Research Article

Exposure Factors to Retail Insect Repellents Based on Household use in South Korea

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Abstract:

Household exposure to insect repellents including hazardous ingredients may play a role in the health risk of users caused by the use of ingredients. A market searching was conducted to elucidate which repellents and major ingredients were commonly used in the market. Furthermore, we investigated valuable exposure factors on respiratory exposure and the combined exposure amounts to insect repellents of household users that are useful to conduct accurate exposure assessments. 254 insect repellents and 10 major ingredients were searched in market. The most prevalent active ingredients of insect repellents were deet and picaridin. Web-survey study evaluated respiratory exposure factors such as the use frequency, the exposure duration, the exposed amount, and the combined exposure amount divided by the various application types of insect repellents. The respondent's groups including respondents with preschool children and children were showing regular household use of various insect repellents. The purpose of this study is to investigate, analyze, and evaluate the use of repellents through a nationwide online survey, and suggest a representative exposure coefficient for the use of repellents.

Keywords: Insect repellents; Exposure factors; Web-survey; Combined exposure; Preschool children and children

1. Introduction

Household insect repellents to harmful insects for infection with multiple arthropods that can cause local or systemic effects to raise several important considerations concerning public safety. Insect repellents are commonly used in and around residential homes. Exposure to insect repellents may result from inhalation, dermal contact from residential applications. There are many inhalable formulations of insect repellents available to users, including aerosol spray and trigger spray. A large number of insect repellents that are effective against specific target insects have been developed with the idea of consumer benefits. Hundreds of insect repellents are marketed to date. It may be inhaled when sprays are used around the body [1, 2]. Indoor contaminants have increased the risk of exposure partly and may pose a special risk to children. The indoor residential environment is a more important route of exposure to hazardous substances than dietary ingestion [3−5].

Mosquitoes are the most medically important arthropod vectors of severe human disease. They transmit the protozoan parasites causing malaria and viruses that cause infections such as dengue, yellow fever, filariasis, chikungunya, Japanese encephalitis, etc. [6, 7]. There are many different species of bloodsucking bedbugs, fleas, mites, and ticks. Bedbugs, which can be found in beds or furniture, feed on humans to obtain blood-meals. Some mites live in people's skin, e.g. the mites that cause scabies. Other mite species and ticks may take blood-meals on humans. Fleas, bedbugs are insects, whereas ticks and mites belong to another group of arthropods, the Acarbina. Bedbugs do not carry disease, but their biting can be a serious nuisance. However, important diseases of humans are transmitted by other arthropods dealt with hence, among them the following: plague and murine typhus (certain fleas), lyme disease, relapsing fever and many viral diseases (ticks), scrub typhus (biting mites) [8].

Insect repellents are not insecticidal; rather they mask the human skin or cover up the local environment to repel the insects and arthropods (mosquitoes, fleas, mites, ticks). N, N-diethyl-3-methylbenzamide (DEET) and [2-(2-hydroxyethyl)-1-piperidinecarboxylic acid 1-methyl propyl ester] (Picaridin) are widely used synthetic ingredients of insect repellents available to the general consumer. The action mechanism of DEET and picaridin are to provide a vapor barrier that deters the insect from coming into contact with the skin [11]. Insect repellents are marketed in every practicable application types such as: trigger, aerosol spray, patch sheet, creams, and grease sticks. Regardless of the application types, the time of protection varies with the active ingredients, the insect species, and the zeal of the insect [12]. Multiple uses of insect repellents may cause the aggregately combined exposure of the multiple ingredients to product users.

The Korean government enacted 'The Korean Biocidal Products Regulation (KBPR)' that concerns the placing on the market and use of biocidal products, which are used to protect humans, materials or articles against harmful organisms, by the action of the active substances contained in the biocidal product. According to this regulation, all biocidal products should undergo exposure and risk assessments to evaluate health and environmental hazards caused by

their use. The exposure assessment component of a risk assessment of hazardous chemicals requires evaluation of exposure of relevant chemicals through all the relevant pathways by all the relevant routes of exposure for all relevant periods. The products of exposure assessment are estimates of the exposure of defined subjects to each chemical by periods and exposure pathways [9]. Exposure assessments were carried out to characterize real-life situations of users, where by potentially exposed populations are identified; potential pathways of exposure are identified; and the magnitude, frequency, duration, and temporal-pattern of contact with a product are quantified [3]. In general, humans in their developmental stages (fetuses, infants, toddlers, and children) appear to be more severely affected by exposure to contaminants than adults [10].

When assessing exposure and health risk to children, more accurate exposure assessment could be estimated by combined exposures from all potential exposure routes [13]. The exposure assessment to chemicals from several resources including insect repellents is suspected to be the cause and the initial goal of the investigation for identification health effects [14, 15]. To conduct exposure assessment for using insect repellents, information on combined exposure (e.g., frequency of multiple-use, and information about the circumstances of usage) are necessary [16]. The purpose of this present study was to develop a database on exposure assessment regarding inhalation and combined exposure pattern to household insect repellents. This study created a sufficient resource database for implementing exposure of insect repellents and also presented an approach for compiling common principles of combined exposure assessment.

2. Methods

2.1 Retail insect repellent products survey

A market searching was conducted to elucidate which household insect repellents were commonly used in the Korean market. Survey-company carried out the market searching for the currently used household insect repellents. The web searching collected current information on the household insect repellents and active ingredients. Household insect repellents, which were provided specifically for the general public to ensure that they use household insect repellents most appropriately, were including the information of the active ingredients.

