often examined in aggregate exposure assessment (Ficheux et al., 2019). Recent aggregate exposure studies conducted on preservatives (Aylward et al., 2018; Ezendam et al., 2018; Garcia-Hidalgo et al., 2018), fragrance compounds (Dornic et al., 2018; Jongeneel et al., 2018) and vitamin A (Tozer et al., 2019) in cosmetics, personal care and household care products. In addition, aggregate exposure modeling that focuses on co-use and receptor oriented approach had been attempted to several cleaning products containing the antibacterial ingredient (Tozer et al., 2015). The probabilistic aggregate consumer exposure model (PACEM) developed in Europe had also considered co-used products (Delmaar et al., 2015; Dudzina et al., 2015; Gosens et al., 2014). Commercial database for cosmetics, such as Kantar World panel (Comiskey et al., 2015; Comiskey et al., 2017), also included co-use information of human subjects.

Applying actual co-use products combination to aggregate exposure assessment was the most realistic method. However, it was difficult to identify the specific combinations used by individuals for every aggregate exposure estimation. Accurately investigating all product combinations for certain populations would be costly and time-consuming. Previous studies had used several methods to identify product co-use patterns and characteristics. First, correlation analysis had been used to analyze the level of agreement between use of two products (Biesterbos et al., 2013; Wu et al., 2010). Correlation analysis determined the relationship between only two products. This method could not analyze the correlation of three or more products. Second, hierarchical cluster analysis had been used to determine the products categories commonly used together and displayed the results as dendrograms (Lang et al., 2016). This method was unable to determine the proportion of the population to the cluster. The population using exact products of specific cluster might be small. Third, frequent pattern mining (FPM) analysis had been used to identify the most frequent co-use combinations and the percentage of users (Garcia-Hidalgo et al., 2017; Manová et al., 2013). FPM analysis presented fractional results with numerous patterns and similar support rates. As the number of target products increased, the number of possible product combinations increased and the support rates for each product combination decreased.

Appropriate co-use patterns should be determined using a national representative exposure factor database for a sufficient number of products in one major category. The Korean national representative exposure factor database about

31 cosmetic products including simultaneous usage-patterns (Lim et al., 2019) could be used to analyze co-use patterns of cosmetics. A sufficient number of products in a single classification need to be analyzed to identify co-use patterns. The number of products in previous studies had been limited to 10-15 products of a specific sub-class that were not all products of one major category (Garcia-Hidalgo et al., 2017; Lang et al., 2016). Furthermore, co-use patterns might be affected by the characteristics of the study population. However, previous studies only considered difference in gender (Garcia-Hidalgo et al., 2017). Using a national representative population, co-use pattern by age and gender could be determined.

The objectives of the study were 1) to characterize co-use patterns of cosmetics by applying and comparing the three aforementioned methods of co-use pattern analysis, and 2) to determine the co-use scenarios applicable to aggregate exposure assessment of cosmetics.

3.2. Methods

Materials

The Korean representative exposure factors of 31 cosmetic products for the simultaneous usage patterns of 1,001 individuals were obtained from home-visit face-to-face interviews. The detailed survey methodology has been described previously (Lim et al., 2019).

In the survey, target cosmetics included four skincare (skin toner, face lotion, face cream, facial sunscreen), three hair care (hair dye, hair treatment, hair styling), four body care (body lotion, hand cream, deodorant, body sunscreen), three cleanser (hand wash, face cleanser, shaving cream), three base makeup (foundation, makeup base/primer, pact/powder), four eye makeup (eyeliner, eyeshadow, mascara, eyebrow), four lip makeup (lip balm, lip tint, lip gloss, lipstick), four nail care (nail polish, gel nail polish, nail strengthener, nail remover), and two fragrance (shower cologne, perfume) products.

Proportionate quota sampling was used to recruit respondents (n = 1001) with quotas based on sex, age, and regional distribution of the Korean population. Subjects were divided into males (n = 509) and females (n = 492) by gender, as well as by age: 19–39 (n = 396) or over 40 (n = 605) years old. Considering both gender and age, the population groups were composed of males aged 19–39 (n = 205), males aged 40+ (n = 304), females aged 19–39 (n = 191), and females aged 40+ (n = 301).

Three methods of co-use pattern analysis

The correlations among pairs of cosmetic products were analyzed using Cohen's kappa (Cohen, 1960). Cohen's kappa measured inter-rater agreement for categorical items. The κ value was calculated using p_o and p_c, where p_o was the proportion of units in which agreement was observed, and p_c was the proportion of units for which agreement was expected by chance. Kappa values less than 0 was indicated poor agreement, values from 0 to 0.20 indicated slight agreement, 0.21 to 0.40 indicated fair agreement, 0.41 to 0.60 indicated moderate agreement, 0.61 to 0.80 indicated substantial agreement, and 0.80 to 1.00 indicated almost perfect agreement (Landis and Koch, 1977).

Hierarchical clustering for binary variables was performed for each gender group. The use and non-use of cosmetics were coded as "1" and "0", respectively, for each respondent. The asymmetric binary distance was measured for clustering. The result of a clustering was presented as a tree-structured dendrogram. The male group included clustering for 16 products and did not include base makeup, eye makeup, lip makeup, and nail care products. The female group included clustering for 30 products and did not include shaving foam. The number of clusters (k) was determined conservatively as the square root of $n/2$ (Mardia et al., 1979), where n was the number of cosmetics in the present analysis.

FPM was performed for each gender-age group using the eclat algorithm. The basic concept of FPM was to find the co-occurrence, which was calculated as the probability of item combinations being included together in a shopping basket. The eclat algorithm used equivalence class clustering schemes and bottom-up lattice traversal to generate all potential maximal itemsets (Zaki et al., 1997). The 'arules' package (Hahsler et al., 2019; Hahsler et al., 2005) was used for the eclat algorithm to reveal frequent co-use patterns. All calculation and statistical analyses were conducted using R version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria).

Determination of co-use scenarios

The cosmetic co-use scenarios were developed using FPM with the eclat algorithm and the distribution of the number of used cosmetics by each population group. Figure 3-1 presents the determination logic of the co-use scenarios for cosmetics. The co-use patterns analyzed using the eclat algorithm were sorted by descending order of support according to the size of combination. Cosmetics were ranked by the frequency of occurrence in the co-use patterns. The cosmetics included in combinations with a small number of cosmetics had a higher rank. For example, a cosmetic that first occurs within a combination size of three would be ranked higher than a cosmetic that first occurs within a combination size of five, even if the two cosmetics occurred in co-use patterns with equal frequency. In addition, the 25th, 50th, 75th and 95th percentile values of distribution of the number of used cosmetics were selected for the four target population groups. The cosmetics were then combined until reaching an equal rank of each percentile value; this combination was selected as a co-use scenario. In this study, a total of 16 cosmetic co-use scenarios were determined for four scenarios (scenario 1 for P25, scenario 2 for P50, scenario 3 for P75 and scenario 4 for P95) of the four population groups (young males, senior males, young females and senior females).

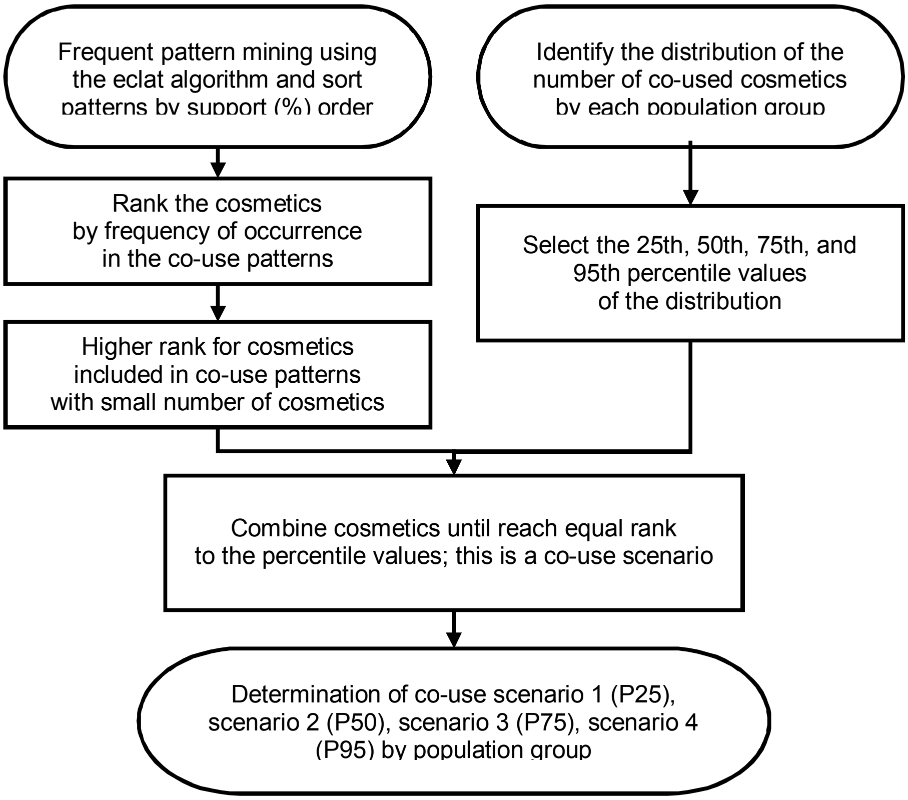


Figure 3-1. Overview of the co-use scenario determination using frequent pattern analysis and the distribution of the number of co-used cosmetics.

3.3. Results

Correlation of cosmetic pairs

Table 3-1 presents the Cohen's kappa values with $p < 0.05$ for all 31 cosmetics in nine categories for the entire study population. The product combination with the highest kappa value was nail polish and nail remover (kappa = 0.88); 92.4% of nail polish users used it with nail remover (97 of 105). Face cream, foundation, and lipstick were also strongly correlated (kappa > 0.70); 71.2% of face cream users also used it in combination with foundation and lipstick (337 of 473). For eye makeup categories, each of the six combinations of the four products were moderately correlated (kappa > 0.40). Shaving foam was negatively correlated (kappa < 0) with other cosmetics, with the exceptions of hair styling (kappa = 0.15) and deodorant (kappa = 0.07).

Table 3-1. Cohen's kappa coefficients for the co-used 31 cosmetics examined for all respondents (n = 1001).

(a) Skincare and hair care products

	Skincare				Hair care		
	FT	FL	FC	FS	HD	HT	HS
Skin toner (FT)	-						
Face lotion (FL)	**0.45**	-					
Face cream (FC)	0.14	0.082	-				
Facial sunscreen (FS)	0.16	0.14	**0.55**	-			
Hair dye (HD)			0.08		-		
Hair treatment (HT)	0.09		**0.56**	0.37	0.06	-	
Hair styling (HS)		0.03					-
Body lotion (BB)	0.13	0.12	**0.54**	0.37		**0.41**	
Hand cream (BH)	0.09	0.07	**0.47**	0.30	0.07	0.36	
Deodorant (BD)				0.03		0.06	0.14
Body sunscreen (BS)			0.07	0.11		0.08	0.09
Hand wash (CH)			0.14	0.10		0.17	0.10
Face cleanser (CF)			0.212	0.19		0.13	
Shaving foam (CS)	-0.01	-0.02	-0.17	-0.06		-0.13	0.15
Foundation (MF)	0.11	0.09	**0.77**	**0.46**	0.08	**0.55**	-0.06
Makeup base/Primer (MB)			0.09	0.04	0.07	0.11	
Pact/Powder (MP)	0.03	0.03	0.33	0.18	0.10	0.24	
Eyeliner (EL)	0.03		0.25	0.15		0.32	
Eyeshadow (ES)	0.06	0.03	**0.46**	0.25		**0.44**	
Mascara (EM)	0.03		0.31	0.18		0.34	
Eyebrow (EB)	0.05		**0.42**	0.21		0.35	
Lip balm (LB)			0.10	0.07		0.11	
Lip tint (LT)			0.12	0.08		0.14	-0.05
Lip gloss (LG)	0.02	0.02	0.17	0.10		0.19	
Lipstick (LS)	0.11	0.09	**0.79**	**0.48**	0.10	**0.55**	-0.07
Nail polish (NP)	0.02		0.20	0.12		0.24	
Gel nail polish (NG)			0.07	0.04	-0.07	0.12	
Nail strengthener (NS)			0.05	0.03		0.09	0.05
Nail remover (NR)	0.02		0.23	0.13		0.27	
Shower cologne (RC)			0.09	0.07		0.12	
Perfume (RP)	0.03		0.17	0.13		0.23	0.18

(b) Body care, cleanser and base makeup products

	Body care				Cleanser			Base makeup		
	BB	BH	BD	BS	CH	CF	CS	MF	MB	MP
BB	-									
BH	0.39	-								
BD	0.05	0.07	-							
BS	0.09	0.15	0.16	-						
CH	0.13	0.11	0.09	0.08	-					
CF	0.17	0.07	0.01	0.02	0.03	-				
CS	-0.09	-0.06	0.07			-0.04	-			
MF	**0.47**	**0.44**		0.08	0.12	0.17	-0.18	-		
MB	0.07	0.06			0.06	0.01	-0.07	0.08	-	
MP	0.19	0.17		0.11	0.10	0.06	-0.13	0.25	0.15	-
EL	0.18	0.18	0.15	0.14	0.11	0.05	-0.13	0.31	0.10	0.23
ES	0.31	0.24	0.08	0.10	0.13	0.09	-0.16	**0.48**	0.14	0.32
EM	0.21	0.20	0.10	0.13	0.17	0.06	-0.14	0.36	0.12	0.22
EB	0.26	0.20	0.07	0.10	0.11	0.07	-0.15	**0.45**	0.13	0.30
LB	0.08	0.09	0.26	0.13	0.09	0.02		0.13	0.10	0.08
LT	0.06	0.06	0.19			0.02	-0.08	0.15	0.05	0.07
LG	0.12	0.13		0.13	0.07	0.03	-0.10	0.21	0.06	0.17
LS	**0.48**	**0.44**		0.08	0.09	0.18	-0.19	**0.76**	0.10	0.38
NP	0.13	0.15		0.10	0.09	0.04	-0.11	0.21	0.09	0.17
NG	0.05	0.06	0.13	0.11	0.06	0.01	-0.06	0.08		0.07
NS	0.04	0.05		0.05	0.07	0.01		0.07	0.08	0.14
NR	0.16	0.16	0.09	0.12	0.12	0.04	-0.12	0.21	0.09	0.20
RC	0.08	0.06	0.07	0.11		0.01		0.11	0.08	0.08
RP	0.19	0.15	0.14	0.14	0.16	0.05	0.08	0.17		0.12

(c) Eye makeup and lip makeup products

	Eye makeup				Lip makeup			
	EL	ES	EM	EB	LB	LT	LG	LS
EL	-							
ES	**0.48**	-						
EM	**0.56**	**0.58**	-					
EB	**0.42**	**0.44**	**0.44**	-				
LB	0.25	0.16	0.25	0.16	-			
LT	0.34	0.23	0.32	0.19	0.29	-		
LG	0.20	0.26	0.25	0.14			-	
LS	0.26	**0.45**	0.29	**0.40**	0.06		0.16	-
NP	0.33	0.29	0.33	0.23	0.12	0.10	0.26	0.21
NG	0.17	0.14	0.21	0.09	0.16	0.08	0.17	0.08
NS	0.15	0.12	0.20	0.12	0.11	0.06	0.23	0.06
NR	0.34	0.32	0.35	0.24	0.15	0.12	0.26	0.23
RC	0.19	0.18	0.18	0.16	0.11	0.20	0.14	0.08
RP	0.24	0.23	0.26	0.16	0.10	0.06	0.14	0.17

(d) Nail care and fragrance products

	Nail care				Fragrance	
	NP	NG	NS	NR	RC	RP
NP	-					
NG	0.14	-				
NS	0.32	0.29	-			
NR	**0.88**	0.34	0.27	-		
RC	0.17	0.15	0.12	0.17	-	
RP	0.17	0.11	0.08	0.23	0.08	-

* Only kappa values with $p < 0.05$ are shown. Values larger than 0.40 are shown in bold.

