Survey of Isothiazolinones and Other Preservatives in Household Wet Tissue Products in Japan

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Summary

Recently, many cases of contact dermatitis due to isothiazolinone preservatives in several types of household products used for cooling the body have been reported. As a result, the concentrations of isothiazolinone preservatives in these products were investigated. However, concentrations of isothiazolinone preservatives in other types of household products have not been studied adequately. In this study, 19 preservatives (including isothiazolinones) in 32 wet tissue products were investigated because these products come in direct contact with the skin. 2-Methyl-4-isothiazolin-3-one (MI), 5-chloro-2-methyl-4-isothiazolin-3-one (CMID), and benzisothiazolin-3-one (BIT) were detected in 19 samples (0.46–48 µg/g-wet), 17 samples (trace amount [tr.]–52 µg/g-wet), and one sample (67 µg/g-wet), respectively. Five types of para-benzenes were detected in 21 samples (tr.–834 µg/g-wet), 2-Bromo-2-nitropropane-1,3-diol (Bronopol), 3-iodo-2-propynyl N-butyricarbamate (IPBC), and phenoxyethanol were detected in 12 samples (4.7–254 µg/g-wet), 11 samples (tr.–62 µg/g-wet), and 4 samples (65–1159 µg/g-wet), respectively. The concentration levels of isothiazolinone preservatives detected in this study perhaps induce allergic contact dermatitis in patients who are already sensitive to these preservatives. However, only 3 products described the use of isothiazolinone preservatives and a cautionary note about the possibility of contact dermatitis due to isothiazolinone preservatives was not provided. We also found that preservatives detected in the samples were different from those indicated on the product (in some cases, names of preservatives were not indicated at all). The use of such products may expose consumers to the risk of contact dermatitis; moreover, when contact dermatitis occurs, the identification of the substance that causes it may be delayed. Therefore, it is desirable that manufacturers provide information about the components of wet tissue products on the product labels.

Key words: wet tissue, preservative, isothiazolinone, contact dermatitis, household product

Introduction

Recently, several types of household products used for cooling the body, such as gel-products (containing superabsorbent polymers) and polyvinyl alcohol (PVA) towels, have been developed, and the sale of these products in Japan has increased. However, several cases of contact dermatitis due to such products containing isothiazolinone preservatives have been reported. As a result, a voluntary recall of gel-products was issued by the suppliers and information about the use of PVA cooling towel was provided by the National Consumer Affair Center of Japan. Therefore, we have studied the concentration levels of several isothiazolinone preservatives in gel-products and PVA cooling towels.

Additionally, many cases of contact dermatitis related to isothiazolinone preservatives in various kinds of household products, such as paints, fabric softeners, detergent for toilet, ironing water, and wet tissue (wet wipe) products, have been reported in Europe and the U.S.A. It is necessary to grasp the actual concentration levels of isothiazolinone preservatives in these products. However, only a few studies have been conducted on isothiazolinone preservatives in household products, such as our previous studies on cooling products and household non-formalin adhesives for wallpaper in Japan. Thus, to prevent the occurrence of allergic contact dermatitis, a survey of isothiazolinone preservatives in household products to which consumers can be exposed is necessary.

Many cases of contact dermatitis due to isothiazolinone preservatives in wet tissue products have been reported in Europe and the USA because wet tissue products come in direct contact with the skin. Thus, we investigated the concentrations of five isothiazolinone preservatives in wet tissue products. Furthermore, non-isothiazolinone preservatives in wet tissue products, such as 2-bromo-2-(bromomethyl)pentanedinitrile (methylidibromo glutaronitrile (MDBGN)) and 3-iodo-2-propynyl N-butyricarbamate (IPBC), have been reported to cause contact dermatitis. Therefore, 14 types of non-isothiazolinone preservatives in wet tissue products were also investigated in this study.

Materials and methods

Samples

Since the consumer can easily purchase wet tissue products, 32 wet tissue products samples were purchased from several 100-yen
stores in Japan from January to February 2014 (details of these samples are provided in Table 1). Wet tissue products for infants were not purchased, because they are classified as cosmetic products in Japan.