2.2 Household insect repellent usages

The purpose of the web-survey was to obtain information about the household exposure of the insect repellents at home. We hired the private survey company (K-STST Research Ltd.) to conduct an extensive online survey across all cities and provinces in Korea regarding household insect repellent usage. The survey company had participant panel pool in all provinces and 15 metropolitan areas. To achieve our target of statistically significant 5000 survey respondents considering the demographic characteristics, an initial e-mail was sent to approximately 60000 to 75000 public panel members, 12 times ~ 15 times participants of 5000 purpose cases. If an e-mail recipient agreed to participate in the survey and had experience using at least one of the identified household insect repellent products, they were sent a web link directing them to the online survey questionnaire. Until the 5000 cases purpose number of respondents was obtained, ‘agree to take part in survey study’ was continued. A total of 5015 households completed the survey questionnaire. Additionally, sex balanced respondents with an equal distribution of age groups were selected using quota

sampling methods. The web-survey questionnaires consisted of purchasing/using the information of insect repellents as follows: list of insect repellents used at home and the frequency of use, estimation of quantitative exposed duration to insect repellents, quantitative amount of insect repellents used, and demographic data. The online survey questionnaire also asked respondents to list and describe all family members in the household to determine the presence of preschool children. Combined exposed amounts of the studied families by insect repellents at home were evaluated. Exposed subjects were constructed to six groups such as: total respondents, families with infants, families with toddlers, families with children, families with youths, and only adult families considering long-term resting inhalation rate for children from birth to 18 years of age (Korean exposure factors handbook for children [17]).

2.3 Household insect repellent exposure analysis

Use information of insect repellents at home was investigated to obtain the frequency of using products, the exposure duration of products, and the amount of use per application by considering the insect repellent application types. The survey questionnaire included questions on the use of information, the exposed information, and the exposed amounts as followed:

- Frequency of the insect repellents used during some periods at home?
- Time from the beginning to end of the insect repellents use including task time
- Total time and number of triggering/spraying action (trigger type, aerosol spray type)
- The time of pressing a button on the aerosol spray products (aerosol spray type)
- Amount of use per product application

To investigate the exposed amount of inhalable application types insect repellents for studied groups, we purchased the surveyed various insect repellents in the market. The survey questionnaire included the used amount per insect repellent application. Based on the surveyed result, the exposure amount of insect repellents was investigated to studied groups. Experiments were conducted to evaluate an accurate amount of use insect repellents per application. The amounts of products used (g/use) were measured by weighing used amounts. To calculate the exposure amount of trigger and aerosol spray insect repellents, the following simple equation was used:

Equation: Exposure amount (g/use) = [time of triggering or spraying (time/use)] × [generated mass (g/time)]

The generated mass rate was determined by squeezing the product trigger 10 times for about 6 seconds (trigger type) or spraying the product for 10 seconds (aerosol spray type); the weight of the product was measured before and after use [18]. For patch type sheets, the amount of sheet used was determined as a difference before and after the use of the sheet. To evaluate combined use amounts of insect repellents, the questionnaire included multiple-use of several application types of insect repellents. To calculate the combined exposure amount of inhalable insect repellents per month, the exposure values of the single-use pattern were used considering application types based on the ubiquitous inhalation exposure of the studied families such as trigger type, aerosol spray type, and patch sheet type. Considering the worst-case scenario, the combined respiratory exposure of inhalable application types of insect repellents to the studied families was calculated as the sum of the

single-use amount per month used by the studied families.

3. Results

3.1 Retail insect repellent product and active ingredients

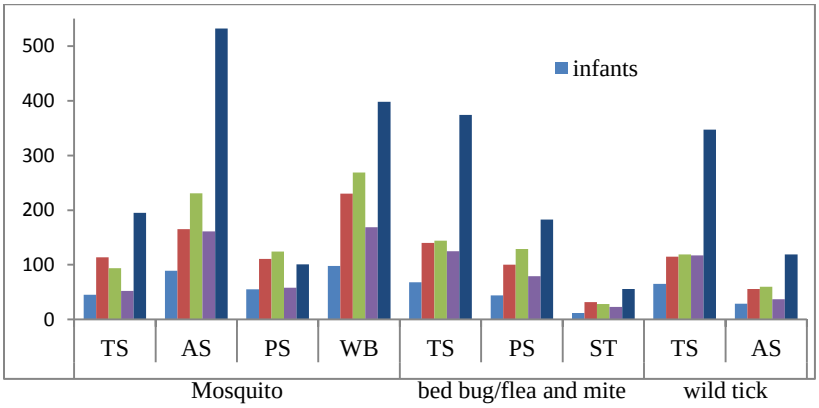
The online product survey for household insect repellents available in retail markets that offered substantial diversity in product purpose, application type, and active ingredients. Based on the results of the household insect repellent usage survey, we selected a subset of 254 products that represent the most prevalent and popular household insect repellents from more in-depth analysis. The purpose for household insect repellents was often defined based on the specific target insect intended for elimination or control. Common target insects included mosquitos, bedbugs/fleas, bed mites, and wild ticks (Table 1). Predominant formulations of surveyed insect repellent products in the market were spraying application types such as trigger type and aerosol spray type. Additionally, various application types of insect repellent products such as patch sheets, wrist bands, and stationary trap were sold in the market. The web survey approach obtained the database about household use patterns and exposure information of insect repellents from the results of the responses of 5015 respondents to the formal questionnaire. Based on survey results, the survey respondents were using various application types of insect repellents in-home and were regularly using them. Responses results of studied respondent groups to survey questionnaires were used were summarized in Figure 1. Insect repellent products in the market were applied to the skin or clothing produce a vapor layer that has an offensive smell or taste to mosquito, bedbug, flea, mite, and wild tick. According to the labeling information of insect repellents, abrasion by clothing, sweating, washing with water, warm temperatures, or high winds will significantly decrease the duration of the effectiveness of insect repellent ingredients; it is necessary to re-apply insect repellents more frequently any of these factors exist. The 254 household insect repellents identified in the online product survey contained several different active ingredients, including DEET, picaridin, clover oil, ethyl byuthylacetylaminopropionate, and others (Table 1). Major active ingredients of studied insect repellents were DEET, picaridin, clover oil, and ethyl byuthylacetylaminopropionate. Among these ingredients, DEET was the most prevalent ingredient in household insect repellents. Of the searched total of 254 insect repellents, 109 products were containing DEET as the active ingredient (42.9%). DEET seems to be the most effective and is the best-studied ingredient of insect repellent available to the public consumer. Picaridin was also predominantly used ingredient of insect repellents (25.6%) for mosquitoes and other insects. Major application types of these insect repellents were trigger type, aerosol spray, and patch sheet. These results addressed that the exposed repellent products to users can present the exposure of active ingredients in products to users and family members of users. The active ingredients in insect repellents can have potent biological and toxicological activity. The biological and toxicological properties of these ingredients are important for the health effect of users of insect repellent [19].

