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Evaluation of the effectiveness of personal protective equipment against occupational exposure to *N*,*N*-dimethylformamide

S.-M. Wang [a], T.-S. Shih [b,c], Y.-S. Huang [d], M.-R. Chueh [d], J.-S. Chou [b], H.-Y. Chang [a,*]

[a] *Department of Environmental and Occupational Health, Medical College, National Cheng Kung University, Tainan, Taiwan, ROC*
[b] *Institute of Occupational Safety and Health, Council of Labor Affairs, Taipei, Taiwan, ROC*
[c] *Graduate Institute of Environmental Health, College of Public Health, China Medical University, Taichung, Taiwan, ROC*
[d] *Center for Environmental, Safety and Health Technology, Industrial Technology Research Institute, Hsin Chu, Taiwan, ROC*

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Abstract

The objectives of this study were to evaluate the protective effectiveness of various personal protective equipment and the respective exposure contributions from respiratory and skin exposures of *N*,*N*-dimethylformamide (DMF) with a self-comparison study design. Two high-, four intermediate- and four low-DMF exposure workers from a synthetic leather factory were monitored in airborne DMF concentrations and *N*-methylformamide (NMF) concentrations in urine across four consecutive days. The workers were designated to wear no personal protective equipment on the first day. The barrier cream, rubber gloves and rubber gloves plus respirator were used on the second, third and fourth days, respectively. Person-to-personal observation was performed in the field to record all high and low exposure tasks during work for each subject. Protective effectiveness index (PEI) was used to evaluate different glove effectiveness. We concluded that the direct skin contact to the strong skin penetrates like DMF could be a more significant exposure source than the respiratory exposure in the actual occupational environment. The provision of protective equipment from skin exposure could be more important than that from respiratory exposure. The application of barrier cream could be as effective as wearing impermeable rubber gloves in the prevention from the skin penetrate in the occupational settings.

Keywords: *N*,*N*-Dimethylformamide; Dermal exposure; Protective effectiveness; Gloves; Biological monitoring

1. Introduction

N,*N*-Dimethylformamide (DMF) is widely used in various industries because of its complete miscibility with water and most organic solvents. The potentially exposed workers and the lowest observed adverse effect level (LOAEL) of DMF estimated by National Occupational Exposure Survey (NOES) and National Toxicology Program (NTP) were over 100,000 workers and less than 250 mg/kg/day. Therefore DMF has been identified as one of four chemicals with the highest priority for human field study [1].

The major health effects after exposure to DMF include alcohol intolerance [2–4], hepatotoxicity [5,6], male reproductive cancers, possible embryotoxicity, teratogenicity in humans and animals [7–9], and sperm motility perturbation in humans [10].

DMF could be administered to humans through the skin or inhalation. A study conducted by volunteers in an exposure chamber reported that about 40.36% of the total DMF uptake was attributed to dermal absorption [11]. Another study conducted in the field concluded that dermal exposure provided a substantial contribution to the total DMF body burden [12]. Therefore, effectively reducing skin exposure to such a potent skin penetrant like DMF becomes an important issue in occupational health.

The DMF skin absorption could originate from vapor exposure and direct skin contact to DMF liquid in the actual occupational setting. A previous study demonstrated that the number of DMF biomarkers in urine after the sole of one hand was immersed in pure DMF solution for 15 min was similar to that after exposure to 60 mg/m^3 (=two-fold concentration of allowable DMF exposure recommended by US-NIOSH) of DMF via the inhalation route for 8 h [13]. Therefore it suggested that to avoid contact with DMF liquid could be more important than contact with DMF vapor. Wearing gloves is the most

* Corresponding author. Tel.: +886 6 2378754; fax: +886 6 2743748.
E-mail address: h7154@mail.ncku.edu.tw (H.-Y. Chang).

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popular way to avoid direct skin contact with liquid hazardous agents. Gloves were extensively used in occupational environments because they provide the capability to effectively reduce skin exposure and protect the skin from injury. Although the impermeable rubber gloves have demonstrated that the ability to reduce the skin exposure was significantly higher than that of cotton gloves [14], they are not feasibly popular in the actually occupational settings because of their discomfort and inconvenience during work. There is a need to consider other alternatives in skin protective equipment. Barrier cream was widely used as a prevention measure in occupational dermatitis [15,16] but rarely used for exposure reduction. In the literature, barrier creams could reduce or prevent chemicals from penetrating into the skin by developing a physical barrier between the skin and the irritant [17–19]. Compared with wearing impermeable gloves, using barrier cream seems more acceptable by workers. Therefore, we also tried to evaluate the protection effectiveness of barrier cream in preventing skin exposure to DMF. The objectives of this study were to evaluate the protective effectiveness of different personal protective equipment including conventional methods like rubber gloves and respirators, and another alternative, barrier cream. The contribution of DMF administered into the body via different routes was also investigated.