Hierarchical clustering

Figure 3-2 presents the clustering dendrograms for each gender group. The male group had three clusters (k) with 16 cosmetics (n). Cluster 1 identified 12 cosmetics: skin toner, face lotion, face cleanser, facial sunscreen, body lotion, hand cream, hair styling, perfume, shaving foam, hand wash, deodorant, and body sunscreen. Cluster 2 included three cosmetics: face cream, hair treatment, and hair dye. Cluster 3 only contained shower cologne. The female group exhibited four clusters (k) with 30 cosmetics (n). Cluster 1 included 23 cosmetics: skin toner, face cleanser, face lotion, face cream, facial sunscreen, lipstick, foundation, body lotion, hand cream, hair treatment, eyebrow, pact/powder, hand wash, hair styling, eyeshadow, mascara, eyeliner, perfume, nail polish, nail remover, lip gloss, body sunscreen, and shower cologne. Cluster 2 identified the two cosmetics of hair dye and makeup base/primer. Cluster 3 contained three cosmetics: deodorant, lip balm, and lip tint. Cluster 4 identified the two nail care cosmetics of gel nail polish and nail strengthener.

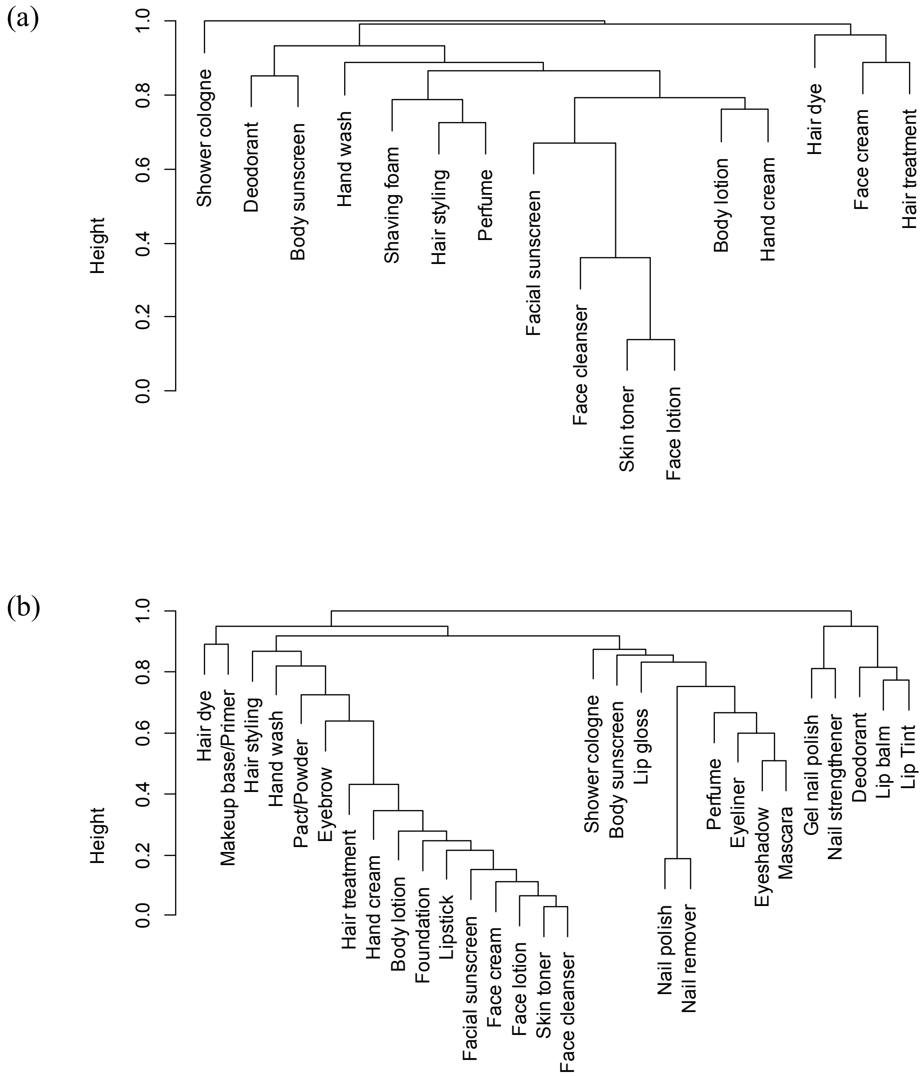


Figure 3-2. Dendrograms representing hierarchical clustering from (a) 16 cosmetics among male respondents (n = 509), and (b) 30 cosmetics among female respondents (n = 492).

Frequent pattern mining

Figure 3-3 presents the number of used cosmetics by the four gender-age population groups. The average number of cosmetics used by females aged 19–39 was 14.0 ± 4.1, which was significantly more than the number used by females aged 40+ (12.2 ± 3.1). While males used fewer cosmetics than female, a similar pattern was observed for the age groups. Males aged 19–39 used more cosmetics (5.1 ± 2.4) compared to males aged 40+ (4.1 ± 1.9). Males aged 19–39 used more cosmetics (5.1 ± 2.4) compared to males aged 40+ (4.1 ± 1.9). The 95th percentile of the number of cosmetics used was 10, 8, 21, and 18 for 19-39 males, 40+ males, 19-39 females, and 40+ females, respectively.

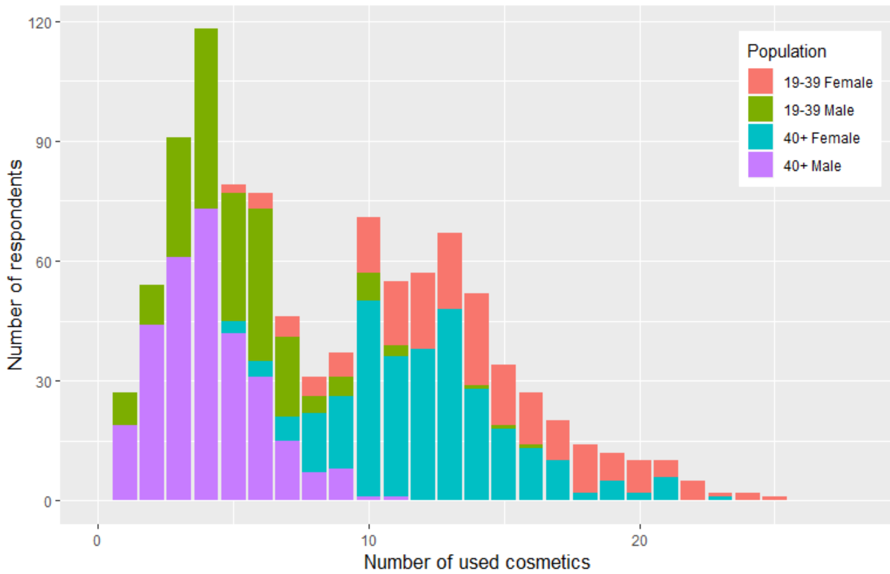


Figure 3-3. The number of used cosmetics and respondents by gender-age population groups.

Tables 3-2 and 3-3 show the possible maximum number of combinations and the five most frequent combinations with support of more than 5% based on the average number of used cosmetics using the eclat algorithm in the male and female populations, respectively. The support for a combination was calculated as the possibility of the combination, and this value existed as a subset among the total number of used products by the respondents.

Table 3-2. The most frequent cosmetic combinations identified by the eclat algorithm with support of more than 5% based on the average number of used cosmetics among male respondents.

(a) 19–39 Male (n = 205)

Number of cosmetics considered	Maximum number of combinations	Combinations	Support (%)
3	30	FT, FL, CF	63.9
		FT, FL, FS	32.7
		FT, FL, HS	31.2
		FL, FS, CF	31.2
		FT, FS, CF	30.2
4	45	FT, FL, FS, CF	28.3
		FT, FL, HS, CF	25.9
		FT, FL, BB, CF	24.9
		FT, FL, CF, RP	19.5
		FT, FL, CF, BH	16.1
5	32	FT, FL, FS, HS, CF	12.7
		FT, FL, HS, CF, RP	11.2
		FT, FL, FS, BB, CF	10.7
		FT, FL, FS, CF, RP	9.8
		FT, FL, HS, BB, CF	9.8
6	38	FT, FL, FS, HS, CF, RP	6.3

(b) 40+ Male (n = 304)

Number of cosmetics considered	Maximum number of combinations	Combinations	Support (%)
3	61	FT, FL, CF	54.3
		FT, FL, FS	25.3
		FT, FL, BH	20.4
		FL, FS, CF	20.4
		FT, FL, BB	19.4
4	73	FT, FL, FS, CF	19.1
		FT, FL, BB, CF	13.5
		FT, FL, BH, CF	12.5
		FT, FL, HD, CF	9.5
		FT, FL, HS, CF	9.2
5	42	FT, FL, FS, BB, CF	5.6
		FT, FL, FS, HS, CF	5.3
		FT, FL, FS, BH, CF	5.3

* The average number of used cosmetics was 5 for males aged 19–39, and 4 for males aged 40+. The cosmetics were abbreviated as follows: FT, skin toner; FL, face lotion; FS, facial sunscreen; HD, hair dye; HS, hair styling; BB, body lotion; BH, hand cream; CF, face cleanser; RP, perfume.

Table 3-3. The most frequent cosmetic combinations identified by the eclat algorithm with support of more than 5% based on the average number of used cosmetics among female respondents.

(a) 19–39 Female (n = 191)

Number of cosmetics considered	Maximum number of combinations	Combinations	Support (%)
11	16	FT, FL, FC, FS, HT, BB, BH, CF, MF, ES, LS	18.8
		FT, FL, FC, FS, BB, BH, CF, MF, ES, EM, LS	16.2
		FT, FL, FC, FS, HT, BB, BH, CF, MF, EB, LS	15.7
		FT, FL, FC, FS, HT, BB, BH, CF, MF, LS, RP	15.2
		FT, FL, FC, FS, HT, BB, CF, MF, ES, EM, LS	15.2
12	19	FT, FL, FC, FS, HT, BB, BH, CF, MF, EL, ES, LS	12.6
		FT, FL, FC, FS, HT, BB, BH, CF, MF, ES, EM, LS	12.6
		FT, FL, FC, FS, HT, BB, BH, CF, MF, ES, LS, RP	12.0
		FT, FL, FS, HT, BB, BH, CF, MF, EL, ES, EM, LS	12.0
		FT, FL, FC, FS, HT, BB, CF, MF, EL, ES, EM, LS	12.0
13	19	FT, FL, FC, FS, HT, BB, BH, CF, MF, EL, ES, EM, LS	10.5
		FT, FL, FC, FS, BB, BH, CF, MF, EL, ES, EM, LS, RP	9.4
		FT, FL, FC, FS, HT, BB, BH, CF, MF, EL, ES, LS, RP	9.4
		FT, FL, FS, HT, BB, BH, CF, MF, EL, ES, EM, EB, LS	9.4
		FT, FL, FC, FS, HT, BB, BH, CF, MF, EL, ES, EM, EB	9.4
14	23	FT, FL, FC, FS, HT, BB, BH, CF, MF, EL, ES, EM, LS, RP	7.9
		FT, FL, FC, FS, HT, BB, BH, CF, MF, EL, ES, EM, EB, LS	7.9
		FT, FL, FC, FS, HT, BB, BH, CF, MF, EL, ES, EM, LS, NR	7.3
		FT, FL, FS, HT, BB, BH, CF, MF, EL, ES, EM, EB, LS, NR	6.8
		FT, FL, FC, FS, HT, BB, BH, CF, MF, EL, EM, EB, LS, NR	6.8
15	15	FT, FL, FS, HT, BB, BH, CF, MF, EL, ES, EM, EB, LS, NP, NR	5.8
		FT, FL, FC, FS, HT, BB, BH, CF, MF, EL, ES, EM, EB, LS, NR	5.8
		FT, FC, FS, HT, BB, BH, CF, MF, EL, ES, EM, EB, LS, NP, NR	5.2
		FT, FL, FC, HT, BB, BH, CF, MF, EL, ES, EM, EB, LS, NP, NR	5.2

		FT, FL, FC, FS, HT, BB, BH, CF, EL, ES, EM, EB, LS, NP, NR	5.2

(b) 40+ Female (n = 301)

Number of cosmetics considered	Maximum number of combinations	Combinations	Support (%)
9	15	FT, FL, FC, FS, HT, BB, CF, MF, LS	42.5
		FT, FL, FC, FS, BB, BH, CF, MF, LS	42.2
		FT, FL, FC, FS, HT, BB, BH, CF, LS	35.9
		FT, FL, FC, FS, HT, BB, BH, CF, MF	32.9
		FT, FL, FC, FS, HT, BH, CF, MF, LS	32.9
10	18	FT, FL, FC, FS, HT, BB, BH, CF, MF, LS	30.6
		FT, FL, FC, FS, HT,BB, CF, MF, ES, LS	22.3
		FT, FL, FC, FS, BB, BH, CF, MF, ES, LS	20.3
		FT, FL, FC, FS, HT, BB, BH, CF, ES, LS	17.6
		FT, FL, FC, FS, HT, BB, CF, MF, LS, RP	17.3
11	49	FT, FL, FC, FS, HT, BB, BH, CF, MF, ES, LS	15.6
		FT, FL, FC, FS, HT, BB, BH, CF, MF, LS, RP	12.3
		FT, FL, FC, FS, HT, BB, CF, MF, ES, EM, LS	11.3
		FT, FL, FC, FS, HT, BB, BH, CF, MF, EM, LS	10.6
		FT, FL, FC, FS, HT, BB, BH, CF, MF, MP, LS	10.3
12	35	FT, FL, FC, FS, HT, BB, BH, CF, MF, ES, EM, LS	8.3
		FT, FL, FC, FS, HT, BB, BH, CF, MF, LS, NP, NR	8.0
		FT, FL, FC, FS, HT, BB, BH, CF, MF, ES, LS, RP	6.6
		FT, FL, FC, FS, HT, BB, CF, MF, LS, NP, NR, RP	6.3
		FT, FL, FC, FS, HT, BB, CF, MF, ES, EM, LS, RP	6.3
13	38	FT, FL, FC, FS, HT, BB, BH, CF, MF, LS, NP, NR, RP	5.3
		FT, FL, FC, FS, HT, BB, BH, CF, MF, EL, ES, EM, LS	5.0

* The average number of used cosmetics was 14 for females aged 19–39, and 12 for females aged 40+. The cosmetics were abbreviated as follows: FT, skin toner; FL, face lotion; FC, face cream; FS, facial sunscreen; HT, hair treatment; BB, body lotion;

BH, hand cream; CF, face cleanser; MF, foundation; MP, pact/powder; EL, eyeliner; ES, eyeshadow; EM, mascara; EB, eyebrow; LS, lipstick; NP, nail polish; NR, nail remover; RP, perfume.

In males aged 19–39 and 40+, 63.9% and 54.3%, respectively, used a combination of three cosmetics, including skin toner, face lotion and face cleanser. In both male groups, skin toner and face lotion were the main skincare products. Among hair care products, hair styling products were used by males aged 19–39, and hair dye was used by males aged 40+. Face cleanser was the most common item included in co-use combinations for all four population groups. Perfume was only included in co-use combinations for males aged 19–39 when the number of cosmetics in the combination was large.