Table 1: Distribution of insect repellents and ingredients used by respondents in home

Active ingredients in insect repellents (products in market; n=254, major 10 ingredients are shown)						
Ingredients	CAS No.[a]	Vapor pressure (mmHg, 25 °C) [a]	No. of repellent products used (% rate, n=254)		Target insects	Application types
N, N-Diethyl-M-toluamide (DEET)	134-62-3	0.002	109 repellents (42.9)		Mosquitoes	Trigger spray, aerosol spray, patch sheet, wrist band
Picaridin (icaridin)	119515-38-7	4.43×10^{-4}	65 repellents (25.6)			
Clover oil (trifolium oil)	8000-34-8	-	31 repellents (12.2)			
Ethyl byuthylacetylamino propionate	52304-36-6	1.1×10^{-3} (20 °C)	23 repellents (9.1)			
Propylene glycol	57-55-6	0.13	14 repellents (5.5)		Bedbugs, fleas and mites	Trigger spray, patch sheet, stationary trap
(3R)-3,7-Dimethyloct-6-enal (citronella java oil)	2385-77-5	-	9 repellents (3.5)			
Metofluthrin	240494-70-6	1.47×10^{-5}	4 repellents (1.6)		Wild ticks	Trigger spray, aerosol spray
Allethrin	584-79-2	1.2×10^{-6} (21°C)	3 repellents (1.2)			
Dipropyl isocinchomeronate	136-45-8	5.18×10^{-8}	2 repellents (0.8)			
Permethrin	52645-53-1	4.92×10^{-7}	2 repellents (0.8)			

[a] As reported in Pubchem (NIH).

Figure 1: A number of household insect repellents used by studied families at home



3.2 Household demographic characteristics

The distributions of 5015 respondents were divided into respondents with infants (0–2 years), respondents with toddlers (3–6 years), respondents with children (7–12 years), respondents with youths (13–18 years), and adults (19 years and older); these groups are based on the long-term resting inhalation rates for children from birth to 18 years of age. The exposure information of insect repellents was investigated to six groups: total respondents (5015 respondents), families with infants (384), families with toddlers (688), families with children (821), families with youths (785), and only adult families (2946) (Table 2).

Table 2: Demographic results of survey study

Distribution of respondents	No. of respondents	No. of male	No. of female
Total respondents	5015	2484	2531
19 – 29 y	967	304	663
30s of age	1848	772	1076
40s of age	1424	862	562
50s + of age	776	546	230
Respondents with infants	384	Male infants: 204	Female infants: 212
1 infant	353	171	182
2 infants	30	32	28
3 infants	1	1	2
Respondents with toddlers	688	Male toddlers: 399	Female toddlers: 410
1 toddler	571	298	273
2 toddlers	113	95	131
3 toddlers	4	6	6
Respondents with children	821	Male children: 541	Female children: 499
1 child	611	311	300
2 children	202	216	188
3 children	7	12	9
4 children	1	2	2
Respondents with youths	785	Male youths: 515	Female youths: 481
1 youth	579	305	274
2 youths	201	203	199
3 youths	5	7	8
Adults only families	2946	Male only: 3818	Female only: 4171

Note-ages: infant, 0−2 y; toddler, 3−6 y; child, 7−12 y; youth, 13−18 y; adult, 19+ y.

Based on the survey result, 384 respondents answered that there were 1 to 3 infants and the total number of

infants in the 384 respondents was 416. 688 respondents answered that there were 809 toddlers in total. The use prevalence of insect repellents was defined as the number of respondents who reported using insect repellents in the home during the last year. The surveyed respondent groups were retaining various application types of insect repellents and showing regular use. Table 3 gives the summary data of insect repellent use patterns by respondent groups divided by respondents with preschool children, children, youth, and only adults. Use of mosquito repellents was more prevalent, with various application type repellents used by 46.8% of total respondents, 45.6% of respondents with infants, and 52.9% of respondents with toddlers than use of bedbug/flea/mite repellents (20.9%, 24%, 21.2%) and wild tick repellents (17.1%, 18.2%, 18%). Primary exposure to insect repellents occurs to the user who actively uses the products. Secondary exposure is the exposure that may occur after the actual use of insect repellents. The user of products may be subject to both primary and secondary exposure whereas the non-user or bystander will only experience secondary exposure [20]. Studied results reveal that preschool children, children, and youths can be exposed to insect repellents through regular household use by adult users (or use to preschool children, children by adults). Primary exposure to insect repellents occurs to adults, youths, and children. Preschool children and children may also experience secondary exposure.

The survey study included the questionnaire about the co-use prevalence of each two insect repellents. The Co-use of repellents that contain the same ingredients results in the combined exposure to those ingredients. In Table 3, the prevalence of co-use insect repellents were presented as follows: numbers of respondent using mosquito repellent and bedbug/flea/mite repellent among 5015 respondents (14.2% of total respondents, 15.6% of respondents with infants, and 16% of respondents with toddlers), numbers of respondent using bedbug/flea/mite repellent and wild tick repellent (7.2% of total respondents, 7% of respondents with infants, and 7.3% of respondents with toddlers), numbers of respondent using mosquito repellent and wild tick repellent (12.4% of total respondents, 12.2% of respondents with infants, and 14.2% of respondents with toddlers). The prevalence of multiple users using mosquito repellent, bedbug/flea/mite repellent, and wild tick repellent among 5015 respondents was 5.9% of total respondents, 5.2% of respondents with infants, and 6.3% of respondents with toddlers.