Materials

2-Methyl-4-isothiazolin-3-one (MI) and 5-chloro-2-methyl-4-isothiazolin-3-one (CMI) were purchased from Waterstone Technology, LLC as a mixture (MI: 3.63%, CMI: 10.85%). Benzisothiazolin-3-one (BIT), 2-ω-ctyl-4-isothiazolin-3-one (OT), parabens (PBs) [methyl-paraben (Me-PB), ethylparaben (Et-PB), propylparaben (Pr-PB), isobutylparaben (Isobu-PB), and benzylparaben (Be-PB)], benzoic acid (BA), phenoxethanol (PE), 2-bromo-2-nitropropane-1,3-diol (Bronopol: BP), 5-bromo-5-nitro-1,3-dioxane (Bromidox), 2-mercaptobenzothiazole (MBT), and 3-iodo-2-propynyl N-butylcarbamate (IPBC) were obtained from Wako Pure Chemical Industries, Ltd. Milli-Q water was produced using a PTFE filter (pore size: 0.2 µm, ADVANTEC) and analyzed by high performance liquid chromatography with a photo diode array detector (HPLC/PDA).

Sample processing

In the first step, several sheets of wet tissue products were taken out from the upper part of the package. Then, these sheets were cut into small pieces and 1.0 g of the sample was weighed. This weighted sample was placed into a glass tube with 20 mL of methanol and shaken for 30 min using a horizontal shaker. After shaking, the sample was filtered using a suction funnel with a glass filter. The residue was washed with methanol and the wash was combined with the filtrate. The sample solution was concentrated to less than 5 mL with a rotary evaporator while the temperature of the water bath was maintained below 40°C. The volume of the sample solution was subsequently adjusted to 5 mL using methanol. The sample solution was filtered using a PTFE filter (pore size: 0.2 µm, ADVANTEC) and analyzed by high performance liquid chromatography with a photo diode array detector (HPLC/PDA).

HPLC/PDA analysis

All samples were analyzed using a Shimadzu NexeraX2 HPLC/mass spectrometry grade of formic acid was obtained from Wako Pure Chemical Industries, Ltd. Milli-Q water was produced using a Milli-Q Synthesis A10 system (Merck Millipore, Tokyo, Japan).