The co-use patterns with high support were similar in females aged 19–39 and 40+. Respectively, 18.8% and 15.6% of these two groups used a combination of 11 cosmetics including four skincare products, hair treatment, body lotion, hand cream, face cleanser, foundation, eyeshadow and lipstick. All four skincare products (skin toner, face lotion, face cream, facial sunscreen) were primarily used by females. As the number of cosmetics considered increased, various types of eye makeup products (eyeliner, eyeshadow, mascara, eyebrow) were added. Foundation and lipstick were the most used products among base makeup products and lip makeup products, respectively. Nail remover and nail polish most frequently occurred together in co-use combinations. Between these two products, the co-use combination including only nail remover showed higher support in the group of females aged 19–39.

Determination of co-use scenarios

Table 3-4 presents four cosmetic co-use scenarios for each of the four population groups. Each co-use scenario was presented as the number of co-used cosmetics and the types of cosmetics. As the scenario number increased, new cosmetics were added to the co-use pattern of the previous scenario. The products that were most common among all co-use scenarios were skin toner and face lotion in the skincare category. The co-use scenario with the largest number of cosmetics was scenario 4 of the young female group, which included one or more cosmetics in each of nine categories. Makeup products (base makeup, eye makeup, lip makeup and nail care products) were only included in the co-use scenarios of females. Hair styling, shaving foam and hair dye were only included in the co-use scenarios of males. Deodorant was only included in scenario 4 of the younger groups for both males and females. A total of 16 co-use scenarios included 24 of 31 possible cosmetics. Seven products (body sunscreen, hand wash, makeup base/primer, lip balm, lip tint, gel nail polish and nail strengthener) were not included in the final co-use scenarios.

Table 3-4. The cosmetic co-use scenarios proposed using the rank of occurrence of frequency in co-use patterns and percentile values of the number of cosmetics used. Co-use scenario 1 represented 25th percentile of co-use pattern, scenario 2 the 50th percentile, scenario 3 the 75th percentile, scenario 4 for 95th percentile for each of the four Korean gender-age populations.

	Number of co-used cosmetics	Co-use pattern
Male, young		
Scenario 1	4	FT, FL, CF, FS
Scenario 2	5	FT, FL, CF, FS, HS
Scenario 3	6	FT, FL, CF, FS, HS, BH
Scenario 4	10	FT, FL, CF, FS, HS, BH, RP, BB, BD, CS
Male, senior		
Scenario 1	3	FL, FT, CF
Scenario 2	4	FL, FT, CF, FS
Scenario 3	5	FL, FT, CF, FS, BB
Scenario 4	8	FL, FT, CF, FS, BB, BH, HS, HD
Female, young		
Scenario 1	11	FT, FL, FS, BB, CF, MF, FC, HT, BH, ES, LS
Scenario 2	14	FT, FL, FS, BB, CF, MF, FC, HT, BH, ES, LS, EM, EB, RP
Scenario 3	17	FT, FL, FS, BB, CF, MF, FC, HT, BH, ES, LS, EM, EB, RP, EL, NR, NP
Scenario 4	21	FT, FL, FS, BB, CF, MF, FC, HT, BH, ES, LS, EM, EB, RP, EL, NR, NP, MP, LG, RC, BD
Female, senior		
Scenario 1	10	FT, FL, FC, CF, LS, FS, BB, BH, MF, HT
Scenario 2	12	FT, FL, FC, CF, LS, FS, BB, BH, MF, HT, ES, RP
Scenario 3	14	FT, FL, FC, CF, LS, FS, BB, BH, MF, HT, ES, RP, EM, NP
Scenario 4	18	FT, FL, FC, CF, LS, FS, BB, BH, MF, HT, ES, RP, EM, NP, MP, EL, NR, EB

* The cosmetics were abbreviated as follows: FT, skin toner; FL, face lotion; FC, face cream; FS, facial sunscreen; HD, hair dye; HT, hair treatment; HS, hair styling; BB, body lotion; BH, hand cream; BD, deodorant; CF, face cleanser; CS, shaving cream; MF, foundation; MP, pact/powder; EL, eyeliner; ES, eyeshadow; EM, mascara; EB, eyebrow; LG, lip gloss; LS, lipstick; NP,

nail polish; NR, nail remover; RC, shower cologne; RP, perfume.

3.4. Discussion

Correlation of cosmetic pairs

The product correlations using the kappa coefficient for the Korean population could be directly compared with the results observed during a study in The Netherlands (Biesterbos et al., 2013). In both studies, high correlations of pairs were observed in the nail care and eye makeup categories. Face cream (day cream and night cream in the Dutch study) was also highly correlated with makeup products. The combination of face cream, foundation and lipstick was characteristic of the cosmetic co-use patterns of Korean females. Negative correlations occurred between the shaving products and makeup products in both studies. The former were used by males, while the latter were used by primarily by females.

In contrast to our study, previous studies in Switzerland (Garcia-Hidalgo et al., 2017) and California (Wu et al., 2010) used Spearman's correlation coefficient for analysis of product pairs. Spearman's correlation coefficient was used for both qualitative and quantitative variables. However, Cohen's kappa coefficient was a specific statistical value for analyzing agreement among categorical data. Comparisons between these previous studies and the present study were challenging, given that the two types of correlations had different statistical values. In addition, the two previous studies used different target products that included both cosmetics and personal care products. Nevertheless, the Swiss study found high correlations between makeup cosmetics and makeup remover product (Garcia-Hidalgo et al., 2017), while the California study reported a high correlation between body lotion and hand lotion (Wu et al., 2010).

Correlation analysis using Cohen's kappa coefficient was applicable for populations without dominant observations (use or non-use). Our study applied this correlation analysis to a database of 1,001 subject and 31 cosmetics. Cohen's kappa coefficient was not appropriate for dominant observation; for example, 907 subjects used skin toner, and 791 of these individuals (87.2%) also used face cleanser. This pair was actually highly correlated; however, the *p*-value of Cohen's kappa coefficient was not significant; this, the kappa value for the pair was not presented in Table 1. The cosmetics primarily used by a particular gender might have "non-use rates" for the opposite gender. Therefore, our combined analysis of male and female populations could compensate for the weakness of Cohen's kappa coefficient.

Hierarchical clustering

To detect differences in the usage patterns between males and females, clustering analysis was applied to data for each gender. The binary linkage distance method was used to cluster the of categorical data (use or non-use). The composition of the classified clusters indicated that cluster 1 contained many cosmetics for both males and females. The smaller clusters represented co-use characteristics of specific populations. Cluster 2 in males consisted of face cream, hair dye and hair styling, all of which had generally low use rates in males. In females, cluster 2 consisted of cosmetics mainly used by senior females, cluster 3 included cosmetics marketed mainly to a young population, and cluster 4 included exclusively nail care products. People tended to use some cosmetics from cluster 1 and from smaller clusters according to their preferences. In this study, principal component analysis (PCA) was not used to analyze the co-use patterns of cosmetics because these were cumulative patterns, which make it difficult to bundle cosmetics into a specific factor or component.

In this study, calculating the k value using the square root of $n/2$ was appropriate for this co-use pattern analysis. When the value of k was increased, the existing clusters were split and re-clustered as subsets. The cosmetics within different clusters were not re-clustered with increases in k. The silhouette score (Rousseeuw, 1987) had been used as an indicator for the appropriation of clustering configurations. In females, the silhouette score was 0.14 with four clusters and reached a maximum of 0.21 with eight clusters. When the value of k was changed from 4 to 8, cluster 1 was divided into four clusters, cluster 2 was divided into two clusters, and clusters 3 and 4 were unchanged. Four of the six clusters that split from clusters 1 and 2 contained only one cosmetic (hair styling, shower cologne, hair dye and makeup base/primer). The clusters with single cosmetic were unnecessary for the co-use pattern analysis.

Frequent pattern mining

FPM looks for repeating relationships between several items in a dataset in the form of association rules (Chee et al., 2018). Among FPM algorithms, the eclat algorithm was a tree-based algorithm suitable for the analysis of long patterns and dense databases (Fiat and Shporer, 2003; Schmidt-Thieme, 2004). The actual number of co-use patterns was much lower than the total number of theoretically possible co-use patterns. For example, if three of 31 cosmetics were selected for a co-use pattern, there were theoretically 4,495 combinations. However, the group of males aged 19–39 had only 30 combinations, and males aged 40+ had 61 combinations. Similarly, Garcia-Hidalgo et al. (2017) also observed lower number of co-use patterns than was theoretically possible. In addition, the present study conducted the FPM analysis separately for the four groups based on gender and age. For males, perfume only occurred in the frequent co-use combinations of the 19–39 group, while hair dye only occurred frequently in the 40+ group. For females, powder/pact was only selected for the 40+ group. This study was the first to determine of co-use patterns of cosmetics by age and gender. Previous studies using FPM analysis had only been based on gender (Garcia-Hidalgo et al., 2017; Manová et al., 2013).

The cosmetic combinations revealed by the FPM analysis method could not be representative co-use patterns of the entire population. The support rate of the FPM for a specific combination did not reflect the percentage of the population using only the selected cosmetics; instead, the support rate represented the proportion of the population who used that specific combination among the total co-used cosmetics of an individual. As the number of cosmetics in the combination increased, the support rate for each pattern decreased. In females aged 19–39, who used the largest number of cosmetics, the co-use patterns of each individual differed. The co-use combinations resulting from the FPM could not be directly applicable for aggregate exposure assessment.

Determination of co-use scenarios

The cosmetic co-use scenarios were developed by determining the number of specific cosmetics in co-use patterns and the percentiles of the distribution of the number of co-used cosmetics. The proposed co-use scenarios could compensate for the disadvantages of the three co-use pattern analysis methods. First, this approach made it possible to determine the relationship between three or more products. The correlation analysis was limited to the relationship between pairs of products. Second, our method provided population distributions for the various co-use scenarios. The co-use scenarios based on the four percentiles ranged from low (25th percentile) to high (95th) exposures. Because hierarchical clustering analysis was only based on the clustering of cosmetics, it did not present population proportions for the clusters. The population distribution of co-used products could not be determined without the population proportions for the clusters. Third, this approach allowed us to directly apply the results to aggregate exposure assessment. The co-use scenarios presented specific cosmetic combinations for various demographic groups. The FPM analysis identified all co-use patterns; however, it did not represent the population with a single co-use pattern.

The cosmetic co-use scenarios revealed in the present study were based on the Korean representative exposure factor database that included the simultaneous usage patterns. Although this study was based on 31 cosmetics in nine categories, it might be nearly impossible to include all types of cosmetics currently available on the market. New databases with more cosmetics would be ideal for more comprehensive co-use scenarios. However, our database included the most common cosmetics on the market. These co-use scenarios could be directly applied to aggregate exposure assessment of cosmetics in Korea. When additional cosmetics were included in the co-use scenarios, aggregate exposure assessment could determine the impact of the additional cosmetics.

3.5. Conclusions

The co-use patterns of 31 cosmetics used by the Korean population were determined using Cohen's kappa coefficient, hierarchical clustering with binary linkage distance and FPM with the eclat algorithm. The cosmetic co-use patterns were significantly influenced by the gender and age of the population. Four co-use scenarios were determined for each of four gender-age population groups. The co-use scenarios were proposed for the 25th, 50th, 75th and 95th percentiles of the target population. The proposed co-use scenarios could be directly applied to aggregate exposure assessment of cosmetics.

Chapter IV.

Application and validation of aggregate exposure assessment for phthalates based on cosmetic co-use scenarios

4.1. Introduction

The use of consumer products is a major exposure source of chemical exposure through multiple sources and multiple routes. Cosmetics and personal care products in direct dermal contact with human body are important sources of chemical exposure. Common ingredient of cosmetics and personal care products, such as preservatives, were often examined in recent aggregate exposure and risk assessment studies (Aylward et al., 2018; Ezendam et al., 2018; Garcia-Hidalgo et al., 2018). Chemical exposure and risk assessment has been implemented in a tiered approach framework (IPCS, 2009; Meek, 2013; Meek et al., 2011; U.S.EPA, 1992, 2004), which can be applied to aggregate exposure assessment. For low-tier screening level risk assessment, aggregate exposure could be determined by simplistic adding up the exposures from all kind of products. Understanding how multiple products were co-used more frequently could be critical for high-tier realistic aggregate exposure assessment. Cosmetic use patterns are highly influenced by consumer preference heterogeneity. Considering co-use and non-use of cosmetic products enables more realistic and accurate aggregate estimation (Cowan-Ellsberry and Robison, 2009), and is one of the important points of cosmetic safety assessment (Ficheux et al., 2019).

Although there is a broad consensus on the correlation of co-used products and aggregate exposure, the process of the methodology to implement co-used products in aggregate exposure assessment is less clear. Previous studies in Switzerland (Garcia-Hidalgo et al., 2017; Manová et al., 2013), France (Ficheux et al., 2015), and Netherlands (Biesterbos et al., 2013) were focused generation of co-used product data through national survey among large population sample. Global database combined United States and Europe had been utilized for usage patterns of cosmetics and personal care products including 20 co-use combinations (Comiskey et al., 2015; Comiskey et al., 2017). The number of cosmetic products used and the co-use combinations in a 24 h or a 48 h-period was assessed in a cohort of US adult women (Parlett et al., 2013) and Canada pregnant women (Lang et al., 2016). These studies presented the results of individual's co-use patterns, and only mentioned the applicability of co-use patterns to aggregate exposure assessment. Aggregate exposure assessment using actual co-use products combination of individuals was the most accurate and realistic estimation. However, it was difficult to survey every co-use products combination for every aggregate exposure estimation due to resource and cost issues.

An aggregate exposure assessment using co-use scenarios could be useful for chemical risk assessment and management without direct surveys of every c-use product. Our previous study (Lim and Lee, co-submitted) proposed cosmetic co-use scenarios for gender-age population groups based on the Korean representative exposure factor database for 31 cosmetics. The cosmetic co-use scenarios were a combination of cosmetics that could be directly applied to aggregate exposure assessment, and provided population distribution from low (25th percentile) to high (95th) exposures for four different demographic groups. The co-use scenarios with chemical compositions of cosmetics could be estimate the population aggregate exposure of chemicals. Simple summation of the chemical exposure doses to aggregate exposure estimation had the potential of overestimation (Delmaar et al., 2015; Gosens et al., 2014). Considering only the products contained in co-use scenarios to aggregate exposure assessment was more realistic and refined estimation as scenario-based high-tier approach. Receptor-based estimation considering individual’s specific exposure factors and simultaneous usage patterns was the most accurate estimation, and 'gold standard' for the sample population. Validation of the aggregate exposure estimation by the co-use scenario based approach would be possible as comparison with aggregate exposure estimation by the receptor-based approach.

Three phthalates, namely di(2-ethylhexyl)phthalate (DEHP), di-n-butyl phthalate (DnBP) and diethyl phthalate (DEP) were selected as target chemicals for this study. Phthalates was used as solvent, additive, plasticizer, vehicle for fragrance and cosmetic ingredients (Api, 2001; Koniecki et al., 2011; U.S.ATSDR, 2002). Especially for low-molecular-weight phthalate, DnBP and DEP, cosmetics and personal care products were the major exposure sources for human body (Buckley et al., 2012; Duty Susan et al., 2005; Hsieh et al., 2019; Huang et al., 2018; Koch et al., 2013; Romero-Franco et al., 2011). In our earlier study (Lim et al., 2019), the chemical composition of three phthalates and daily mass (g/day) for 31 cosmetics were presented. Aggregate exposure dose (AED) based on co-use scenarios could be estimated combining the cosmetic combinations in the co-use scenario with daily mass and chemical composition for each cosmetic. Lim et al. (2019) calculated receptor-based AED for three phthalates. Therefore, aggregate exposure estimation by co-use could be validated by comparison of the two AED values.