2. Experimental/materials and methods

2.1. The orientation of the manufacturing process and the subject recruitment and classification

A factory located in Southern Taiwan in the production of synthetic leather sheets was selected for this study. In the synthetic leather manufacturing procedure, dry and wet processes are classified based on the way solvent are expelled from the products, although both processes are virtually the same. In the wet process raw materials, resin, dyes and cellulose are mixed homogeneously and dissolved in a solvent containing only water and DMF (mixing). The mixture is then applied onto a base-textile made of cotton, man-made cotton, or polyester sheet. The coated textile is then washed with water several times to remove the residual solvents (coating). The product of the wet process (coated textile) is then further used in the dry process. Dry process mixing is similar to that in the wet process except that the solvents are a mixture of DMF, methyl ethyl ketone, and toluene, instead of DMF and water. The mixture is then applied onto the wet process coated textile (coating) and then heated in an oven to remove the solvents. The products achieved from wet and dry processes are then examined and further color and surface texture modified by adding pigments and/or mounting materials to accommodate the individual customers' requests (post treatment). Basically, DMF exposure is the highest in the "coating" process because it involves an open operation with a heating condition. The second highest exposure is in the "mixing" process because it involves a vigorous rotation procedure. DMF evaporation in "mixing" is not as high as in "coating" because the former occurs in an enclosed condition.

Fifteen workers were selected from three major processes. They were classified into three exposure groups: high, intermediate, and low based on their main job. Ten workers were defined as "high exposure" and intermediate exposure" groups (five for each) whose main tasks (over 50% in their total working hours) were "coating" and "mixing", respectively. Another five workers were grouped into "low exposure" if their main job were "post treatment". Each worker in the factory was designated to do other tasks during the whole 8 h work shift in addition to their main job. To ascertain the exact task allocation for each worker, we recorded their detailed activities from the beginning to the end of work using close on site observation. The task-time allocation for each worker was completed by recording their time proportion as "high exposure task" if his tasks were "coating" or "mixing" and as "low exposure task" if his tasks were "post treatment".

2.2. Personal protective equipment scenario

Different types of personal protective equipment (PPE) were used across four consecutive days to evaluate the protective

Table 1
Demographic information and the exposure characteristics for 10 selected workers from the synthetic leather factory in this study

Job[a]	Task[b]		Age	Work duration (years)	Cigarette smoking	Alcohol drinking
	High exposure time (%)	Low exposure time (%)				
High	75	25	40	14	Yes	Yes
High	75	25	42	13.4	Yes	Yes
Intermediate	60	40	40	8.2	No	No
Intermediate	60	40	36	12.8	Yes	Yes
Intermediate	50	50	43	14	Yes	Yes
Intermediate	50	50	45	19.3	Yes	Yes
Low	20	80	30	8	No	No
Low	25	75	47	16	No	Yes
Low	25	75	37	11	Yes	Yes
Low	25	75	32	9	Yes	Yes

[a] The workers were classified into three exposure groups: high, intermediate, and low based on their main job. "High exposure" and "intermediate" groups were defined as the workers whose main tasks (over 50% in their total working hours) were "coating" and "mixing", respectively. Other workers were grouped into "low exposure" if their main job was "post treatment".

[b] The task-time allocation for each worker was completed by recording their time proportion as "high exposure task" if his tasks were "coating" or "mixing" and as "low exposure task" if his task was "post treatment".

effectiveness. For the first experiment day the selected workers wore no PPE because PPE were not usually used in this industry. Barrier cream, rubber gloves (MAPA NS-450; 30 mil in thickness, 16 in. in length, flock-lined lining; polymer, natural rubber inner layer and neoprene outer layer), and rubber gloves plus respirator (R95 respirator, 3M 8247, St. Paul, MN, USA; this product was tested and met the performance requirements of AS/NZS 1716-1994 and has been approved by WorkCover NSW, approval number 2142) were used on the second, third and fourth experiment days respectively. The rubber gloves and respirator were used only in the higher DMF exposure task, such as DMF liquid contact. Moreover, in order to evaluate the effectiveness more accurately we observed the work process for each worker and recorded the task details and the frequency of using solvents and PPE. We excluded several workers that exhibited little willingness to follow the experimental strategy, wearing PPE during work and asking for leave during the experiment period. Finally, only 10 workers were used in the daily analysis (Table 1).

2.3. Calculation of the contribution of total body burden from different exposure routes

All of the DMF-exposed workers were expected to have high and low DMF exposure via skin and inhalation exposure routes. According to different exposure routes and exposure types, high and low DMF exposure, the total body burden (TBB) could be contributed from high and low DMF exposure via both skin and inhalation routes. The TBB contribution equations are shown in Table 2. The contribution from different exposure routes was calculated using these equations.