Table 3: Multiple use patterns by studied groups

Repellents products	No. of respondents used mosquitoes, bedbugs/fleas/mites, wild ticks repellents (% ratio)	No. of respondents used bedbugs/fleas/mites, wild ticks repellents (% ratio)	No. of respondents used wild ticks repellents (% ratio)
Mosquitoes	Total respondents: 2348/5015 [a] Infants: 175/384 (45.6) [a] Toddlers: 364/688 (52.9) [a] Children: 386/821 (47) [a] Youths: 372/785 (47.4) [a] Only adults: 1356/2946 (46) [a]		
Bedbugs/fleas/mites	Total respondents: 714/5015 [b] Infants: 60/384 (15.6) [b] Toddlers: 110/688 (16) [b] Children: 119/821 (14.5) [b] Youths: 116/785 (14.8) [b] Only adults: 407/2946 (13.8) [b]	Total respondents: 1050/5015 [a] Infants: 92/384 (24) [a] Toddlers: 146/688 (21.2) [a] Children: 163/821 (19.9) [a] Youths: 173/785 (22) [a] Only adults: 606/2946 (20.6) [a]	
Wild ticks	Total respondents: 623/5015 [b] Infants: 47/384 (12.2) [b] Toddlers: 98/688 (14.2) [b] Children: 101/821 (12.3) [b] Youths: 103/785 (13.1) [b] Only adults: 356/2946 (12.1) [b] Total respondents: 300/5015 [c] Infants: 20/384 (5.2) [c] Toddlers: 43/688 (6.3) [c] Children: 51/821 (6.2) [c] Youths: 54/785 (6.9) [c] Only adults: 174/2946 (5.9) [c]	Total respondents: 364/5015 [b] Infants: 27/384 (7) [b] Toddlers: 50/688 (7.3) [b] Children: 57/821 (6.9) [b] Youths: 64/785 (8.2) [b] Only adults: 213/2946 (7.2) [b]	Total respondents: 860/5015 [a] Infants: 70/384 (18.2) [a] Toddlers: 124/688 (18) [a] Children: 140/821 (17.1) [a] Youths: 130/785 (16.6) [a] Only adults: 499/2946 (17) [a]

Note: Infants, respondents with infants in family; toddlers, respondents with toddlers in family; children, respondents with children in family; youths, respondents with youths in family; only adults, respondents with only adults; mosquito repellents include application types-TS, AS, PS, WB; bedbugs/fleas/mites repellents include application types-TS, AS, PS, ST; wild tick repellents include application types-TS, AS.

[a]numbers of respondents using single repellent, [b]numbers of respondents using two repellents, [c]numbers of respondents using multiple repellents.

3.3 Household use frequency of insect repellents

The use frequency of insect repellents varied based on the applications of repellent, target insects, and seasons. The household use frequencies of insect repellents for total respondents and studied family groups were investigated. Season variations on use frequency were also considered. The use frequency varied according to the respondent groups with preschool children, children, youths, and only adults. Table 4 summarizes the mean, SD, and 50^{th} to 75^{th} percentile product use frequency values for each of the demographic groups considered. Mosquito repellents and wild tick repellents were found to be used more frequently in the summer when mosquitoes and wild tick are frequently active; mosquito repellents and wild tick repellents were used more than once a week in summer and were used more than once a month in other seasons. The use frequency of bedbug/flea/mite repellents did not show the seasonal variation. Compare to the use frequencies of mosquito repellents and bedbug/flea/mite repellents, respondents with preschool children or children showed little use (or no use) of wild tick repellent products in the seasons other than the summer (Table 4). Comparatively, to control wild tick, aerosol spray insect repellents had the highest use frequency.

3.4 Use duration and respiratory exposure times of insect repellents

Exposure to insect repellents occurs to the users who actively use the products during the time spent using the insect repellents. In order to investigate the time spent applying the insect repellents, respondents were asked how long they took to use the product, from the beginning to the end, in one application. The time spent to use insect repellents was evaluated as the time taken for a series of tasks involving the use of each product. Table 5 summarized the use duration parameters used to calculate the exposure amounts by product application type for all survey respondents and for families with infants and toddlers. Most application types of repellents that could be exposed to the user or bystanders in the home via inhalation were trigger and aerosol spray types. The use of these inhalable application type products may cause exposure of active ingredients to users or bystanders such as preschool children, children, and youths in the home. Inhalation exposure is usually derived from the airborne concentration in the zone in which the exposed user breathes [20].

To calculate the actual use amount of studied respondent groups to inhalable application type products, we investigated the time spent operating the trigger and the time spent pressing the button on the aerosol spray products. For trigger type insect repellents, the exposure time was defined as the time taken per use during triggering actions during the total use duration. The exposure time of the aerosol spray products was defined as the time the button was pressed per use during the total use duration. Table 6 summarized the numbers of triggering actions, the time spent during triggering actions of trigger types products and spraying times of aerosol spray type products reported by respondents. In the case of mosquito repellents, the mean task time of trigger type repellents per use by total respondents was 3.4 h/use (2.9 h/use by respondents with infants) (Table 5). During the using task time, the number of triggering actions was 5.27 times/use and the meantime of 5.27 triggering actions was 2.6 sec/use by total respondents (4.6 times/use, 2.3 sec/use by respondents with infants) (Table 6).