HPLC/PDA analysis  

All samples were analyzed using a Shimadzu NexeraX2 HPLC/

| No. | Country of manufacture | The ingredients described on the product¹ |
|-----|------------------------|---------------------------------------|
| 1   | Japan                  | ethanol, bactericide, benzalkonium chloride |
| 2   | Japan                  | water, propylene glycol, cetylpyridinium chloride, ethyl benzoate, methyl benzoate, alo extract |
| 3   | Japan                  | water, ethanol, PG, benzalkonium chloride, methylparaben, ethylparaben |
| 4   | Japan                  | water, PG, methylparaben, ethylparaben, benzalkonium chloride |
| 5   | Japan                  | water, benzalkonium chloride, BG, isopropylbutylcarbamate, grapefruit seed extract, sodium hydroxide carbonate |
| 6   | Japan                  | water, propylene glycol, cetylpyridinium chloride, ethylparaben, methylparaben, silver ion water |
| 7   | Japan                  | water, ethanol, PG, methylparaben, ethylparaben, benzalkonium chloride |
| 8   | Japan                  | ethanol, bactericide, benzalkonium chloride |
| 9   | Japan                  | ethanol, paraben, catam, PG, purified water |
| 10  | Japan                  | ethanol, benzalkonium chloride, paraben, purified water, perfume |
| 11  | Japan                  | propylparaduxonechloride, chlorhexidine gluconate, ethanol, perfume, purified water |
| 12  | South Korea            | water, ethanol, propylene glycol, chlorobenzal, methylchloroisothiazolinone, methylisothiazolinone, polymamipropyl biguanide, green tea extract |
| 13  | Japan                  | water, PG, benzalkonium chloride, isopropylbutykarbamate |
| 14  | Japan                  | water, BG, benzalkonium chloride, isopropylbutykarbamate, tea extract |
| 15  | Japan                  | water, propylene glycol, methylparaben, organic compound containing nitrogen and sulfur, ethylparaben, propylparaben, silver ion |
| 16  | Japan                  | purified water, ether, bactericide |
| 17  | Japan                  | water, PG, methylparaben, ethylparaben, propylparaben, propylene glycol, paraben, benzalkonium chloride |
| 18  | Japan                  | water, benzalkonium chloride, benzalkonium chloride, isopropylbutykarbamate |
| 19  | Japan                  | water, ethanol, BG, benzalkonium chloride, isopropylbutykarbamate |
| 20  | Japan                  | water, PG, methylparaben, ethylparaben, propylparaben, benzalkonium chloride |
| 21  | Japan                  | water, propylene glycol, ethylparaduxonebenzate, methylparaduxonebenzate, benzalkonium chloride |
| 22  | Japan                  | water, propylene glycol, benzal, nicotine, cetylpyridinium chloride, alo extract, perfume |
| 23  | Japan                  | water, PG, methylparaben, ethylparaben, benzalkonium chloride |
| 24  | Japan                  | water, propylene glycol, methylparaben, ethylparaben, benzalkonium chloride |
| 25  | Japan                  | water, propylene glycol, methylparaben, ethylparaben, benzalkonium chloride |
| 26  | Japan                  | purified water, propylene glycol, polhosanethanol, paraben, benzethionium chloride, glycerine, cetylpyridinium chloride, alo extract, perfume |
| 27  | Japan                  | water, PG, methylparaben, ethylparaben, propylparaben, tea extract, benzalkonium chloride |
| 28  | Japan                  | purified water, benzalkonium chloride |
| 29  | Japan                  | water, propylene glycol, benzalkonium chloride, alo vera, vitamin E, citric acid, methylparaben, bronopol, ethylenediaminetetraacetic acid, methylisothiazoline |
| 30  | Japan                  | water, purified water, benzalkonium chloride |
| 31  | Japan                  | ethanol, purified water, benzalkonium chloride, paraben, BG |

¹ List of ingredients provided on the product label.
system (Shimadzu, Kyoto, Japan) consisting of two LC-30AD pumps, a CTO-30A column oven, an SPD-M30A photodiode array detector, an SIL-30AC auto sampler, and a CBM-20A communication bus module. System control and data calibration were carried out using the Lab Solutions software (ver. 6.11) (Shimadzu, Kyoto, Japan). An InertSustain® Phenyl column (length 150 mm, internal diameter 3.0 mm, particle size 3 µm; GL Sciences, Inc., Tokyo, Japan) was used for separating the target compounds. Eluent A of ultrapure water containing 0.1% formic acid and eluent B of acetonitrile were used as the mobile phase. The gradient elution began with 25% of eluent B, which was held constant for 2 min, and increased linearly to 30% over 9 min, which was held constant for another 3 min. Then, eluent B increased linearly to 90% over 6 min, which was held constant for another 5.5 min. These gradient conditions are similar to those in the previous study\(^\text{5}\) with minor modifications. The flow rate, injection volume, and oven temperature were 0.6 mL/min, 5 µL, and 40°C, respectively. The monitoring wavelength ranged from 190 to 600 nm and UV-Vis spectra of the preservatives measured by PDA were used for identification of target compounds. The wavelengths used for the quantification of the analytes are shown in Table 3.

Results and discussion

Limits of detection and quantification

The HPLC chromatogram of the standard solution is shown in Fig. 1. Good separation of all the preservatives was observed. The retention times of the compound are listed in Table 3. The relative standard deviation of the retention times of every compound was below 0.06% (n=5).