2.4. Environment monitoring

The sampling and analytical methods previously published by our group were adopted in this study [12]. A passive air sampler containing activated charcoal (3M Co., Model 3500, St. Paul, USA) was used to monitor the 8-h time weighted average airborne DMF concentrations across four experimental days in this study. All air samplers were stored at −20 °C prior to analysis. The collected samples were extracted with 1.5 mL mixture solvent containing 80% carbon disulfide (HPLC grade; Tedia, Fairfield, OH, USA) and 20% *n*-pentanol (American Chemical Society Certified; Fisher Scientific, Pittsburgh, PA, USA) for 30 min and then were analyzed using a gas chromatograph (GC) equipped with thermionic sensitive detector (Varian 3600CX GC/TSD; GenTech Scientific Inc., Arcade, NY, USA) coupled to an auto-sampler (Varian 8200 CX, GenTech).

2.5. Biological monitoring

Post shift urine samples were collected for four consecutive days from each worker. Each urine sample was kept in an ice bucket right after collection and then stored at −80 °C before instrumental analysis. Urinary *N*-methylformamide (NMF) was analyzed according to a previously published method [12]. In brief, promptly thawed urine samples at 37 °C were centrifuged at 5000 rpm for 20 min. The supernatant (0.5 mL) was added to 0.5 mL methanol (HPLC grade, Tedia), kept in a 4 °C ice bath for 15–20 min, and then further centrifuged at 5000 rpm for 10 min before GC analysis.

3. Results

3.1. Environmental monitoring

Airborne DMF concentrations across four consecutive days showed the concentration ranges were group-dependent (Fig. 1). The high exposure concentrations were consistently highest, following by the intermediate, and the low exposure the lowest. The airborne DMF concentrations for high DMF exposure workers ($n = 2$) across four working days all higher than the permissible exposure limit (10 ppm). Although, in general, there were no statistical differences across 4 days in airborne DMF concentrations except for the low exposure group, in which the variability across the 4 days were substantial. Moreover, the concentrations for the third and the fourth days were significantly higher than those for the second day ($p < 0.05$). This suggested that higher variations of airborne DMF concentrations existed for

Table 2
The conditions of wearing personal protective equipment on four consecutive days and their exposure scenarios

Weekday	PPE scenario	Exposure route and type[a,b]	Total body burden (urine concentration, mg/L)[c,d,e]
1	Without wearing any PPE	Skin: H and L Inhalation: H and L	Cskin-H + Cskin-H + Cinh-L + Cinh-L
2	Applying barrier cream	Skin: unexposed Inhalation: H and L	
3	Wearing rubber gloves in high exposure task	Skin: L Inhalation: H and L	Cskin-L + Cinh-H + Cinh-L
4	Wearing rubber gloves plus respirator in high exposure task	Skin: L Inhalation: L	Cskin-L + Cinh-L

[a] H: high exposure task.
[b] L: low exposure task.
[c] Cskin: total body burden concentration contributed from skin exposure.
[d] Cinh: total body burden concentration contributed from inhalation exposure.
[e] Equation for calculation of total body burden contribution: Cskin-P = [Cskin-P + Cskin-R + Cinh-P + Cinh-R (week day 1)] − [Cskin-R + Cinh-P + Cinh-R (week day 3)]; Cinh-P = [Cskin-R + Cinh-P + Cinh-R (week day 3)] − [Cskin-R + Cinh-R (week day 4)].

Table 3
Concentrations of urinary NMF (mg/l) across four consecutive days for the workers among the three groups

	Day 1 Without wearing any PPE[a]		Day 2 Applying barrier cream[a]		Day 3 Wearing rubber gloves[a]		Day 4 Wearing rubber and respirator[a]	
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
High exposure group ($n = 2$)	32.6	10.5	13.2	6.8	19.2	14.2	13.1	3.3
Intermediate exposure group ($n = 4$)	10.7	5.6	7.9	4.3	5.7	3.8	7.0	2.2
Low exposure group ($n = 4$)	3.0	0.7	0.9	0.4	2.4	0.8	3.9	3.2

[a] PPE (personal protective equipment) condition.

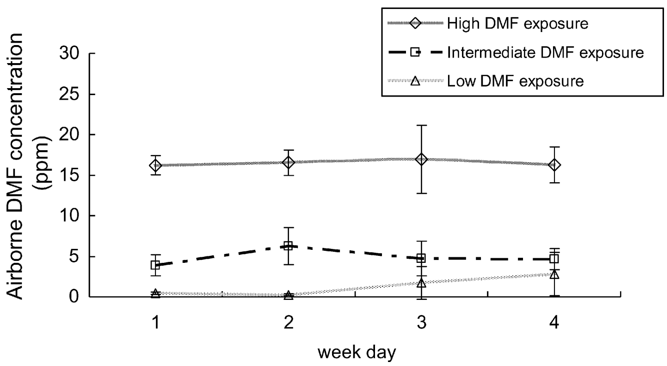

Fig. 1. Airborne DMF concentrations among three groups across four experimental days.

low DMF exposure workers than high and intermediate DMF exposure workers.