The objectives of this study were 1) to assess aggregate exposure based on co-use scenarios for DEHP, DnBP, and DEP in cosmetics, and 2) to validate the aggregate exposure assessment methodology of co-use scenario by comparing with receptor-based AED.

4.2. Methods

Materials

Lim et al. (2019) described the detailed national representative exposure factor survey and phthalates analysis methodologies. The Korean cosmetic exposure factor database were obtained from home-visit face-to-face surveys of 1,001 individuals over 19 years old. A total of 31 cosmetics were classified into 9 categories (4 skin care, 3 hair care, 4 body care, 3 cleansing, 3 base makeup, 4 eye makeup, 4 lip makeup, 4 nail care, and 2 fragrance products). The daily mass (g/day) for each cosmetic was calculated by multiplying the use frequency (use/day) by the use amount (g/use). The DEHP, DnBP, and DEP concentrations representing 31 cosmetics were analyzed by GC-MS-MS.

Our previous study determined four cosmetic co-use scenarios (scenario 1 for 25th, scenario 2 for 50th, scenario 3 for 75th and scenario 4 for 95th percentiles) for each of the four population groups (19-39 years old young males, 40+ years old senior males, 19-39 years old young females, and 40+ years old senior females). A co-use scenario was proposed using percentile values of the number of cosmetics used and the rank of occurrence frequency in frequent co-use patterns. Each co-use scenario was presented as the number of co-used cosmetics and the cosmetics combination. Within a single population, the co-use scenarios had cumulative property that new cosmetics were added to previous low-percentile co-use scenarios.

Co-use scenario based aggregate exposure assessment

For 19-39 years old males, co-use scenario 1 consisted of 4 cosmetics (skin toner, face lotion, face cleanser, facial sunscreen), scenario 2 consisted of 5 cosmetics (scenario 1 and hair styling), scenario 3 consisted of 6 cosmetics (scenario 2 and hand cream), and scenario 4 consisted of 10 cosmetics (scenario 3 and perfume, body lotion, deodorant, shaving cream). For 40+ years old males, co-use scenario 1 consisted of 3 cosmetics (face lotion, skin toner, face cleanser), scenario 2 consisted of 4 cosmetics (scenario 1 and facial sunscreen), scenario 3 consisted of 5 cosmetics (scenario 2 and body logion), and scenario 4 consisted of 8 cosmetics (scenario 3 and hand cream, hair styling, hair dye). For 19-39 years old females, co-use scenario 1 consisted of 11 cosmetics (skin toner, face lotion, facial sunscreen, body logion, face cleanser, foundation, face cream, hair treatment, hand cream, eyeshadow, lipstick), scenario 2 consisted of 14 cosmetics (scenario 1 and mascara, eyebrow, perfume), scenario 3 consisted of 17 cosmetics (scenario 2 and eyeliner, nail remover, nail polish), and scenario 4 consisted of 21 cosmetics (scenario 3 and pact/powder, lip gloss, shower cologne, deodorant). For 40+ years old females, co-use scenario 1 consisted of 10 cosmetics (skin toner, face lotion, face cream, facial cleanser, lipstick, body lotion, hand cream, foundation, hair treatment), scenario 2 consisted of 12 cosmetics (scenario 1 and eyeshadow, perfume), scenario 3 consisted of 14 cosmetics (scenario 2 and mascara, nail polish), and scenario 4 consisted of 18 cosmetics (scenario 3 and pact/powder, eyeliner, nail remover, eyebrow).

The exposure dose (μg/kg/day) values of cosmetics were calculated from the

Korean representative exposure factor survey results (Lim et al., 2019). Only 24 of the 31 cosmetics in the exposure factor database were used in co-use scenario, and this study only targeted those cosmetics. The exposure dose values of skin toner (n = 907), face lotion (n = 903), face cream (n = 473), facial sunscreen (n = 596), hair dye (n = 171), hair treatment (n = 362), hair styling (n = 195), body lotion (n = 538), hand cream (n = 490), deodorant (n = 69), face cleanser (n = 867), shaving cream (n = 97), foundation (n = 415), pact/powder (n = 167), eyeliner (n = 146), eyeshadow (n = 236), mascara (n = 162), eyebrow (n = 215), lip gloss (n = 88), lipstick (n = 415), nail polish (n = 105), nail remover (n = 112), shower cologne (n = 66), and perfume (n = 277) were calculated using following equation:

$$\mathrm{ED}(\mathrm{\mu g}/kg/day) = \frac{C_i(\mu g/g) \times f_i(use/day) \times q_i(g/use) \times RF_i}{BW\ (kg)}$$

where C_i is the maximum phthalates concentration in these cosmetic products (μg/g), f_i is the frequency of cosmetic use (use/day), q_i is the amount of cosmetic use (g/use), RF_i is the retention factor on the skin (unitless), and BW is the body weight (kg). The use frequency (f_i) and use amount (q_i) of each product were obtained from the survey results. The values of C_i used for DEHP, DnBP, and DEP were the maximum value for each cosmetic product. The value of RF was 1 for leave-on cosmetic products and 0.01 for wash-off cleanser products, face cleanser and shaving foam (SCCS, 2015). The BW value used in the calculation was taken from the survey respondent's actual questionnaire answer.

Co-use scenario based AEDs were calculated by Monte Carlo simulations as a probabilistic approach. Probability distributions were assumed by Anderson-Darling goodness-of-fit tests for the exposure doses of each 24 cosmetics used in the co-use scenarios for DEHP, DnBP and DEP. The aggregate exposures were calculated by summing through 10,000 repeated sampling from cosmetic exposure dose distributions for DEHP, DnBP, and DEP. The contribution of cosmetics was derived by sensitivity analysis. All simulations and analyses were conducted using Oracle Crystal Ball (Oracle Corporation, Redwood Shores, CA, USA).

Comparison of co-use scenario based AED and receptor-based AED

For validation of co-use scenario based aggregate exposure estimation, probabilistic estimated co-use scenario based AED was compared with the distribution of receptor-based AEDs in each population group. The receptor-based AED (Lim et al., 2019) was calculated from each individual's simultaneous cosmetic usage exposure factor database for 19-39 years old young males (n = 205), 40+ years old senior males (n = 304), 19-39 years old young females (n = 191), and 40+ years old senior females (n = 301). Both receptor-based and co-use scenario based AEDs were calculated from the same exposure factor databases (Lim et al., 2019), and phthalates concentration for each product were taken from the maximum value of the analytical results. The co-use scenario based AED was compared with 25th, 50th, 75th, and 95th percentile of DEHP, DnBP, and DEP exposure levels of population groups.

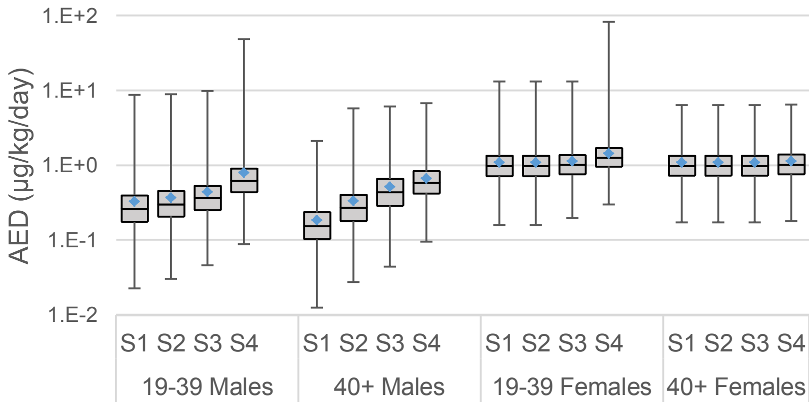
4.3. Results

Co-use scenario based aggregate exposure assessment

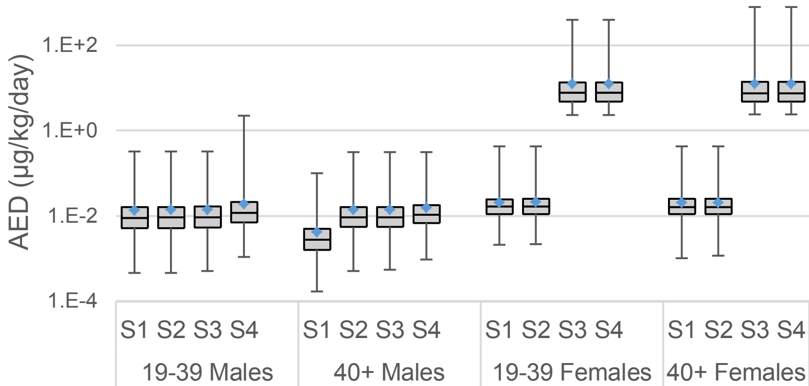
Figure 4-1 shows the distribution of co-use scenario based AED values (μg/kg/day) estimated by probabilistic simulation of the three phthalates. For all three phthalates, the averages of the co-use scenario based AED was increased by increased number of co-use scenarios. The more cosmetics were, the higher number of the co-use scenario.

For DEHP, the averages of co-use scenario based AED were higher than 1 μg/kg/day for females and lower than 1 μg/kg/day for males in all scenarios. The maximum values of DEHP's AED increased considerably from co-use scenario 3 to scenario 4 in 19-39 years old males and 19-39 years old females. For DnBP, the average values of co-use scenario based AED were higher than 10 μg/kg/day for scenarios 3 and 4 of females and lower than 1 μg/kg/day in all males and scenarios 1 and 2 of females. The differences were more than two orders of magnitude. For DEP, the average values of co-use scenario based AED were higher than 1 μg/kg/day in scenario 2, 3, and 4 of 19-39 years old males and all females. The averages of scenario 1 for 19-39 years old males and scenarios 2, 3 and 4 for 40+ years old males were lower than 0.001 μg/kg/day. The maximum value of DEP's AED was calculated in scenario 4 of 40+ years old males.

(a)



(b)



(c)

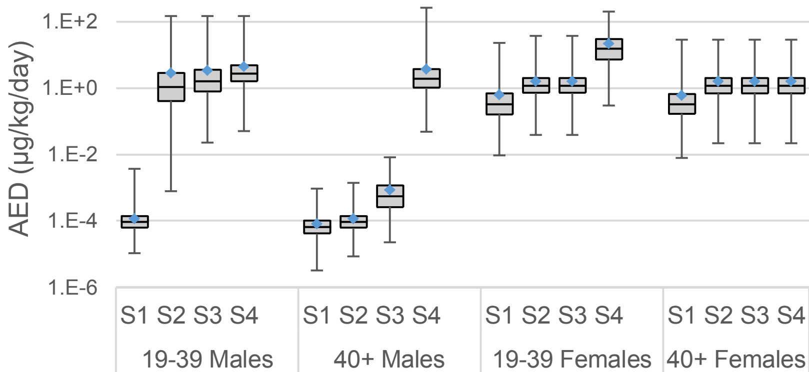


Figure 4-1. Probabilistic aggregate estimation based on co- use scenarios (a) DEHP, (b) DnBP, and (c) DEP. The horizontal lines showed the median, the boxes showed the quartiles, the whisker caps showed the minimum and maximum values, and blue diamond showed average values.

Product contribution

Table 4-1 shows the contribution of cosmetics for co-use scenario based AED values to DEHP, DnBP, and DEP. The contribution was based in scenario 4 of each population group. Cosmetic contributions in co-use scenarios 1, 2, and 3 are shown in Table S1-S3. The important cosmetics for male groups were body lotion and facial sunscreen for DEHP, facial sunscreen and skin toner for DnBP, and hair styling and perfume for DEP. The important cosmetics for female groups were face cream and body lotion for DEHP, nail polish for DnBP. The import cosmetics of DEP exposure was shower cologne for 19-39 years old females, and perfume for 40+ years old females. Nail polish was a major contributor with 99.8% for DnBP aggregate exposures in female groups. Shower cologne was a major contributor with 98.9% for DEP aggregate exposures in 19-39 years old females. Perfume (69.9%) and hand cream (29.2%) had high contribution for DEP exposure in 40+ years old females.

Table 4-1. Contribution of cosmetics and rank correlation for DEHP, DnBP, DEP aggregate exposure estimations about co-use scenario 4 by each population group.

(a) 19-39 Males

	DEHP	DBP	DEP
FT	2.2%	16.5%	0.0%
FL	11.1%	0.2%	0.0%
FS	21.2%	69.1%	0.0%
HS	3.1%	0.1%	75.2%
BB	39.4%	0.0%	0.0%
BH	5.7%	0.1%	7.6%
BD	16.4%	13.8%	0.0%
CF	0.6%	0.1%	0.1%
CS	0.2%	0.1%	0.0%
RP	0.0%	0.0%	17.1%

(b) 40+ Males

	DEHP	DBP	DEP
FT	13.0%	19.2%	0.0%
FL	3.7%	0.0%	0.0%
FS	24.9%	77.1%	0.0%
HD	2.7%	3.5%	1.0%
HS	3.5%	0.0%	88.5%
BB	44.3%	0.0%	0.0%
BH	7.4%	0.0%	10.5%
CF	0.6%	0.0%	0.0%

RP	0.0%	0.0%	0.7%

(c) 19-39 Females

	DEHP	DBP	DEP
FT	0.7%	0.0%	0.0%
FL	4.0%	0.0%	0.0%
FC	48.8%	0.0%	0.0%
FS	9.5%	0.0%	0.0%
HT	0.1%	0.0%	0.0%
BB	14.9%	0.0%	0.0%
BH	1.9%	0.0%	0.2%
BD	8.1%	0.0%	0.0%
CF	0.2%	0.0%	0.0%
MF	1.6%	0.0%	0.0%
MP	0.0%	0.0%	0.0%
EL	0.0%	0.0%	0.0%
ES	0.0%	0.0%	0.0%
EM	0.0%	0.0%	0.0%
EB	0.0%	0.0%	0.0%
LG	0.0%	0.0%	0.0%
LS	0.0%	0.0%	0.0%
NP	0.0%	99.8%	0.1%
NR	0.4%	0.0%	0.0%
RC	9.6%	0.0%	98.9%

(d) 40+ Females

	DEHP	DBP	DEP
FT	1.2%	0.0%	0.0%
FL	4.4%	0.0%	0.0%
FC	58.1%	0.0%	0.0%
FS	10.4%	0.0%	0.0%
HT	0.1%	0.0%	0.7%
BB	19.2%	0.0%	0.0%
BH	3.2%	0.0%	29.2%
CF	0.1%	0.0%	0.0%
MF	2.6%	0.0%	0.1%
MP	0.0%	0.0%	0.0%
EL	0.0%	0.0%	0.0%
ES	0.0%	0.0%	0.0%
EM	0.0%	0.0%	0.0%
EB	0.0%	0.0%	0.0%
LS	0.0%	0.0%	0.0%
NP	0.0%	99.8%	0.0%
NR	0.6%	0.0%	0.0%
RP	0.0%	0.0%	69.9%

* The cosmetics were abbreviated as follows: FT, skin toner; FL, face lotion; FC, face cream; FS, facial sunscreen; HD, hair dye; HT, hair treatment; HS, hair styling; BB, body lotion; BH, hand cream; BD, deodorant; CF, face cleanser; CS, shaving cream; MF, foundation; MP, pact/powder; EL, eyeliner; ES, eyeshadow; EM, mascara; EB, eyebrow; LG, lip gloss; LS, lipstick; NP, nail polish; NR, nail remover; RC, shower cologne; RP, perfume.