Recovery tests were conducted by adding every compound to the sample (No.5) that did not contain the target compounds, except for IPBC that was detected below the limit of quantification (LOQ). The added amounts of the compounds were as follows: MI: 1.08 µg/g-wet; Bronidox, MDBGN, and IPBC: 50 µg/g-wet; other analytes: 5.0 µg/g-wet. The recovery tests were conducted in quadruplicate. The recoveries of target compounds and their coefficients of variation were 71–109% and 1.2–5.5%, respectively (Table 3). The limit of detection (LOD) was calculated according to JIS K 0124:2011\(^\text{21}\) using the standard deviation (SD) and t-value (t=1.71 for n=4) obtained from the recovery tests. LOQ was calculated as ten times of SD\(^\text{21}\). The LODs and LOQs are listed in Table 3. The LODs and LOQs of the analytes were in the ranges of 0.12–5.6 µg/g and 0.25–12 µg/g, respectively. The LODs and LOQs of bronidox, MDBGN, and IPBC were higher than those of other compounds because of their lower sensitivity than other chemicals.

Concentrations of the target compounds in wet tissue samples

The concentrations of the target compounds in the wet tissue samples are listed in Table 4. Three types of isothiazolinones (MI, CMI, and BIT), five types of paraBens (Me-PB, Et-PB, Pro-PB, Isobu-PB, and Bu-PB), BP, PE, and IPBC were detected in the samples. Other preservatives were not detected. A representative HPLC chromatogram obtained from sample No.6 is shown in Fig. 2. MI and CMI were detected in 19 samples (0.46–48 µg/g-wet) and 17 samples (trace amount [tr.]-52 µg/g-wet), respectively. BIT was detected in one sample (67 µg/g-wet). The detection frequencies of PBs were in the following order: Me-PB (21 samples, tr.-834 µg/g-wet), Et-PB (20 samples, tr.-748 µg/g-wet), Pro-PB (6 samples, 30–328 µg/g-wet), Isobu-PB (one sample, 42 µg/g-wet), and Bu-PB (one sample, 73 µg/g-wet). BP, IPBC, and PE were detected in 12 samples (4.7–254 µg/g-wet), 11 samples (tr.-62 µg/g-wet), and 4 samples (65–1159 µg/g-wet), respectively.

| Abbreviation | CAS number | Chemical formula | Molecular weight |
|--------------|------------|------------------|-----------------|
| 2-Methyl-4-isothiazolin-3-one | MI | 2662-20-4 | C₈H₇NO₂S | 115.15 |
| 5-Choro-2-methyl-4-isothiazolin-3-one | CMI | 26172-55-4 | C₈H₇CINO₂ | 149.60 |
| Benzisothiazolin-3-one | BIT | 2634-33-5 | C₇H₇NO₂S | 151.19 |
| 2-n-Octyl-4-isothiazolin-3-one | OIT | 26530-20-1 | C₁₃H₁₄NO₂S | 213.30 |
| 4,5-Dichloro-n-octyl-4-isothiazolin-3-one | 2C-OIT | 64359-81-5 | C₁₄H₁₃Cl₂NO₂S | 282.20 |
| Methy14-hydroxybenzoate (methylparaben) | Me-PB | 99-76-3 | C₈H₇O₃ | 152.15 |
| Ethyl14-hydroxybenzoate (ethylparaben) | Et-PB | 120-47-8 | C₈H₇O₃ | 166.18 |
| Isopropyl14-hydroxybenzoate (isopropylparaben) | Isoprop-PB | 4191-73-5 | C₁₁H₁₄O₂ | 180.20 |
| Propyl14-hydroxybenzoate (propylparaben) | Pro-PB | 94-13-3 | C₁₁H₁₀O₂ | 180.20 |
| Isobutyl14-hydroxybenzoate (isobutylparaben) | Isobu-PB | 2427-02-3 | C₁₁H₁₄O₂ | 194.23 |
| Butyl14-hydroxybenzoate (butylparaben) | Bu-PB | 94-26-8 | C₁₁H₁₀O₂ | 194.23 |
| Benzyl14-hydroxybenzoate (benzylparaben) | Be-PB | 94-18-8 | C₁₁H₁₀O₂ | 228.25 |
| 2-Bromo-2-nitropropane-1,3-diol (branopol) | BP | 52-51-7 | C₉H₉BrNO₂ | 199.99 |
| 2-Phenoxyethanol | PE | 122-99-6 | C₈H₁₀O₃ | 138.16 |
| Benzonic acid | BA | 65-85-0 | C₈H₈O₂ | 122.12 |
| 5-Bromo-5-nitro-1,3-dioxane | Bronidox | 30007-47-7 | C₈H₇BrNO₂ | 212.00 |
| 2-Mercaptobenzothiazole | MBT | 149-30-4 | C₇H₇NS₂ | 167.24 |
| 2-Bromo-(2-bromomethyl)-pentanediimine (methylkibromo glutaninitride) | MDBGN | 35691-65-7 | C₁₀H₁₀BrN₂O₂ | 265.93 |
| 3-Iodo-2-propynyl N-butylcarbamate | IPBC | 55406-53-6 | C₁₁H₁₆I NO₂ | 281.09 |
types of other preservatives were detected in the same sample. Although BIT was not detected in the gel-products used for cooling, an organic compound contained nitrogen and sulfur –49–, which might be intentionally used as preservatives because of their minimum inhibitory concentrations (MICs) for fungi and bacteria, which are 2–9 ppm (as mixture of MI and CMI) and 0.75–9 ppm (as mixture of MI and CMI) 23), respectively. However, it is also possible that MI and CMI were contaminated during manufacturing because several types of other preservatives were detected in the same sample. Although BIT was not detected in the gel-products used for cooling, PVA towels4–6, and adhesives for wall-paper 27–29), it was detected in the wet tissue sample (No. 15) in this study. For this product, the use of “organic compound contained nitrogen and sulfur” was indicated on the product label; this compound may correspond to BIT. The concentration of BIT detected from No. 15 was higher than its MIC (5–49 ppm for fungi and bacteria) 24). PBs were detected in many samples; some PBs detected in the sample did not coincide with the descriptions provided with the products. Although the use of BP was indicated for two products (No. 22 and 29), we also detected BP in other samples. BP was detected in the samples together with MI and CMI. A similar tendency was observed in PVA cooling towels5. Since a mixture of BP, MI, and CMI is used as a water-treatment agent in various industrial processes25), the mixture may also be used for wet tissue products.