3.5 Exposed amount of insect repellents

In order to evaluate the exposed amount of studied

respondent groups to inhalable insect repellents, we compared the difference in the weight of the product before and after use at room temperature (Table 7). Additionally, we measured the generated mass (g/sec) for trigger type and spraying type repellents after they were applied. For trigger spray repellents, the exact exposed amounts were calculated as the used weight of trigger type repellent per one operating triggering multiply the numbers of operating the triggering. In the case of aerosol spray type repellents, the exposed amount was calculated as the generated mass of repellents per second multiply the time spent pressing the button on the aerosol spray repellents per use. The exposed amount of repellents per use differed among insect repellents and their application types (g/use, Table 7). The mean exposed amount of trigger type mosquito repellents was determined to be 1.2 g/use by total respondents (1.1 g/use by respondents with infants, 1.3 g/use by respondents with toddlers, and 1.3 g/use by respondents with children). Comparatively, for aerosol repellents used to control mosquitoes, bedbug/flea/mites, and wild tick, the mean product use time was higher than trigger spray repellents. These results implied that respondents using aerosol type repellents were exposed to active ingredients in aerosol type repellents 4−6 times more than active ingredients in trigger type repellents. The mean exposed amount of trigger type mosquito repellents was determined to be 7.7 g/use by total respondents (6.2 g/use by respondents with infants, 7.0 g/use by respondents with toddlers, and 7.8 g/use by respondents with children) (Table 7). The exposed amounts of bedbug/flea/mite repellents and wild tick repellents did not show a significant difference between the studied respondent groups.

Table 4: Comparison of use frequency by studied groups

Insect repellents	Total respondents (n=5015)				Respondents with infants (n=384)			Respondents with toddlers (n=688)			Respondents with children (n=821)			Respondents with youths (n=785)			Respondents only adults (n=2946)		
	Mean	SD	50^{th}–75^{th}		Mean	SD	75^{th}	Mean	SD	75^{th}	Mean	SD	75^{th}	Mean	SD	75^{th}	Mean	SD	75^{th}
Mosquites repellents		Summer season Other seasons																	
TS	7.5 [a] 3.0 [b]	18.7 7.9	3.0–7.0 0.0–3.0		8.2 4.9	11.6 12.6	7.5 4.0	10.6 4.3	29.0 7.9	7.0 4.0	5.9 2.1	11.1 4.8	7.0 4.0	6.8 2.4	11.3 5.5	7.5 4.0	6.1 2.5	12.9 7.8	7.0 1.0
AS	8.0 [a] 3.5 [b]	27.7 18.3	3.0–7.0 0.0–3.0		5.8 2.9	7.7 9.3	7.0 4.0	5.8 2.2	7.4 5.2	7.0 2.0	5.7 2.4	7.7 5.2	7.0 2.6	8.1 3.9	13.8 12.8	7.5 3.0	9.4 3.9	36.9 23.8	7.0 3.0
PS	5.3 [a] 1.7 [b]	10.8 5.4	2.0–7.0 0.0–0.5		5.8 1.4	8.7 3.2	7.0 2.0	3.6 1.3	3.6 3.2	7.0 1.0	4.4 1.6	5.5 4.1	7.0 1.0	5.4 1.5	9.6 4.5	7.0 0.1	7.3 1.9	16.6 7.6	7.0 0.0
WB	5.0 [a] 1.4 [b]	12.1 4.9	2.5–7.0 0.0–0.1		4.4 1.8	6.9 5.3	5.0 0.5	4.0 1.5	5.0 4.3	7.0 1.0	4.5 1.3	14.8 4.1	6.0 0.3	4.3 1.1	7.2 3.6	7.0 0.0	5.8 1.5	13.0 5.7	7.0 0.17
Bedbugs/fleas/mites repellents			Four seasons																
TS	5.5 [b]	11.6	2.0–6.0		5.0	5.1	8.0	5.7	8.2	8.0	4.9	5.9	8.0	5.7	13.1	6.0	5.4	12.9	4.0
PS	2.4 [b]	7.4	0.5–2.0		3.1	5.2	4.0	2.2	3.9	2.0	1.4	2.2	2.0	4.0	14.9	3.0	2.2	5.0	2.0
ST	3.3 [b]	2.5	2.0–4.0		6.0	2.4	6.0	3.3	2.6	6.0	3.1	1.9	6.0	2.9	2.6	4.0	3.5	2.7	6.0
Wild ticks repellents			Summer season Other seasons																
TS	4.7 [a] 1.0 [b]	9.7 1.3	2.0–4.0 1.0–2.0		4.0 NS	7.4 NS	2.0 NS	3.8 NS	4.8 NS	5.0 NS	3.9 2.0	5.8 -	4.5 2.0	3.6 2.0	5.5 -	3.0 2.0	6.2 0.1	13 -	5.0 0.1
AS	30.5 [a] 11.0 [b]	49.8 7.9	14–28 8.0–20		30.6 8.0	46.4 -	21 8.0	37.5 NS	77.3 -	28 NS	30.6 NS	43.0 -	28.0 NS	33.5 5.0	48.5 -	35.0 5.0	27.8 20.0	40.0 -	28.0 20.0

Abbreviations: TS, trigger spray; AS, aerosol spray; PS, patch sheet; WB, wrist band; ST, Stationary traps; NS, not surveyed.

[a] use per week, [b] use per month.