Comparison of co-use scenario based AED to receptor-based AED

Figure 4-2, Figure 4-3 and Figure 4-4 compares AED values determined by co-use scenario method and receptor-based method for three phthalates in different population groups for DEHP, DnBP, and DEP, respectively. For DEHP, all differences of AED using co-use scenario and receptor-based was lower than one order magnitude. The AEDs estimated by co-use scenario 1 (P25, AED_{c1}) and scenario 2 (P50, AED_{c2}) were higher than receptor-based AEDs (AED_r) in the entire population. The AEDs estimated by using co-use scenario 3 (P75, AED_{c3}) and co-use scenario 4 (P95, AED_{c4}) was higher than AED_r in the male groups, and lower than AED_r in the female groups.

For DnBP, most differences of AED using co-use scenario and receptor-based was lower than one order magnitude except scenario 3 for 40+ years old females. The AED_{c1} were higher than AED_r in the entire population. The AED_{c2} were higher than AED_r in the three population except 19-39 years old females. The AED_{c3} were higher than AED_r in the entire population. The AED_{c4} were higher than AED_r in the male groups, and lower than AED_r in the female groups.

For DEP, most differences of AED using co-use scenario and receptor-based was lower than one order magnitude except scenario 3 for 40+ years old males. The AED_{c1} were higher than AED_r in the entire population. The AED_{c2} were higher than AED_r in the three population except 40+ years old males. The AED_{c3} were lower than AED_r in the three population except 19-39 years old males. The AED_{c4} were lower than AED_r in the three population except 40+ years old males.

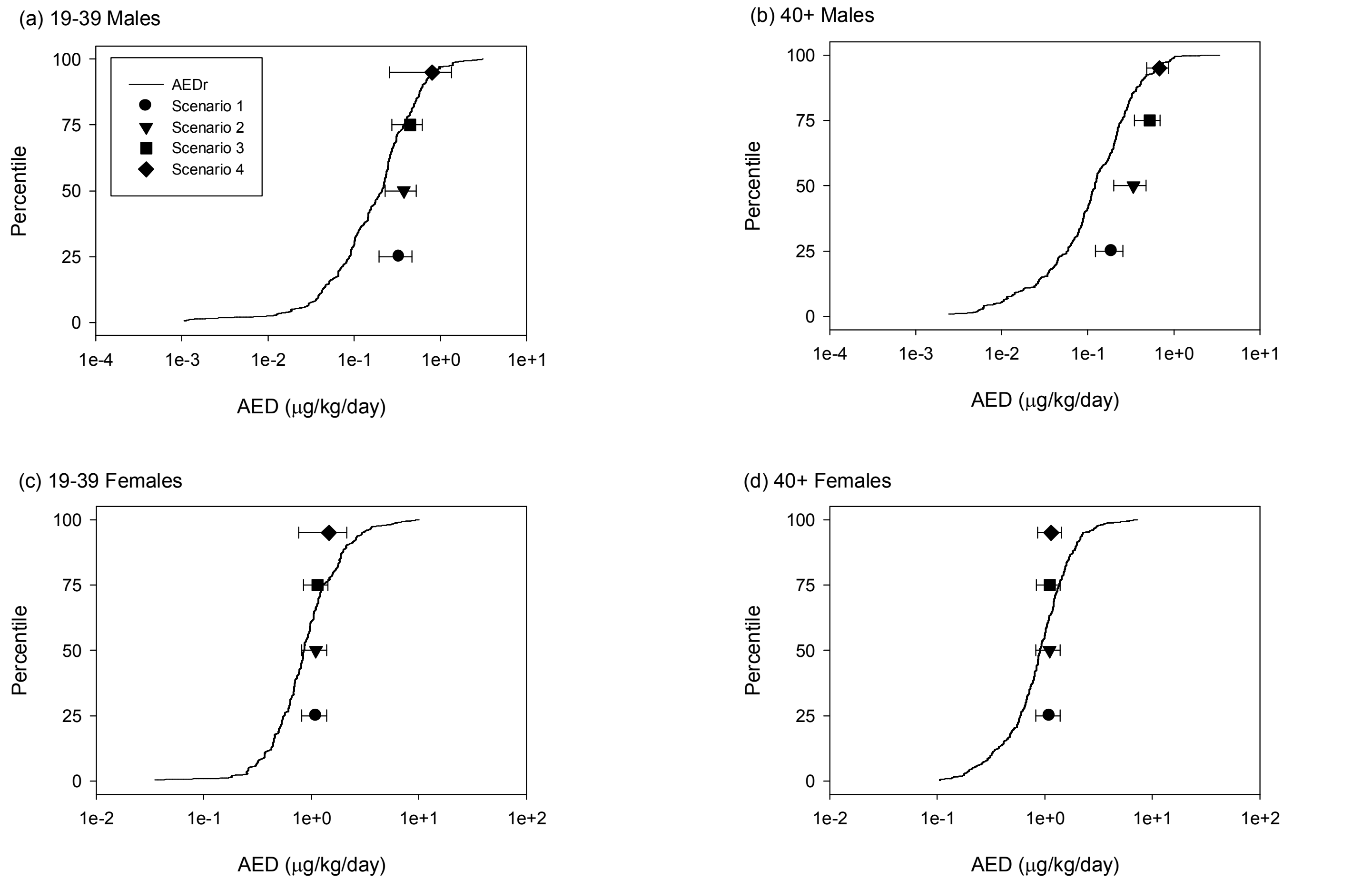


Figure 4-2. Comparison of co-use scenario based aggregate exposure estimation and receptor-based aggregate exposure estimation of (a) 19-39 years old males, (b) 40+ years old males, (c) 19-39 years old females, and (d) 40+ years old females for DEHP. The line shows receptor-based AED, dot and error bar shows the average and standard deviation of co-use scenario based AED for scenario 1 (P25), scenario 2 (P50), scenario 3 (P75) and scenario 4 (P95).

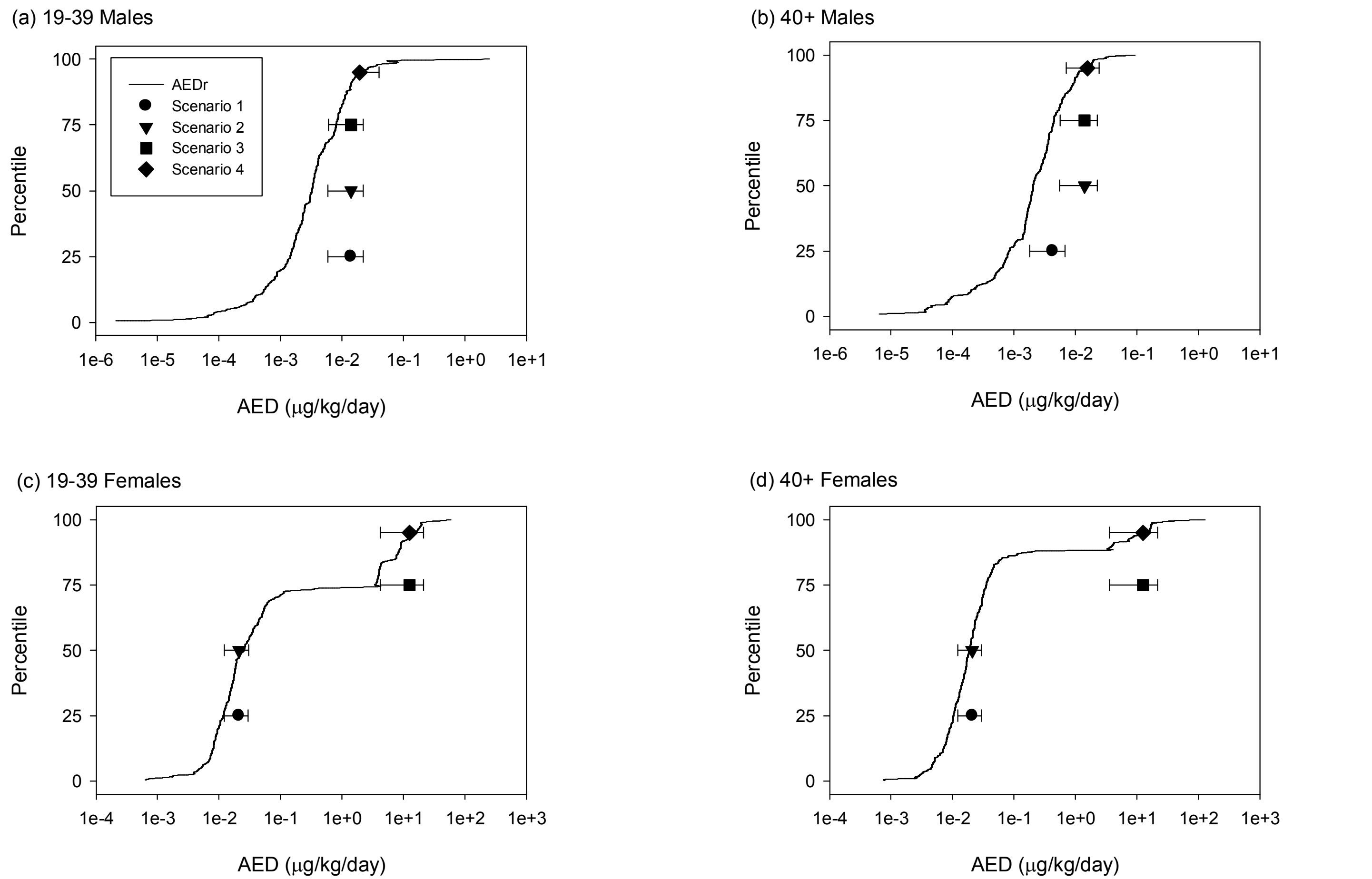


Figure 4-3. Comparison of co-use scenario based aggregate exposure estimation and receptor-based aggregate exposure estimation of (a) 19-39 years old males, (b) 40+ years old males, (c) 19-39 years old females, and (d) 40+ years old females for DnBP. The line shows receptor-based AED, dot and error bar shows the average and standard deviation of co-use scenario based AED for scenario 1 (P25), scenario 2 (P50), scenario 3 (P75) and scenario 4 (P95).

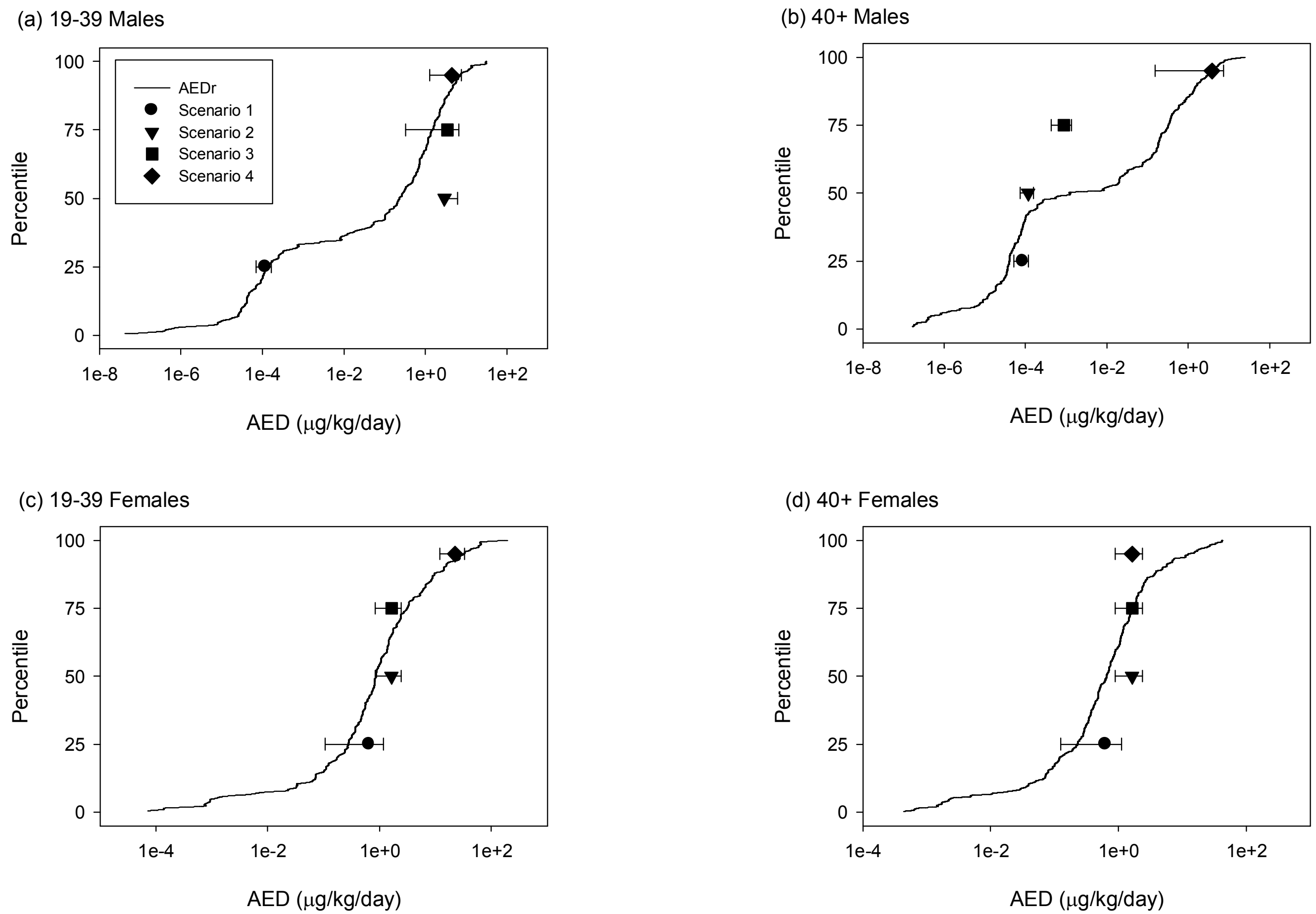


Figure 4-4. Comparison of co-use scenario based aggregate exposure estimation and receptor-based aggregate exposure estimation of (a) 19-39 years old males, (b) 40+ years old males, (c) 19-39 years old females, and (d) 40+ years old females for DEP. The line shows receptor-based AED, dot and error bar shows the average and standard deviation of co-use scenario based AED for scenario 1 (P25), scenario 2 (P50), scenario 3 (P75) and scenario 4 (P95).

4.4. Discussion

Co-use scenario based aggregate exposure assessment

The aggregate exposure assessment of three phthalates in cosmetics based on co-use scenarios were performed in probabilistic approach. The AEDs of females were higher than those of males. Females used more cosmetics than males. Makeup products were mainly used by females. The AEDs of young population were higher than those of senior population. The young population used more cosmetics than senior population within the same gender.

The major contributing cosmetics to aggregate exposure were different by phthalates. Body lotion was the major contributor of the DEHP's aggregate exposure in all population groups. Face cream was the major contributor of the DEHP's aggregate exposure only in the females. Nail polish contributed to the DnBP's aggregate exposure by more than 99% in 75th and 95th percentiles of females. The DnBP concentration of nail polish was overwhelmingly high (Lim et al., 2019). DnBP was a substance added for the purpose of the binder to improve the persistence of nail polish. The DEP's AED values were similarly estimated for 95th percentile of males and females. However, major contributing cosmetics were different by gender. Hair styling products contributed to the DEP's aggregate exposure only in males. Hair styling products were included only in male's co-use scenarios and not in female's co-use scenarios. For females, shower cologne was the major contributor of DEP's aggregate exposure. The DEP concentration in shower cologne was 9.63 times higher than hair styling product (Lim et al., 2019).

Although hair styling product had a lower DEP concentration, their use frequency and use amount in males were much higher.