### Table 3  Retention time, quantifying wavelength, limit of detection (LOD), limit of quantification (LOQ), and recovery of target compounds

| Chemicals | Retention time (min) | Wavelength (nm) | LODa (µg/g-wet) | LOQb (µg/g-wet) | Recoveryb (%) | CVc (%) |
|-----------|---------------------|----------------|----------------|----------------|---------------|--------|
| MI        | 1.73                | 273            | 0.12           | 0.25           | 106           | 1.5    |
| BP        | 2.17                | 195            | 0.40           | 0.84           | 95            | 1.8    |
| CMI       | 2.72                | 273            | 1.1            | 2.3            | 96            | 4.8    |
| BIT       | 3.29                | 226            | 0.72           | 1.5            | 104           | 3.0    |
| PE        | 4.22                | 195            | 1.0            | 2.2            | 94            | 4.6    |
| BA        | 4.52                | 195            | 0.14           | 0.30           | 106           | 1.3    |
| Mc-PB     | 4.93                | 256            | 0.35           | 0.75           | 108           | 2.3    |
| Bronidox  | 6.33                | 195            | 5.6            | 12             | 81            | 2.9    |
| Et-PB     | 7.37                | 256            | 0.41           | 0.87           | 108           | 3.0    |
| MBT       | 8.27                | 322            | 0.91           | 1.9            | 71            | 5.5    |
| MDBGN     | 8.67                | 195            | 4.5            | 10             | 92            | 2.6    |
| Isopro-PB | 10.37               | 256            | 0.45           | 0.95           | 107           | 1.8    |
| Pro-PB    | 11.02               | 256            | 0.61           | 1.3            | 107           | 2.4    |
| Isobu-PB  | 15.16               | 256            | 0.36           | 0.76           | 109           | 1.4    |
| Bu-PB     | 15.88               | 256            | 0.30           | 0.64           | 109           | 1.2    |
| IPBC      | 17.00               | 195            | 2.8            | 5.9            | 89            | 1.3    |
| OIT       | 17.46               | 273            | 0.64           | 1.4            | 107           | 2.5    |
| Be-PB     | 17.68               | 256            | 0.73           | 1.6            | 105           | 3.0    |
| 2CI-OIT   | 19.80               | 283            | 0.93           | 2.0            | 80            | 5.0    |

a The definition of abbreviations are described in Table 2.