Table 5: Comparison of use duration by studied groups

Insect repellents	Total respondents (n=5015)			Respondents with infants (n=384)			Respondents with toddlers (n=688)			Respondents with children (n=821)			Respondents with youths (n=785)			Respondents only adults (n=2946)		
	Mean	SD	50th–75th	Mean	SD	75th	Mean	SD	75th	Mean	SD	75th	Mean	SD	75th	Mean	SD	75th
Mosquitoes repellents																		
TS (h/use) [a]	3.4	3.2	2.5−5.0	2.9	3.0	5.0	3.6	3.5	5.0	3.3	2.7	5.0	3.0	3.0	4.7	3.4	3.1	5.0
AS (h/use) [a]	3.2	3.2	2.1−5.0	2.9	2.8	5.0	2.9	2.4	4.5	3.1	2.9	5.0	3.0	2.8	5.0	3.3	3.5	5.0
PS (h/use) [a]	5.7	4.4	5.0−8.0	5.2	4.2	8.0	5.7	3.8	8.0	6.0	4.1	8.0	6.2	4.9	8.1	5.6	4.7	6.5
WB (h/use) [a]	6.3	5.2	5.0−8.0	5.0	4.7	6.0	5.2	4.1	7.0	5.8	4.2	8.0	6.8	5.5	8.0	7.0	5.8	9.0
Bedbugs/fleas/mites repellents																		
TS (min/use) [a]	6.9	18.7	2.0−6.0	5.1	6.4	5.0	11.8	38.6	10.0	13.1	38.5	10.0	7.2	10.4	10.0	5.7	12.3	5.0
(h/day) [b]	6.0	3.5	7.0−8.0	6.2	3.5	8.5	6.1	3.4	8.5	5.8	3.4	8.0	6.6	2.8	8.0	6.0	3.8	8.0
PS (h/day) [b]	7.5	5.7	7.5−8.1	6.6	5.9	8.0	7.4	5.2	8.4	7.7	4.6	8.2	6.8	5.6	8.0	7.8	6.6	8.5
ST (h/day) [b]	7.5	6.0	7.0−8.0	9.4	7.8	10.0	7.4	6.1	9.0	7.6	5.3	8.0	6.9	2.9	8.5	7.7	6.9	8.0
Wild ticks repellents																		
TS (h/use) [a]	3.6	3.0	3.0−5.0	3.2	2.1	5.0	4.1	3.1	5.0	3.4	2.7	5.0	3.0	2.9	4.5	3.5	3.1	5.0
AS (h/use) [a]	3.4	3.0	3.0−5.0	2.2	1.8	3.0	3.0	2.8	4.0	3.2	2.7	5.0	3.7	3.8	5.0	3.5	2.9	5.0

Abbreviations: NU, no use.

[a] total time spent per use that used and exposed by repellents in the place where the repellents applied, [b] time exposed to articles applied by repellent per day.

Table 6: Comparison of respiratory exposure duration to spraying repellents by studied groups

Insect repellents		Total respondents (n=5015)				Respondents with infants (n=384)			Respondents with toddlers (n=688)			Respondents with children (n=821)			Respondents with youths (n=785)			Respondents only adults (n=2946)		
		Mean	SD	50^{th}–75^{th}		Mean	SD	75^{th}	Mean	SD	75^{th}	Mean	SD	75^{th}	Mean	SD	75^{th}	Mean	SD	75^{th}
Mosquitoes repellents																				
TS	No [a]	5.27	4.93	4.0−5.0		4.6	3.4	5.0	5.5	5.8	6.0	5.7	6.3	6.0	4.6	3.7	5.0	5.4	4.8	5.0
	Time [b]	2.6	2.4	2.0−5.0		2.3	1.7	2.5	2.7	2.9	3.0	2.8	2.1	3.0	2.3	1.8	2.5	2.7	2.4	2.5
AS (Time [c])		11.9	12.6	10.0−15.0		9.6	9.9	10.0	10.8	11.6	10.0	12.1	12.3	20.0	12.5	12.2	20.0	12.0	13.0	15.0
Bedbugs/fleas/mites repellents																				
TS	No [a]	10.3	12.5	5.0−10.0		11.6	17.3	10.0	9.8	13.8	10.0	9.7	13.0	10.0	14.7	16.2	20.0	9.8	10.9	10.0
	Time [b]	4.6	5.5	2.2−4.4		5.1	7.7	4.4	4.3	6.1	4.4	4.3	5.7	4.4	6.5	7.2	8.9	4.3	4.8	4.4
Wild ticks repellents																				
TS	No [a]	5.7	6.2	3.0−5.0		5.3	5.4	5.0	5.3	5.2	5.0	5.1	4.8	5.0	6.0	6.2	6.0	6.4	7.6	6.0
	Time [b]	2.5	2.7	2.2−2.6		2.4	2.4	2.2	2.3	2.3	2.2	2.3	2.1	2.2	2.7	2.8	2.6	2.9	3.4	2.6
AS (Time [c])		13.4	18.1	10−15		11.9	16.3	15.0	11.1	10.2	15.0	14.1	14.5	20.0	14.5	22.7	15.0	13.4	18.4	15.0

No[a]; the number of operating the trigger (time/use), Time[b]; the time spent operating the trigger (second/use), Time[c]; the time spent pressing the button on the aerosol spray repellents (second/use).

Table 7: Comparison of worst-case exposed amount by studied groups

Insect repellents	Total respondents (n=5015)			Respondents with infants (n=384)			Respondents with toddlers (n=688)			Respondents with children (n=821)			Respondents with youths (n=785)			Respondents only adults (n=2946)		
	Mean	SD	50th–75th	Mean	SD	75th	Mean	SD	75th	Mean	SD	75th	Mean	SD	75th	Mean	SD	75th
Mosquitoes repellents																		
TS (g/use) [a]	1.2	1.1	0.9−1.1	1.1	0.8	1.1	1.3	1.3	1.4	1.3	1.4	1.4	1.1	0.8	1.1	1.2	1.1	1.1
(g/s) [b]	2.2	2.1	1.7−2.1															
AS (g/use) [a]	7.7	8.1	6.4−9.7	6.2	6.4	6.4	7.0	7.5	6.4	7.8	7.9	11.3	8.0	7.9	12.9	7.8	8.4	9.7
(g/s) [b]	0.6	0.02	0.6−0.6															
PS (g/use) [c]	0.3	0.2	0.2−0.4	0.3	0.2	0.4	0.3	0.2	0.4	0.3	0.2	0.2	0.3	0.2	0.4	0.3	0.2	0.4
WB (g/each) [c]	0.1	0.1	0.08−0.4	ND														
Bedbugs/fleas/mites repellents																		
TS (g/use) [a]	3.2	3.9	1.5−3.1	3.6	5.5	3.1	3.1	4.4	3.1	3.1	4.1	3.1	4.6	5.1	6.3	3.1	3.4	3.1
(g/s) [b]	0.7	0.4	0.6−1.1															
PS (g/use) [c]	16.1	9.6	12.0−24.1	14.5	8.1	18.1	14.1	9.1	18.1	15.7	8.8	24.1	15.6	9.3	24.1	17.3	10.6	24.1
ST (g/s) [c]	0.4	0.2	0.2−0.6	ND														
Wild ticks repellents																		
TS (g/use) [a]	1.0	1.1	0.9−1.1	1.0	1.0	0.9	1.0	1.0	0.9	0.9	0.9	0.9	1.1	1.1	1.1	1.2	1.4	1.1
(g/s) [b]	0.4	0.2	0.3−0.4															
AS (g/use) [a]	4.7	6.4	3.5−5.2	4.2	5.7	5.2	3.9	3.6	5.2	4.9	5.1	6.1	5.1	8.0	5.2	4.7	6.4	5.2
(g/s) [b]	0.3	0.06	0.3−0.4															