Comparison of co-use scenario based AED and receptor-based AED

This study proposed a novel method of aggregate exposure assessment based on co-use scenario. The aggregate exposure estimation by the co-use scenario was validated by comparison with the receptor-based aggregate exposure assessment. Receptor-based aggregate exposure assessment was the highest tier approach because individual's actual product usage patterns were considered. In this study, receptor-based AED was considered as 'true value' for the validation of co-use scenario based aggregate exposure assessment.

The receptor-based AED distribution curve for DEHP showed a relatively modest increase. DEHP's aggregate exposure did not show the effect of any one specific cosmetic. The receptor-based AED distribution curve for DnBP showed a sharp increase near the 75th percentile for 19-39 years old females and 85th percentile for 40+ years old females. It was due to the nail polish user. The use rates of nail polish were 28.8% for 19-39 years old females and 16.3% for 40+ years old females (Lim et al., 2019). The receptor-based AED distribution curve for DEP showed a clear increase near the 35th percentile for 19-39 years old males. It was due to the hair styling product user. The use rate of hair styling product was 38.0% for 19-39 years old males (Lim et al., 2019).

The AEDs based on co-use scenario showed similar trends to the receptor-based AED distribution. The increase of DnBP's AED in 75th percentile for 19-39 years old females by nail polish was similar to the distribution of receptor-based

AED. The increase in DEP' AED in 50th percentile for 19-39 years old males by shower cologne was similar to the distribution of receptor-based AED. The receptor-based AEDs were within one standard deviation of the mean AED by the co-use scenario, in the 7 of 16 scenarios for DEHP, 7 of 16 scenarios for DnBP, and 9 of 16 scenarios for DEP. The AEDs based on co-use scenario values were slightly higher than receptor-based AED values at 25th, 50th, and 75th percentiles of population groups. For most cases, the AED differences were less than one order of magnitude.

The tier of exposure assessment could be classified by the amount of resources used in the assessment. High tier approach was recommended for refined and realistic estimation. Realistic aggregate exposure estimation required a big database of exposure factors. While the aggregate exposure assessment using co-use scenarios used less resources than receptor-based aggregate exposure assessment, co-use scenario AEDs were similar to receptor-based AEDs. Especially at 95th percentiles of the entire population, co-use scenario based AED values were similar or slightly lower than receptor-based AED values. Risk assessment and management were mainly conducted for high exposure (95th percentile) group. When exposure factor information is limited, aggregate exposure assessment using co-use scenarios can provide reasonable aggregate exposure. In addition, the aggregate exposure assessment using co-use scenarios could identify a product with a high contribution among limited cosmetics.

Need of more accurate aggregate exposure assessment

This study estimated aggregate exposure of phthalates in cosmetics. The aggregate exposure estimates might not be close to 'true value'. The exposure algorithm of cosmetics used in this study was consisted of (1) chemical concentration, (2) use frequency, (3) use amount, (4) retention factor, and (5) body weight. For calculating the exposure dose of cosmetics, chemical concentration and retention factor were used as fixed values, and use frequency, use amount and body weight used as distributions from individual's survey responses. This study fixed phthalate concentrations at the maximum value assuming worst-case assumption.

The parameter uncertainty accounted for a large part of the total uncertainty (U.S. EPA, 1992, 1997) in the co-use scenario based aggregate exposure assessment, rather than the scenario uncertainty and model uncertainty. Uncertainty due to the survey results was a minor contribution in aggregate exposure assessment compared with other parameters in the previous study (Gosens et al., 2014). There was unevaluable uncertainty due to the concentration of phthalates in cosmetics. The uncertainty of phthalate concentrations might be considered by using phthalate concentration as a probability distribution.

In this study, the external dose of phthalates was calculated using the exposure scenarios. Since the dermal absorption rate of three phthalates were assumed to be 100%, internal dose was not estimated. Delmaar et al (2015) conducted a validation of aggregate exposure model for DEP in personal care products compared to doses from urinary level of biomonitoring studies. Internal dose of DEP was calculated by considering skin permeability, which had largest uncertainty for exposure model. In addition, the internal doses included other exposure sources than cosmetics. It could be considered other consumer products, diet, and environment even though low-molecular weight phthalates. Therefore, validation of AED values using co-use scenarios with biomarker level was not possible at this stage. Further study might evaluate co-use scenario based aggregate exposure assessment methodology by comparing AED levels with biomarker levels, considering dermal absorption rate and other exposure sources.

Limitations

The co-use scenario used in this study was derived from the Korean national representative exposure factor database for cosmetics. Without a big database, neither co-use scenario based AED nor receptor-based AED could be estimated. Further research was needed on how to determine co-use scenario simply without national representative survey. It was necessary to confirm that the same co-use scenario was derived from simple usage survey rather than comprehensive exposure factor survey. It would also be applied to other populations or other consumer products to verify the versatility of aggregate exposure assessment using co-use scenario method.

4.5. Conclusions

The co-use scenario based aggregate exposure assessment for three phthalates in cosmetics were performed by probabilistic approach. The co-use scenario AEDs were slightly higher than receptor-based AEDs at 25, 50, and 75th percentiles of population, and slightly lower that at 95th percentile. Since co-use scenario based aggregate exposure assessment required relatively less resources, it could be useful as an alternate method of receptor based aggregate exposure assessment.

Chapter V.

Summary and Conclusions

Chemicals causing adverse health effects should be managed by risk. Traditional chemical exposure and risk assessments were often limited to a single exposure source. For a realistic exposure assessment of chemical, aggregate assessment of a chemical across multiple exposure sources should be considered. Even if exposure from a single source was under a safe level, it was possible that total exposure from multiple sources could not be a safe level.

For aggregate exposure assessment to consumer products, it was necessary to consider simultaneously co-used products. Two aggregate exposure assessment approaches for consumer products were utilized and they were product-based and receptor-based approaches. The product-based approach estimated aggregate exposure as a sum of exposures from all consumer products. The receptor-based approach estimated aggregate exposure as a sum of each individual's actual used product exposure. Higher tier of aggregate exposure assessment required big database through large scale and comprehensive exposure factor survey.

The objective of this study was to develop a middle tier aggregate exposure assessment methodology based on co-use scenarios of multiple consumer products. Conducting aggregate exposure assessment using co-use scenario needed less exposure factor resources, nevertheless refined estimation rather than product-based approach. The target consumer products were cosmetic products, and the target chemicals were three of phthalates, that is, DEHP, DnBP, and DEP. The Korean national representative exposure factor database to 31 cosmetics were utilized.

The first study estimated aggregate exposures to phthalates through cosmetics by receptor-based and product-based approaches. The exposure factors for 31 cosmetic products were collected by face-to-face interviews with 1,001 members of the Korean population through national representative sampling. The concentrations of phthalates in 214 cosmetic products were analyzed by GC-MS-MS. The receptor-based aggregate exposure could be more realistic estimation. However, this method required significant data of individual's simultaneous cosmetics usage pattern. Product-based aggregate exposures significantly overestimated, especially in 95th percentiles of product-based aggregate exposures for DnBP and DEP. Although product-based aggregate exposure could be conducted with minimal information, it could significantly overestimate aggregate exposure.

The second study characterized co-use patterns of cosmetics and determined the co-use scenarios for gender-age population groups. The co-use patterns of cosmetics should be critical for accurate aggregate exposure assessment. The Korean national representative exposure factor database was used to analyze the co-use patterns of cosmetics. The use or non-use of 31 cosmetics was treated as a categorical variable. Three analytical methods were applied to determine the co-use patterns: 1) Cohen's kappa coefficient, 2) Hierarchical clustering analysis and 3) Frequent pattern mining. In addition to the three analytical methods, a co-use scenario was proposed using the rank of frequency of occurrence in co-use patterns and percentile values of the distribution of the number of used cosmetics. The 16 co-use scenarios for the 31 cosmetics were determined to the 25, 50, 75, and 95th percentiles of the distribution of four gender-age population groups. The co-use scenarios were applied for aggregate exposure assessment in the third study.

In the third study, co-use scenario based aggregate exposure assessment were performed and validated by comparison with receptor-based AED for three phthalates in cosmetics. The aggregate exposure was estimated for DEHP, DnBP, and DEP of 16 co-use scenarios by probabilistic approach. The most contributing cosmetics to co-use scenario based AED were determined by sensitivity analysis. The aggregate exposure using co-use scenarios was similar to the result of the receptor-based AED. The AEDs by co-use scenario were slightly overestimated below 75th percentiles of population, and underestimated at 95th percentiles. Aggregate exposure assessment using co-use scenarios could simplify assessments with specific product information in large datasets.

We proposed and evaluated co-use scenario based aggregate exposure estimations. The co-use scenario could be useful for aggregate exposure assessment with less exposure factor information. It could be easier to identify the main contributor among cosmetics. When new cosmetics were included in the co-use scenarios, impact of the new cosmetics could be determined.

The aggregate exposure assessment in this study might not be realistic value, since all assessments used maximum concentration as fixed value for each product. The values would have influenced the AED estimation for DnBP and DEP, because the DnBP in the nail care products and the DEP in the fragrance products were extremely high. The skin retention factor and absorption factor were determined conservatively. Nevertheless, it did not affect the validation of co-use scenario aggregate exposure assessment method since concentration value was equal to both co-use scenario method and receptor-based method.

Important implication of this study was the characteristics of high exposure groups. Aggregate DEHP exposures were similar for the three methods. However, aggregate DnBP and DEP exposures were different. In high exposure populations, aggregate DnBP and DEP exposures by receptor-based method were much higher than those by product-based estimation and slightly higher than the co-use scenario based estimates. General concept was that receptor-based estimates was lower than product-based estimates. However, this study identified the opposite outcome in DnBP and DEP. Therefore, receptor-based method was more suitable for aggregate exposure assessment of high-exposure populations. If comprehensive database of exposure factors was not available, co-use based aggregate exposure could provide reasonable estimate of aggregate exposure of high exposure group.

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Supplements

Table S-1. Multiple reaction monitoring (MRM) transitions for the measurement of phthalates with GC/MS/MS.

Compounds	Precursor ions (m/z)	Production ions (m/z)
DEP	149.2	65.0
DnBP	149.2	65.0
DEHP	279.4	149.0
d4-DEP	153.2	69.1
d4-DnBP	153.2	69.1
d4-DEHP	153.2	69.0

Table S-2. The use rates (%) of cosmetic products by gender and age group.

Products	Overall	Female					Male				
		19-29	30-39	40-49	50-59	60+	19-29	30-39	40-49	50-59	60+
	N	93	98	115	112	74	102	103	118	114	72
Skincare											
Skin toner	90.6	96.8	96.9	98.3	100.0	94.6	83.3	82.5	84.7	83.3	86.1
Lotion	90.2	88.2	92.9	96.5	99.1	100.0	79.4	93.2	85.6	82.5	86.1
Cream	47.3	83.9	88.8	97.4	98.2	97.3	5.9	3.9	0.8	1.8	1.4
Face sunscreen	59.5	90.3	81.6	93.0	90.2	77.0	40.2	38.8	28.0	31.6	23.6
Hair care											
Hair dye	17.1	12.9	10.2	15.7	32.1	37.8	4.9	8.7	7.6	19.3	30.6
Hair treatment	36.2	72.0	69.4	69.6	64.3	52.7	7.8	10.7	8.5	5.3	1.4
Hair styling	19.5	10.8	16.3	13.0	14.3	24.3	36.3	39.8	19.5	14.0	4.2
Body care											
Body lotion	53.7	78.5	81.6	82.6	86.6	77.0	31.4	35.9	25.4	22.8	15.3
Hand cream	49.0	71.0	75.5	76.5	73.2	70.3	24.5	29.1	24.6	19.3	30.6
Deodorant	6.9	25.8	6.1	4.3	0.9	0.0	14.7	12.6	3.4	0.9	0.0
Body sunscreen	12.1	20.4	17.3	18.3	11.6	8.1	7.8	8.7	11.0	8.8	6.9
Cleanser											
Hand wash	18.0	21.5	38.8	27.8	17.9	10.8	16.7	12.6	15.3	9.6	4.2
Face cleanser	86.6	100.0	98.0	97.4	99.1	97.3	86.3	79.6	71.2	70.2	68.1
Shaving cream	9.7	0.0	0.0	0.0	0.0	0.0	24.5	22.3	19.5	14.9	12.5
Base makeup											
Foundation	41.5	82.8	81.6	84.3	86.6	82.4	1.0	1.9	0.0	0.0	0.0

Products	Overall	Female					Male				
		19-29	30-39	40-49	50-59	60+	19-29	30-39	40-49	50-59	60+
	N	93	98	115	112	74	102	103	118	114	72
Makeup base/Primer	4.6	9.7	4.1	8.7	10.7	14.9	0.0	0.0	0.0	0.0	0.0
Fact/Powder	16.7	28.0	33.7	37.4	27.7	44.6	1.0	0.0	0.0	0.0	0.0
Eye makeup											
Eyeliner	14.6	67.7	30.6	26.1	17.9	4.1	0.0	0.0	0.0	0.0	0.0
Eyeshadow	23.6	67.7	53.1	48.7	38.4	29.7	0.0	0.0	0.0	0.0	0.0
Mascara	16.2	62.4	38.8	29.6	25.0	5.4	0.0	0.0	0.0	0.0	0.0
Eyebrow	21.5	62.4	43.9	41.7	33.9	35.1	1.0	0.0	0.0	0.0	1.4
Lip makeup											
Lip balm	8.2	41.9	15.3	6.1	2.7	4.1	3.9	3.9	3.4	1.8	1.4
Tint	7.4	57.0	7.1	6.1	3.6	2.7	0.0	1.0	0.0	0.0	0.0
Lip gloss	8.8	19.4	26.5	27.0	6.3	8.1	0.0	0.0	0.0	0.0	0.0
Lipstick	41.5	61.3	80.6	89.6	94.6	94.6	0.0	0.0	0.0	0.0	0.0
Nail care											
Nail polish	10.5	29.0	28.6	18.3	19.6	8.1	0.0	1.0	0.0	0.0	0.0
Gel nail polish	3.7	10.8	16.3	7.0	2.7	0.0	0.0	0.0	0.0	0.0	0.0
Nail strengthener	2.7	9.7	6.1	7.0	1.8	1.4	0.0	1.0	0.0	0.0	0.0
Nail remover	11.2	31.2	31.6	20.9	19.6	8.1	0.0	0.0	0.0	0.0	0.0
Fragrance											
Shower cologne	6.6	22.6	9.2	9.6	7.1	8.1	2.9	2.9	4.2	0.0	0.0
Perfume	27.7	43.0	49.0	39.1	26.8	20.3	29.4	32.0	16.1	12.3	4.2

Table S-3. Use frequency and use amount by sub product types.