b LOD was calculated according to JIS K0124:2011 using the standard deviation (SD) and t-value (t = 4.71 for n = 4) obtained from the recovery test. (MI: 1.67 µg/g-wet; Bronidox, MDBGN, and IPBC: 50 µg/g-wet; others: 5 µg/g-wet)

c LOQ was calculated as ten times of SD.

d Coefficient of variation.

### Safety of wet tissue products

In December 2014, Cosmetics Europe - The Personal Care Association recommended that the use of MI in leave-on skin products (including cosmetic wet wipes) be discontinued because of an increase in the number of patients showing a positive reaction to MI30). The wet tissue products investigated in this study are not cosmetic products, and hence, they fall under this recommendation. The concentrations of the mixture of MI and CMI (in µg/g-wet) observed in two samples (No. 6 and 28) were higher than the regulated values (as a mixture: 15 µg/g, MI: 3.75 µg/g, CMI: 11.25 µg/g) for cosmetic products in the EU27), the USA32), and Japan34). Furthermore, cases of contact dermatitis caused by wet tissue products containing MI or the mixtures of MI and CMI (10–34 µg/g) have been reported in previous studies11, 13, 15). Therefore, it is necessary to use wet tissue products with care, especially for patients who are already sensitive to isothiazolinone preservatives, because wet tissue products come in direct contact with the skin. Furthermore, since some cases of perianal allergic contact dermatitis due to the use of wet tissues containing MI and CMI around the anus have been reported11, 12, 14, 15), these wet tissues should be used carefully in sensitive areas such as the perianal area.

In the EU, the concentration of BP in the cosmetic products is regulated to be below 0.1%27). Case of occupational contact dermatitis due to BP30) and positive reactions to BP in patch tests have been reported15, 31). These papers reported that skin irritation and allergic responses in the patch test were induced at BP concentrations of 0.5% and 0.25%, respectively30–32). Since the highest concentration of BP detected in this study was 254 µg/g-wet, skin sensitization by BP in the
Fig. 1 HPLC chromatograms of the standard solution (MI: 6.73 µg/mL; other preservatives: 20 µg/mL). (a: 195 nm, b: 226 nm, c: 256 nm, d: 273 nm, e: 283 nm, f: 322 nm) (The definition of abbreviations are described in Table 2)
wet tissue products studied in this survey is not likely to occur.

Regulated values of IPBC in leave-off products, leave-on products, and deodorant products are below 0.02%, 0.01%, and 0.0075%, respectively, in the EU. In Japan, the concentration of IPBC in cosmetic products must be less than 0.02%. Although the use of 0.2% IPBC solution was recommended for the patch test, a positive reaction to 0.1% IPBC solution was reported for a patient who worked in a wood widow frame manufactory. However, IPBC concentrations in wet tissue products have not been reported in the cases of contact dermatitis due to wet tissue products. Furthermore, the concentrations of IPBC detected in this study were lower than the regulated value in the EU. Thus, skin sensitization due to IPBC in wet tissue products studied in this survey probably did not occur. However, because IPBC was also used as a wood preservative and a household antimicrobial agent, it is necessary to carefully use wet tissues containing IPBC for patients who are already sensitive to IPBC. Cross-reactivity between IPBC and thiurams has also been reported because both compounds contain carbamate functionalities. Therefore, it is necessary that patients who are already sensitized to thiurams should be careful while handling household products containing IPBC.

In Japan, the concentrations of PBs and PE used in cosmetic products and quasi-drugs must be less than 1.0%. The concentrations of PBs detected in this study were higher than the concentrations of other preservatives; however, the PB concentrations were below 1.0% in all samples. Furthermore, a negative patch test reaction was reported in the patch test using PE.