Abbreviations: ND, not determined.

[a] exposed amount per application (weight of trigger type repellent per one operating trigger × numbers of operating the trigger or mass generated of aerosol sprayed repellent per second × the time spent pressing the button on the aerosol spray repellents per use), [b] generated mass (g/second) by spraying repellents per time, [c] amount of use per use (g/use).

3.6 Combined exposed amount of insect repellents

As a final task in the present study, we evaluated the effects of combined household insect repellents based on the combined repellents exposure amounts per month. The individual mean monthly exposure amounts were summed to determine the combined insect repellents exposure amounts per month. 5015 respondents reported that mosquito repellents were used 5 to 8 times per week and wild tick repellents were used 4 to 30 times per week in summer. In other seasons, mosquito repellents were used 1 to 3 times per month and wild tick repellents were used 1 to 11 times per month (Table 4). Table 8 summarized the key parameters (e.g., mass generation rate, and emission rate) used to calculate the exposure amounts by product application type for all survey respondents and for families with infants and toddlers considering the worst-case scenario about exposure amounts. The exposed amounts of respondents to insect repellents per month implied the exposure of respondents to the combined exposed amounts of active ingredients per month. In case of mosquito repellents, the mean exposed amount of trigger application type to total respondents was determined to be 38.5 g/month in summer (38.6 g/month by respondents with infants, 59.0 g/month by respondents with toddlers, 32.8 g/month by respondents with children). The total mean combined exposed amount of mosquito repellents was 309.3 g/month in summer (200.1 g/month by respondents with infants, 237.6 g/month by respondents with toddlers, 228.9 g/month by respondents with children) (Table 8). The combined exposed amount of studied repellents (mosquito repellents, bedbug/flea/mite repellents, and wild tick repellents) to total respondents was determined to be 976.6 g/month in summer (856.3 g/month by respondents with infants, 929.1 g/month by respondents with toddlers, 923.5 g/month by respondents with children) (Table 2). The combined exposed amount of mosquito, bedbug/flea/mite repellents, and wild tick repellents in summer was comparatively higher than that in other seasons. The combined use of insect repellents that contain several (or same) ingredients results in aggregate exposure to those ingredients. Therefore, it is necessary to understand the key patterns of the current use of different insect repellents to calculate the combined exposure [21].

Table 8: Combined worst-case exposed amount of studied groups

Insect repellents		Combined exposed amount (g/month, mean (75th))					
		Summer season	Other seasons	Summer season	Other seasons	Summer season	Other seasons
		Total respondents		**Respondents with toddlers**		**Respondents with youths**	
Mosquitoes	TS	38.5 (35.3)	3.6 (3.3)	59.0 (63.6)	5.5 (5.6)	32.0 (32.0)	2.6 (4.4)
	AS	264.0 (332.5)	26.9 (29.1)	174 (15.9)	15.4 (12.8)	277.7 (447.8)	31.2 (38.7)
	PS	6.8 (9.0)	0.5 (0.2)	4.6 (6.1)	0.3 (0.4)	6.9 (9.2)	0.4 (0.04)
TS+AS+PS [a]		309.3 (376.8)	31.0 (32.6)	237.6 (85.6)	21.2 (18.8)	316.6 (489.0)	34.2 (43.1)
Bedbugs/fleas/ mites	TS	17.6 (17.0)	NS	17.6 (17.6)	NS	26.2 (35.9)	NS
	PS	15.3 (17.2)		31.0 (39.8)		62.4 (96.4)	
TS+PS [b]		32.9 (34.2)	-	48.6 (57.4)	-	88.6 (132.3)	-
Wild ticks	TS	20.1 (22.1)	1 (2.2)	16.2 (14.6)	NS	16.9 (16.9)	2.2 (2.2)
	AS	614.3 (679.7)	4.7 (104)	626.7 (835.7)	NS	732.2 (746.5)	25.5 (26)
TS+AS [c]		634.4 (701.8)	5.7 (106.2)	642.9 (850.3)	-	749.1 (763.4)	27.7 (28.2)
		Respondents with infants		**Respondents with children**		**Respondents only adults**	
Mosquitoes	TS	38.6 (38.6)	5.3 (4.4)	32.8 (35.4)	2.7 (5.6)	31.3 (28.7)	3.0 (1.1)
	AS	154.1 (159.0)	17.9 (25.6)	190.5 (276.0)	18.7 (29.3)	314.2 (390.7)	30.4 (29.1)
	PS	7.4 (9.9)	0.4 (0.8)	5.6 (3.7)	0.4 (0.2)	9.3 (12.5)	0.5 (0.0)
TS+AS+PS [a]		200.1 (207.5)	23.6 (30.8)	228.9 (315.1)	21.8 (35.1)	354.8 (431.9)	33.9 (30.2)
Bedbugs/fleas/ mites	TS	15.8 (13.6)	NS	15.1 (15.1)	NS	16.7 (16.7)	NS
	PS	72.5 (90.5)		21.9 (33.7)		38.0 (53.0)	
TS+PS [b]		88.3 (104.1)	-	37.0 (48.8)	-	54.7 (69.7)	-
Wild ticks	TS	17.1 (15.4)	NS	15.0 (15.0)	1.8 (1.8)	31.8 (29.2)	0.1 (0.1)
	AS	550.8 (681.9)	33.6 (41.6)	642.6 (799.9)	NS	559.9 (619.5)	94.0 (104.0)
TS+AS [c]		567.9 (697.3)	33.6 (41.6)	657.6 (814.9)	1.8 (1.8)	591.7 (648.7)	94.1 (104.1)

Abbreviations: NS, not surveyed.