Products	Sub product types	Use frequency (use/day)					Use amount (g/use)				
		Mean	SD*	P50	P75**	P95**	Mean	SD*	P50	P75**	P95**
Skincare											
Skin toner	Liquid	1.92	0.34	2.00	2.00	2.00	0.47	0.51	0.36	0.36	1.06
	2nd liquid	1.48	0.82	2.00	2.00	2.00	0.32	0.34	0.15	0.36	1.06
	3rd liquid	2.00		2.00			0.15		0.15		
	Gel	2.08	1.05	2.00	2.00	3.00	0.58	0.45	0.30	0.85	1.86
	Aerosol spray	2.47	2.07	2.00	2.00	5.00	2.39	0.74	2.06	3.10	3.44
	Pump spray	1.87	1.00	2.00	2.00	3.25	0.50	0.26	0.47	0.66	0.93
	Men’s skin toner	1.76	0.49	2.00	2.00	2.00	0.37	0.29	0.21	0.43	1.15
	Aftershave	1.00	0.00	1.00			0.21	0.00	0.21		
Face lotion	Lotion	1.90	0.38	2.00	2.00	2.00	0.44	0.42	0.43	0.43	1.11
	2nd lotion	1.72	0.55	2.00	2.00	2.00	0.26	0.16	0.20	0.43	0.43
	3rd lotion	1.51	0.68	2.00			0.20	0.00	0.20		
	Men’s lotion	1.71	0.51	2.00	2.00	2.00	0.61	0.55	0.30	0.80	2.11
Face cream	Cream	1.71	0.52	2.00	2.00	2.00	0.68	0.55	0.72	0.72	1.52
	2nd cream	1.47	0.65	2.00	2.00	2.00	0.61	0.58	0.34	0.72	1.44
	3rd cream	1.00	0.00	1.00			0.73	0.56	0.53		
	Eye cream	1.50	0.63	2.00	2.00	2.00	0.25	0.31	0.21	0.21	1.20
Face sunscreen	Lotion	1.13	0.70	1.00	1.00	2.00	0.75	1.00	0.60	0.60	2.75
	Cream	1.21	1.03	1.00	1.00	3.00	0.42	0.56	0.31	0.31	1.74
	Balm/solid	0.89	0.49	1.00			0.02	0.01	0.01		

Products	Sub product types	Use frequency (use/day)					Use amount (g/use)				
		Mean	SD*	P50	P75**	P95**	Mean	SD*	P50	P75**	P95**
Hair care											
Hair dye	Bubble	0.01	0.01	0.01	0.02	0.03	89.7	23.9	100.7	100.7	100.7
	Cream	0.02	0.02	0.02	0.03	0.07	47.6	21.9	65.5	65.5	65.5
	Powder	0.02	0.02	0.01			100.0	50.0	100.0		
Hair treatment	Lotion	0.84	0.59	1.00	1.00	1.00	0.51	0.48	0.43	0.43	1.79
	Pump spray	0.90	0.53	1.00	1.00	1.00	0.95	0.36	1.04	1.30	1.50
Hair styling	Gel	0.74	0.45	1.00	1.00	1.00	0.81	1.31	0.58	0.58	1.54
	Wax	0.76	0.81	0.71	1.00	1.05	1.19	0.91	1.02	1.02	2.74
	Aerosol spray	0.85	1.48	0.71	1.00	1.00	1.90	1.50	1.80	2.40	3.00
Body care											
Body lotion	Lotion	0.82	0.70	1.00	1.00	2.00	2.14	2.24	1.52	3.23	6.47
	Oil	0.62	0.51	0.43	1.00	1.70	0.72	0.79	0.78	1.05	2.24
Hand cream		1.61	1.44	1.00	2.00	4.00	0.73	0.53	0.53	0.82	2.15
Deodorant	Roll-on	0.61	0.50	0.57	1.00	1.00	0.12	0.07	0.09	0.15	0.31
	Stick	0.51	0.61	0.29	0.86	1.00	0.08	0.05	0.06	0.15	0.15
	Aerosol spray	0.44	0.36	0.29	0.68	1.00	3.34	2.91	2.31	3.85	5.93
Body sunscreen	Cream	0.54	0.62	0.29	1.00	2.00	0.77	0.58	0.41	0.94	2.08
	Roll-on/stick	0.65	1.09	0.29	0.86	1.95	0.01	0.01	0.01	0.01	0.02
	Aerosol spray	0.22	0.26	0.12	0.32	0.59	5.79	4.29	5.03	6.54	10.57
	Pump spray	0.43					0.93				
Cleanser											
Hand wash	Bubble	1.84	1.90	1.00	3.00	5.00	0.18	0.15	0.18	0.18	0.35
	Gel	1.52	3.74	0.43	2.00	3.00	0.29	0.42	0.21	0.30	0.58

Products	Sub product types	Use frequency (use/day)					Use amount (g/use)				
		Mean	SD*	P50	P75**	P95**	Mean	SD*	P50	P75**	P95**
	Soap	1.91	1.03	2.00	3.00	3.00	0.50	0.27	0.46	0.60	0.92
Face cleanser	Foam	1.48	0.62	1.00	2.00	2.00	1.13	0.99	1.15	1.15	2.52
	Bubble	1.42	0.73	1.00	2.00	2.00	0.45	0.40	0.32	0.69	1.43
	Oil	0.92	0.50	1.00	1.00	2.00	0.39	0.38	0.26	0.68	1.32
	Water	1.22	0.96	1.00	1.00	2.85	0.60	0.61	0.35	0.80	1.85
	Cream	0.91	0.39	1.00	1.00	1.55	0.71	0.70	0.51	1.18	2.19
	Lip-and-eye remover	0.89	0.43	1.00	1.00	1.80	0.20	0.27	0.08	0.15	0.87
	Tissue	0.92	1.02	0.71	1.00	2.55	4.49	1.60	5.41	5.41	6.89
	Soap	2.28	1.62	2.00	2.00	5.55	0.33	0.23	0.25	0.50	0.75
	Powder	2.52	2.26	2.00			0.23	0.00	0.23		
Shaving cream		0.85	1.06	0.71	1.00	2.00	2.39	1.76	2.32	4.24	4.24
Base makeup											
Foundation	BB/CC cream	0.97	0.67	1.00	1.00	1.20	0.30	0.23	0.19	0.59	0.59
	Liquid foundation	0.88	0.43	1.00	1.00	1.00	0.21	0.14	0.17	0.17	0.40
	Cushion foundation	1.30	0.98	1.00	2.00	3.00	0.17[a]				
Makeup base/Primer		0.82	0.34	1.00	1.00	1.00					
Fact/Powder		1.13	0.93	1.00	1.00	2.00	0.045[a]				
Eye makeup											
Eyeliner		0.83	0.51	1.00	1.00	1.00	0.007[a]				
Eyeshadow		0.74	0.51	0.79	1.00	1.00	0.007[a]				
Mascara		0.70	0.43	0.71	1.00	1.00	0.016[a]				
Eyebrow		0.88	0.37	1.00	1.00	1.00	0.003[a]				

Products	Sub product types	Use frequency (use/day)					Use amount (g/use)				
		Mean	SD*	P50	P75**	P95**	Mean	SD*	P50	P75**	P95**
Lip makeup											
Lip balm		2.26	2.70	2.00	3.00	6.00	0.011 [a]				
Tint		2.33	2.62	2.00	3.00	5.00	0.006 [a]				
Lip gloss		1.33	1.06	1.00	2.00	3.00	0.006 [a]				
Lipstick	Stick	1.70	1.12	2.00	2.00	3.00	0.006 [a]				
	Pencil	1.23	0.73	1.00			0.006 [a]				
Nail care											
Nail polish		0.10	0.12	0.07	0.14	0.25	0.15 [a]				
Gel nail polish		0.05	0.04	0.03			0.15 [a]				
Nail strengthener		0.21	0.31	0.10	0.14	1.00	0.15 [a]				
Nail remover		0.10	0.12	0.07	0.14	0.25	2.68 [a]				
Fragrance											
Shower cologne	Body mist	0.77	0.65	1.00	1.00	2.00	1.31	0.67	1.29	1.49	2.59
	Cologne	0.67	0.41	0.71	1.00	1.00	0.75	0.29	0.78	0.78	1.35
Perfume	Women's perfume	0.66	0.50	0.57	1.00	1.00	0.14	0.06	0.12	0.19	0.19
	Men's perfume	0.70	0.53	0.71	1.00	2.00	0.12	0.05	0.12	0.12	0.19

* SD is displayed if n is greater than 3.

** P75 and P95 displayed if n is greater than 20.

a. MFDS, 2016.

Table S-4. Frequency of detection, median and maximum concentrations (μg/g) of phthalates by cosmetic products.

	DEHP			DnBP			DEP		
	Frequency	Median	Max	Frequency	Median	Max	Frequency	Median	Max
All products	143/214	0.94	75.24	97/214	0.09	46337.68	41/214	0.28	1578.27
Skincare	30/43	1.24	18.62	9/43	0.13	0.78	2/43	0.03	0.05
Skin toner	10/12	0.46	2.94	2/12	-	0.24	0/12	-	-
Face lotion	10/12	1.13	7.29	1/12	-	0.02	1/12	-	0.002
Face cream	6/9	1.46	1862	3/9	0.01	0.26	1/9	-	0.05
Sunscreen*	4/10	0.02	11.82	3/10	0.01	0.78	0/10	-	-
Hair care	9/15	0.93	2.91	3/15	0.03	0.08	15/15	2.37	163.97
Hair dye	4/4	1.82	2.91	3/4	0.02	0.08	4/4	0.63	11.72
Hair treatment	1/6	-	0.87	0/6	-	-	6/6	2.50	8.88
Hair styling	4/5	0.63	2.42	0/5	-	-	5/5	2.85	163.97
Body care	11/21	2.93	13.55	4/21	0.26	0.39	6/21	0.02	24.66
Body lotion	4/9	0.02	6.38	0/9	-	-	3/9	0.006	0.03
Hand cream	2/3	-	2.93	0/3	-	-	1/3	-	24.66
Deodorant	5/9	0.33	13.55	4/9	0.06	0.39	2/9	-	0.08
Cleanser	28/42	2.67	75.24	22/42	0.07	0.66	0/42	-	-
Hand wash	2/5	-	2.57	1/5	-	0.20	0/5	-	-
Face cleanser	23/34	1.12	75.24	20/34	0.01	0.55	0/34	-	-
Shaving foam	3/3	1.24	37.93	1/3	-	0.66	0/3	-	-
Base makeup	7/20	0.47	12.25	13/20	0.06	0.24	1/20	0.06	0.06
Foundation	3/11	0.01	12.25	5/11	0.05	0.12	0/11	-	-

	DEHP			DnBP			DEP		
	Frequency	Median	Max	Frequency	Median	Max	Frequency	Median	Max
Makeup base/primer	1/5	-	0.47	4/5	0.06	0.07	1/5	-	0.06
Pact/powder	3/4	0.16	0.78	4/4	0.15	0.24	0/4	-	-
Eye makeup	9/13	0.34	3.73	9/13	0.12	1.26	1/13	0.28	0.28
Eyeliner	1/3	-	0.06	3/3	0.02	1.26	0/3	-	-
Eyeshadow	2/4	-	0.13	3/4	0.09	0.13	1/4	-	0.28
Mascara	3/3	2.19	3.73	1/3	-	0.05	0/3	-	-
Eyebrow	3/3	0.34	0.84	2/3	-	0.15	0/3	-	-
Lip makeup	16/16	0.46	2.39	6/16	0.11	0.22	4/16	0.10	0.31
Lip balm	3/3	0.86	1.32	1/3	-	0.01	1/3	-	0.31
Lip tint	3/3	0.36	0.49	0/3	-	-	0/3	-	-
Lip gloss	4/4	0.53	2.39	2/4	-	0.12	0/4	-	-
Lipstick	6/6	0.37	0.62	3/6	0.02	0.22	3/6	0.02	0.14
Nail care	23/34	1.27	37.89	30/34	0.15	46337.68	2/34	0.02	0.02
Nail polish	10/11	1.57	8.52	10/11	0.44	46337.68	1/11	-	0.02
Gel nail polish	7/11	0.18	37.89	11/11	0.12	0.53	0/11	-	-
Nail strengthener	4/9	0.02	7.23	6/9	0.02	1.88	0/9	-	-
Nail remover	2/3	2.15	4.52	3/3	0.31	0.88	1/3	-	0.02
Fragrance	9/10	0.53	12.29	4/10	0.06	0.34	8/10	0.37	1578.27
Shower cologne	3/4	0.39	12.29	1/4	-	0.06	2/4	-	1578.27
Perfume	6/6	0.36	1.66	3/6	0.03	0.34	6/6	0.52	643.92

* The phthalates analysis of sunscreen products was carried out without distinction between facial products and body use products.

Table S-5. The receptor-based AED / product-based AED ratio of phthalates by population groups.

	DEHP			DnBP			DEP		
	P50	P75	P95	P50	P75	P95	P50	P75	P95
Female									
19-29	1.74	1.37	1.23	0.03	3.57	5.50	0.58	0.97	4.22
30-39	1.67	1.54	1.15	0.03	1.49	8.06	0.33	0.72	3.16
40-49	1.81	1.68	1.20	0.01	0.02	6.19	0.41	0.68	2.92
50-59	1.92	1.53	1.42	0.02	0.02	5.59	0.42	0.59	1.85
60+	1.81	1.65	1.30	0.02	0.02	0.52	0.40	0.46	2.62
Total	1.85	1.61	1.24	0.02	0.03	5.07	0.43	0.60	2.75
Male									
19-29	0.77	0.75	0.46	0.52	0.78	0.53	0.25	0.51	1.58
30-39	0.74	0.66	0.65	0.01	0.03	0.09	0.21	0.66	1.45
40-49	0.53	0.52	0.77	0.48	0.48	0.74	0.02	0.28	1.73
50-59	0.28	0.45	0.56	0.21	0.35	0.61	0.00	0.22	1.03
60+	0.29	0.36	0.50	0.32	0.36	0.42	0.01	0.21	0.65
Total	0.58	0.55	0.46	0.01	0.02	0.06	0.04	0.37	1.11
Total									
19-29	1.16	1.12	1.02	0.01	0.03	4.42	0.35	0.56	3.10
30-39	1.13	1.12	0.92	0.01	0.02	4.15	0.30	0.62	2.41
40-49	0.79	1.24	0.97	0.00	0.01	2.22	0.23	0.54	1.36
50-59	0.76	0.99	1.05	0.01	0.01	1.35	0.14	0.37	1.16
60+	0.81	1.15	1.05	0.01	0.01	0.00	0.23	0.31	1.02
Total	1.01	1.17	1.00	0.01	0.01	2.46	0.22	0.44	1.59

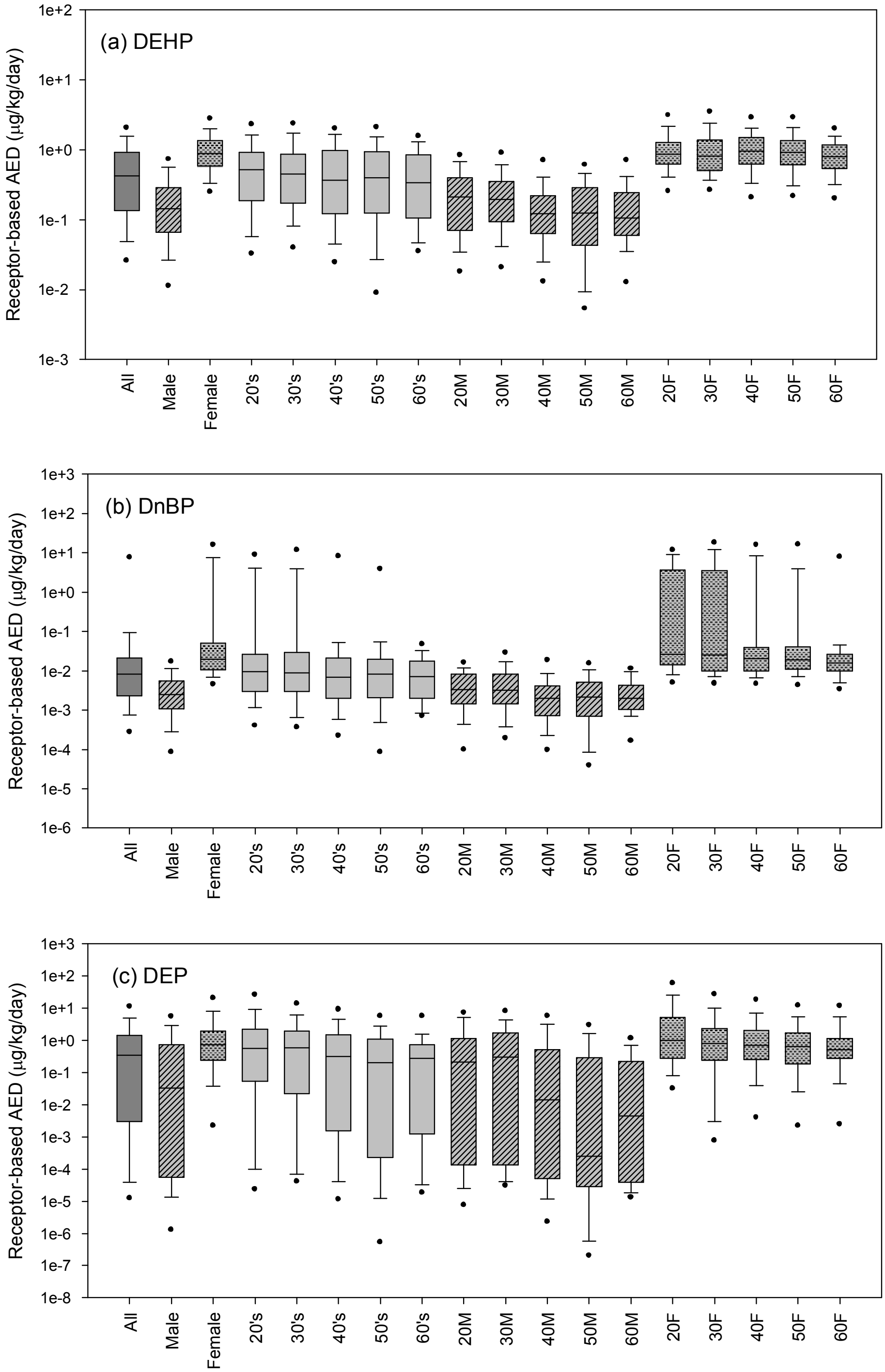

Figure S-1. Distribution of receptor-based aggregate exposure dose by gender and age groups. The horizontal lines show the median, the boxes show the quartiles, the whisker caps show the 10th and 90th percentile values, with the 5th and 95th percentiles plotted as dots.