Table 4  Concentrations of preservatives in the wet tissue samples

| No. | Isothiazolinones (µg/g-wet) | Parabens (µg/g-wet) | Other preservatives (µg/g-wet) |
|-----|--------------------------|----------------|-----------------------------|
|     | MI | CMI | BIT | Me-PB | Et-PB | Pro-PB | Isobu-PB | Bu-PB | BP | PE | IPBC |
| 1   | b | - | - | 723 | 748 | - | - | - | - | - | - |
| 2   | 3.0 | - | - | 58 | 66 | - | - | - | - | - | - |
| 3   | 0.62 | 0.87 | - | 317 | 357 | - | - | - | 25 | - | - |
| 4   | 0.54 | 2.6 | - | - | - | - | - | - | 6.5 | - | - |
| 5   | - | - | - | - | - | - | - | - | - | - | - |
| 6   | 8.6 | 19 | - | 103 | 122 | - | - | - | 120 | - | - |
| 7   | 3.7 | 11 | - | 366 | 176 | - | - | - | 46 | - | - |
| 8   | - | - | - | 695 | 729 | - | - | - | - | - | - |
| 9   | 1.3 | 5.6 | - | 207 | 100 | - | - | - | 5.0 | - | - |
| 10  | 0.80 | 4.6 | - | 382 | 186 | - | - | - | 4.7 | - | - |
| 11  | - | - | - | 507 | 198 | - | - | - | - | - | - |
| 12  | 3.6 | 7.5 | - | - | - | - | - | - | - | - | - |
| 13  | 0.46 | 3.8 | - | - | - | - | - | - | 6.4 | 16 | - |
| 14  | - | - | - | - | - | - | - | - | - | - | 7.8 |
| 15  | - | - | 67 | 389 | 206 | 70 | - | - | - | - | - |
| 16  | 2.2 | tr. | - | - | - | - | - | - | 209 | 27 | - |
| 17  | - | - | - | 278 | 147 | 161 | - | - | 82 | 19 | - |
| 18  | - | - | - | - | - | - | - | - | - | - | 6.2 |
| 19  | - | - | - | - | - | - | - | - | - | - | 20 |
| 20  | - | - | - | 834 | 310 | 328 | - | - | - | - | - |
| 21  | 5.0 | 6.5 | - | 57 | 65 | - | - | - | 33 | - | - |
| 22  | 1.1 | 3.1 | - | tr. | tr. | - | - | - | 245 | 62 | - |
| 23  | - | - | - | 615 | 640 | - | - | - | - | - | - |
| 24  | 3.7 | 10 | - | 426 | 199 | - | - | - | 33 | - | - |
| 25  | 3.3 | 9.0 | - | 381 | 192 | - | - | - | 28 | - | - |
| 26  | - | - | - | 159 | 54 | 30 | 42 | 73 | 1159 | - | - |
| 27  | - | - | - | 219 | 118 | 136 | - | - | - | 65 | - |
| 28  | 48 | 52 | - | - | - | - | - | - | - | - | - |
| 29  | 1.1 | tr. | - | - | - | - | - | - | 254 | 42 | - |
| 30  | 3.3 | 6.2 | - | 783 | 3.3 | - | - | - | - | - | - |
| 31  | 1.1 | 4.9 | - | 262 | 135 | - | - | - | 6.7 | - | - |
| 32  | 26 | - | - | - | - | - | - | - | - | - | 48 |

* The definition of abbreviations are described in Table 2.  b Not detected.  ^ Between the LOD and LOQ.
tion by PBs and PE is not likely to occur in wet tissue products investigated in this survey.

Although isothiazolinone preservatives were detected in 20 products in this study, only three products indicated the use of isothiazolinone preservatives, and a cautionary note informing about the possibility of contact dermatitis due to isothiazolinone was not provided. We also found that preservatives detected in the samples were different from those indicated on the products (in some instances, name of preservatives were not indicated at all). The use of these products may expose consumers to the risk of contact dermatitis. Furthermore, it is likely that in such a situation, the identification of the substance causing contact dermatitis may be delayed when contact dermatitis due to these products occurs. Thus, it is desirable that manufacturers provide information about the components of wet tissue products on product labels.

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