[a] combined amount of target application types of mosquitoes insecticide; [b] combined amount of target application types of budbugs/fleas/mites insecticide; [c] combined amount of target application types of wild ticks insecticide.

4. Discussion

The study mainly showed that the non-occupational prevalent household use of insect repellents in South Korea caused the potential exposure of their hazardous ingredients to users and their family including preschool children and children at home. The main users of insect repellents were adult consumers at home. Based on survey results, compared to use frequency and use amount of respondents with only adults, respondents with preschool children and children did not show the significantly different use frequency and use the number of insect repellents in the home. Preschool children and children are unintentionally exposed to insect repellents and their ingredients. The preschool children and children may be subject to both primary and secondary exposure of insect repellents. Preschool children and children could be applied to repellents used by adults at home or could experience secondary exposure as the non-user or bystander. Primary exposure is invariably higher than secondary exposure, however, preschool children and children may experience higher secondary exposure because of their high inhalation rate [20]. Preschool children and children exposed to household insect repellents occurs through any or all of two potential exposure routes: inhalation and dermal contact. Inhalation is the predominant exposure route of household insect repellents. This study is about exposure assessment study of insect repellents for household use via the respiratory route and is helpful to create the exposure database for household use in exposure assessments of insect repellents in terms of preschool children and children's health. This database includes the frequency, duration, amount per application, and the pattern of combined use, which is needed for exposure assessments. The lack of insect repellent exposure assessment was a major limitation of the health risk assessment study. Estimating human exposure to insect repellents is a fundamental element of the risk assessment process that requires quantifying the levels to which users are exposed to insect repellents.

Household insect repellents are most effective when used in combination with physical control measures, which aim at the elimination and reduction of pest breeding sites or keeping them away from human habitation [19]. Therefore, children in the home are exposed to several insect repellents and active ingredients. The predominant synthetic ingredients of insect repellent were DEET and picaridin in South Korea. *In vivo* toxicity mechanisms of DEET was reported as the catalase, acetylcholinesterase, glutathione-S-transferase activities inhibition, reduced oxygen flux, decreased triacylglycerol, enhanced acetylcholinesterase activity in cerebellum and others. Potential health hazard to human of DEET was cardiac arrest, poor fetal growth, and genotoxic [22]. A wide variation in applied concentrations has been associated with the reported cases of pediatric seizures or other major effects [23]. The mechanism of action of Picaridin is unknown [24].

Precaution should be measured to balance the risks between the prevention of insect-borne diseases and possible adverse effects of insect repellents on health. The duration and amounts of using insect repellents are an important parameter along with the dose/concentration level. The preschool children and children must not be exposed to any insect repellents or should be exposed to the only limited amount of insect repellents whatever the composition may be. The adverse event reports suggest that multiple combined applications of insect repellents can play a

role in toxicity and strengthen the need to follow the product label on reapplication. Despite the benefit of using repellent, the development of it may bring a concern to society. There are still major gaps in knowledge on the influence of insect repellent on human health and the environment.

This study results were based on the web-survey. Methods for data collection using web surveys have been well established. Online questionnaires have been demonstrated to be an inexpensive, convenient, and quick data collection method [25]. Considering these advantages, several researchers have used web surveys to collect data on exposure factors for consumer products [26−29]. In the web-survey study, respondents had to declare the frequency, duration, and amount of product used per application of insect repellents, given several options (S1).

Biocidal products such as insect repellents may be a valuable part of biocidal regulation in Korea. This approach might be useful in establishing guidelines of exposure assessment for studied respondents groups. To protect insect repellents users, preschool children, and children from several hazardous ingredients, more comprehensive exposure estimation and assumptions are needed. To improve the database available for assessing the exposure of insect repellent users, preschool children, and children, further research is required.

Conclusion

This study investigated a fundamental approach to assess human exposure to insect repellents used in daily life. The process of assessing exposure to insect repellents used in the home requires determining the patterns of use, exposure routes, and quantifying potential ingredients intake. This study determined the recent exposure factors of household insect repellents used by respondents group with preschool children, respondents group with children, respondents group with youths, and respondents group with only adults. The results of the present study substantially contribute to the state of knowledge regarding the combined inhalation exposure to retail insect repellents for preschool children. This knowledge will support recent efforts in Korea to accurately quantify and the health and safety of all inhabitants. Further research is required to improve overall health risk assessment methods by accounting for differences among infants, toddlers, children, youth, and adults in inhalation rates, body weights, exposure times, and other factors that may affect health, as well as the combined risks from inhalation and dermal contact exposures.

This study is meant to calculate the representative exposure coefficient value of Korean people by surveying the use of repellents and exposure coefficient on the nationwide scale. Compared with the overseas exposure coefficient handbook, the data is highly up-to-date, representative and reliable, and can be used as a basis for preparing objective evaluation data on risk assessment. Also, it is possible to simulate risk/stability of repellents in various home environments or use situations by estimating exposure coefficients, and provide guidance on how to use repellents properly for consumers and can be used for consumer education and information provision.

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Conflicts of Interest

The authors declare no competing financial interest.

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