Table S-6. Contribution of cosmetics for DEHP, DnBP, and DEP aggregate exposure estimations about co-use scenario 1 by each population group.

(a) 19-39 Males

	DEHP	DBP	DEP
FT	7.4%	20.2%	38.7%
FL	34.3%	0.3%	33.9%
FS	56.3%	79.4%	27.4%
CF	2.0%	0.1%	0.1%

(b) 40+ Males

	DEHP	DBP	DEP
FT	75.5%	98.0%	52.5%
FL	19.7%	1.5%	47.5%
CF	4.8%	0.5%	0.0%

(c) 19-39 Females

	DEHP	DBP	DEP
FT	1.2%	12.2%	0.0%
FL	5.0%	0.1%	0.0%
FC	58.7%	25.9%	0.0%
FS	11.4%	61.2%	0.0%
HT	0.1%	0.0%	4.9%
BB	18.6%	0.0%	0.0%
BH	2.5%	0.0%	94.9%
CF	0.3%	0.0%	0.1%
MF	2.2%	0.5%	0.0%
ES	0.0%	0.0%	0.0%
LS	0.0%	0.0%	0.0%

(d) 40+ Females

	DEHP	DBP	DEP
FT	1.2%	14.0%	0.0%
FL	4.4%	0.0%	0.0%
FC	58.4%	25.2%	0.0%
FS	10.5%	60.1%	0.0%
HT	0.1%	0.0%	5.0%
BB	19.4%	0.0%	0.0%
BH	3.2%	0.0%	94.9%
CF	0.1%	0.1%	0.0%
MF	2.6%	0.5%	0.0%
LS	0.0%	0.0%	0.0%

* The cosmetics were abbreviated as follows: FT, skin toner; FL, face lotion; FC, face cream; FS, facial sunscreen; HT, hair treatment; BB, body lotion; BH, hand cream; CF, face cleanser; MF, foundation; ES, eyeshadow; LS, lipstick.

Table S-7. Contribution of cosmetics for DEHP, DnBP, and DEP aggregate exposure estimations about co-use scenario 2 by each population group.

(a) 19-39 Males

	DEHP	DBP	DEP
FT	6.8%	20.2%	0.0%
FL	31.6%	0.3%	0.1%
FS	52.2%	79.3%	0.1%
HS	7.6%	0.1%	99.9%
CF	1.7%	0.1%	0.1%

(b) 40+ Males

	DEHP	DBP	DEP
FT	33.5%	20.5%	39.0%
FL	7.9%	0.0%	33.2%
FS	56.8%	79.4%	27.9%
CF	1.8%	0.0%	0.0%

(c) 19-39 Females

	DEHP	DBP	DEP
FT	1.2%	12.2%	0.0%
FL	5.0%	0.1%	0.0%
FC	58.7%	25.9%	0.0%
FS	11.4%	61.2%	0.0%
HT	0.1%	0.0%	0.6%
BB	18.6%	0.0%	0.0%
BH	2.5%	0.0%	30.2%
CF	0.3%	0.0%	0.0%
MF	2.2%	0.5%	0.0%
ES	0.0%	0.0%	0.0%
EM	0.0%	0.0%	0.0%
EB	0.0%	0.0%	0.0%
LS	0.0%	0.0%	0.0%
RP	0.0%	0.0%	69.2%

(d) 40+ Females

	DEHP	DBP	DEP
FT	1.2%	14.0%	0.0%
FL	4.4%	0.0%	0.0%
FC	58.4%	25.2%	0.0%
FS	10.5%	60.1%	0.0%
HT	0.1%	0.0%	0.7%
BB	19.4%	0.0%	0.0%
BH	3.2%	0.0%	29.3%
CF	0.1%	0.1%	0.0%
MF	2.6%	0.5%	0.1%
ES	0.0%	0.0%	0.0%
LS	0.0%	0.0%	0.0%
RP	0.0%	0.0%	69.9%

* The cosmetics were abbreviated as follows: FT, skin toner; FL, face lotion; FC, face cream; FS, facial sunscreen; HT, hair treatment; HS, hair styling; BB, body lotion; BH, hand cream; CF, face cleanser; MF, foundation; ES, eyeshadow; EM, mascara; EB, eyebrow; LS, lipstick; RP, perfume.

Table S-8. Contribution of cosmetics for DEHP, DnBP, and DEP aggregate exposure estimations about co-use scenario 3 by each population group.

(a) 19-39 Males

	DEHP	DBP	DEP
FT	5.4%	20.2%	0.0%
FL	27.0%	0.3%	0.0%
FS	46.4%	79.3%	0.0%
HS	6.6%	0.1%	89.3%
BH	13.1%	0.1%	10.6%
CF	1.5%	0.1%	0.1%

(b) 40+ Males

	DEHP	DBP	DEP
FT	15.6%	20.5%	0.7%
FL	4.2%	0.0%	0.6%
FS	29.4%	79.4%	0.7%
BB	50.2%	0.0%	98.0%
CF	0.7%	0.0%	0.0%

(c) 19-39 Females

	DEHP	DBP	DEP
FT	1.2%	0.0%	0.0%
FL	4.9%	0.0%	0.0%
FC	58.4%	0.0%	0.0%
FS	11.3%	0.0%	0.0%
HT	0.1%	0.0%	0.6%
BB	18.6%	0.0%	0.0%
BH	2.5%	0.0%	30.1%
CF	0.3%	0.0%	0.0%
MF	2.2%	0.0%	0.0%
EL	0.0%	0.0%	0.0%
ES	0.0%	0.0%	0.0%
EM	0.0%	0.0%	0.0%
EB	0.0%	0.0%	0.0%
LS	0.0%	0.0%	0.0%
NP	0.0%	99.9%	0.0%
NR	0.4%	0.0%	0.0%
RP	0.0%	0.0%	69.1%

(d) 40+ Females

	DEHP	DBP	DEP
FT	1.2%	0.0%	0.0%
FL	4.4%	0.0%	0.0%
FC	58.4%	0.0%	0.0%
FS	10.5%	0.0%	0.0%
HT	0.1%	0.0%	0.7%
BB	19.4%	0.0%	0.0%
BH	3.2%	0.0%	29.3%
CF	0.1%	0.0%	0.0%
MF	2.6%	0.0%	0.1%
ES	0.0%	0.0%	0.0%
EM	0.0%	0.0%	0.0%
LS	0.0%	0.0%	0.0%
NP	0.0%	99.9%	0.0%
RP	0.0%	0.0%	69.9%

* The cosmetics were abbreviated as follows: FT, skin toner; FL, face lotion; FC, face cream; FS, facial sunscreen; HT, hair treatment; HS, hair styling; BB, body lotion; BH, hand cream; CF, face cleanser; MF, foundation; ES, eyeshadow; EM, mascara; EB, eyebrow; LS, lipstick; RP, perfume.

국문초록

화장품 동시사용 시나리오에 기반한 종합노출평가법 개발

서울대학교 보건대학원
환경보건학과 환경보건학 전공
임 미 영

전통적인 화학물질 노출평가는 단일 노출원을 통한 노출에 한정된다. 인체에 노출되는 화학물질의 양을 현실적으로 추정하기 위해서는 단일 화학물질의 다양한 노출원과 노출경로를 고려한 종합노출평가를 실시할 필요가 있다. 화학물질의 노출 및 위해성평가에 사용되는 단계적 접근법은 종합노출평가에도 적용이 가능하지만, 구체적인 적용방법은 아직 논의된 바 없다. 본 연구의 목표는 소비자제품의 동시사용을 고려한 높은 단계의 종합노출평가법을 개발하는 것이다. 대상 제품은 화장품이며, 대상 화학물질은 디에틸헥실프탈레이트(di(2-ethylhexyl) phthalate, DEHP), 디부틸프탈레이트(di-n-butyl phthalate, DnBP), 디에틸

프탈레이트(diethyl phthalate, DEP)의 프탈레이트 3종이다. 인구구성비에 근거한 비례대표추출을 통해 한국인 1,001명의 표본을 구축하고 가정방문설문조사를 통해 화장품 31종 사용에 대한 노출계수를 수집하였다. GC-MS-MS를 통해 214개 화장품 내의 프탈레이트 농도를 분석하였다.

첫번째 연구(chapter 2)는 화장품 사용을 통한 프탈레이트 노출을 수용체 기반 노출평가를 통해 추정하고 제품 기반 노출평가 결과와 비교하고자 하였다. 수용체 기반 노출평가는 개인이 동시에 사용(co-use)하거나 사용하지 않는(non-use) 제품을 고려하여 제품별 실제 노출계수를 통해 노출평가가 이루어진다. 제품 기반 노출평가는 제품 사용자의 노출계수에 인구집단의 사용률을 반영하여 노출평가가 이루어지며, 두가지 방법으로 추정한 노출량을 비교하였다. 수용체 기반 노출평가 방법으로 추정한 프탈레이트의 평균 종합노출량은 DEHP가 0.68 ± 0.87 μg/kg/day, DnBP가 1.08 ± 5.71 μg/kg/day, DEP가 2.47 ± 9.05 μg/kg/day이다. 수용체 기반 노출평가량에 기여율이 높은 화장품 분류는 DEHP는 스킨케어용품와 바디케어용품, DEP는 손톱케어용품, DEP는 방향용품과 헤어케어용품이었다. 인구학적 분류로는 젊은 여성 집단의 프탈레이트 노출량이 가장 높았다. 수용체 기반 노출평가 방법은 인구집단의 평균노출을 제품 기반 노출평가 방법보다 낮게 추정하였으나, DnBP와 DEP의 경우, 90분위수 이상의 고노출군의 노출량은 제품 기반 노출평가 방법보다 높게 추정하였다.

두번째 연구(chapter 3)는 화장품의 동시사용 패턴의 특징을 파악하고 성별과 연령에 따른 인구집단의 화장품 동시사용 시나리오를 작성하고자 하였다. 화장품의 동시사용 패턴은 정확한 종합노출평가를 위해 중요한 요소이다. 한국인의 국민대표 화장품 노출계수 데이터베이스가 화장품 동시사용 패턴 분석에 사용되었다. 1,001명의 화장품 31종의 사용여부를 사용과 비사용의 범주형 변수로 처리하였다. 동시사용 패턴 분석을 위해 세가지 분석법을 사용하였다. 첫째, 제품쌍의 상관성 분석을 위해 Cohen의 kappa 상관계수를 사용하였고, 화장품의 동시사용 패턴에 성별의 차이가 미치는 영향을 확인하였다. 둘째, 계층적 군집 분석을 위해 이원적 연결법을 사용하였고, 화장품의 군집이 많은 수의 제품이 포함된 거대한 하나의 클러스터와 1개 혹은 2개의 제품이 포함된 작은 클러스터로 분류되는 현상을 확인하였다. 셋째, 빈발 패턴 마이닝을 위해 eclat 알고리즘을 사용하였고, 사용하는 화장품의 개수와 동시사용 패턴은 성별과 연령이 모두 영향을 미치는 것을 확인하였다. 화장품의 동시사용 패턴은 새로움 제품이 기존의 제품 사용 패턴에 더해지는 누적성이 나타났다. 세 가지 분석법을 통해 확인한 화장품의 동시사용 패턴의 특징을 모두 반영하여, 동시사용 패턴 내 빈발 순위와 인구집단의 화장품 사용개수 분포를 결합하여 화장품 동시사용 시나리오를 작성하였다. 4가지 인구집단의 25, 50, 75, 95 분위수에 대한 화장품 31종의 동시사용 시나리오 16가지를 결정하였다.

세번째 연구(chapter 4)는 제품 동시사용 시나리오를 기반으로

종합노출평가를 실시하고 수용체 기반 노출평가법과의 비교를 통해 새로운 평가법을 검증하고자 하였다. 제품의 동시사용을 고려한 종합노출평가법은 모든 제품의 노출량을 합산하는 종합노출평가법보다 높은 단계의 평가법이다. 화장품 동시사용 시나리오를 통해 화장품 사용을 통한 DEHP, DnBP, DEP의 종합노출량을 확률론적 방법으로 추정하였다. 성별과 연령에 의한 4가지 인구집단의 25, 50, 75, 95분위수에 해당하는 종합노출량이 도출되었다. 민감도 분석을 통해 동시사용 시나리오 기반 종합노출량에 기여율이 큰 화장품을 규명하였다. 동시사용 기반 종합노출평가량은 인구집단의 75분위수 이하에서는 수용체 기반 종합노출평가량보다 컸고, 95분위수에서는 수용체 기반 종합노출평가량 보다 작았다. 새로운 종합노출평가법이 낮은 단계의 평가법인 제품 기반 노출평가법보다 가장 높은 단계의 평가법인 수용체 기반 노출평가법에 근접하여 ‘중간’ 단계의 평가법임을 알 수 있었다.

본 연구를 통해 개발한 동시사용 시나리오 기반 종합노출평가법을 통해 개인의 실제 사용 제품의 패턴과 노출계수를 매번 새롭게 조사할 필요없이 적은 종류의 입력값만으로도 종합노출평가를 실시할 수 있다. 동시사용 시나리오 기반 종합노출평가법은 수용체 기반 노출평가법보다 간단하고, 모든 제품이 아닌 동시사용과 비사용 제품을 고려한 현실적인 추정법이며, 종합 노출 및 위해성에 기반한 화학물질 및 제품 관리에 활용할 수 있다.

주요어: 종합노출평가, 동시 사용, 소비자 노출, 화장품, 프탈레이트,
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