3.2. Biological monitoring

With the urinary NMF (U-NMF) concentrations distribution across 4 days, the highest concentrations were observed on day 1 for the high, intermediate exposure groups (Table 3). For the high exposure group the airborne DMF concentrations were almost constant across the four working days. However, the U-NMF concentrations were highest (32.6 ± 10.5 mg/L) in the day 1(without wearing any PPE) which was not only higher than the BEI value (15 mg/L) suggested by ACGIH but also apparently higher than the rest of the days, which were about 13.2, 19.2, and 13.1, for the second, third, and fourth days, respectively. For the intermediate exposure group, the highest U-NMF concentrations of 10.7 mg/L were found on the day 1, following by 7.9, 5.7, and 7.0 on the days 2, 3, and 4, respectively. For the low exposure group, the A-DMF concentrations were almost constant for the days 1 and 2. However, the U-NMF concentrations for day 1 (without wearing any PPE) were 3.0 mg/L, marginally higher than day 2 (applying barrier cream) ($p = 0.07$ by Wilcoxon matched pairs test). Therefore applying barrier cream during the work shift could actually reduce the DMF exposure. In contrast, the U-NMF concentrations on days 3 (wearing rubber gloves) and 4 (all PPE) were 2.4 and 3.9 mg/L, even higher than that on day 1 (without wearing any PPE), possibly because of apparently higher A-DMF concentrations on days 3 and 4 (almost as four- and seven-fold) than the day 1.

We could evaluate the average of the total body burden reduction with different PPE conditions for different exposure groups if the average U-NMF concentration on day 1 (without wearing any PPE) was considered as 100%. For the high exposure group, about 60%, 40% and 60% reductions were found when applying barrier cream (day 2), wearing rubber gloves (day 3), and wearing rubber gloves plus respirator (day 4) (Fig. 2). For intermediate exposure group, comparing with the U-NMF concentrations on the day 1 (without wearing any PPE), the reduction percentages on days 2, 3 and 4 were about 25%, 45%, and 35%, respectively. For the low DMF exposure group, they were 70%,

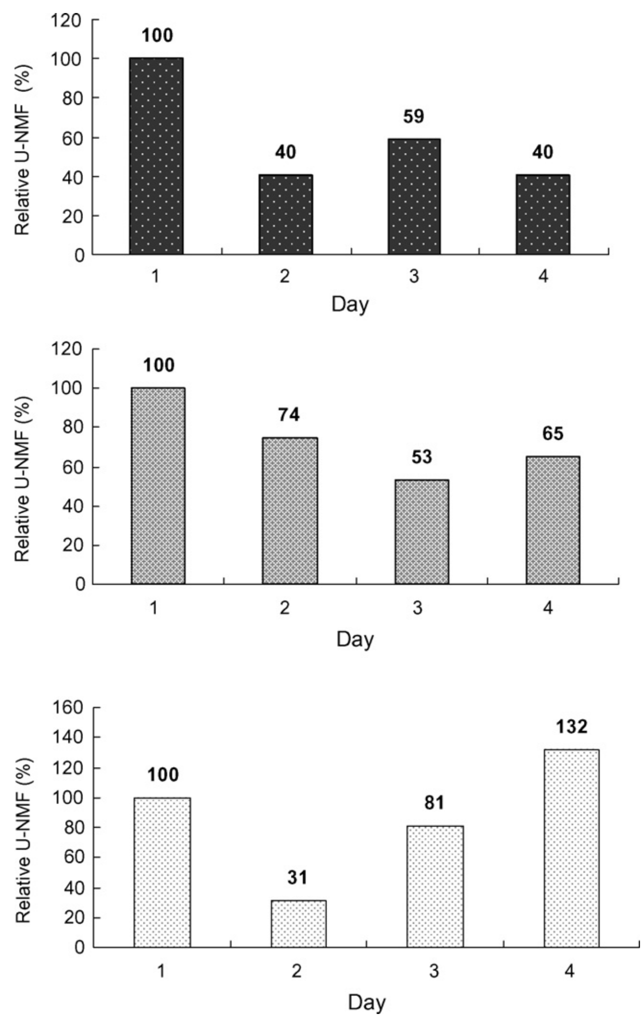

Fig. 2. The relative U-NMF concentration across four consecutive days compared with U-NMF on the day 1 (%). *Note:* (1) top, high exposure group; (2) middle, intermediate exposure group; (3) bottom, low exposure group.

Table 4
The contribution of different exposure routes with high/low DMF exposure task to U-NMF and adjusted U-NMF

Subject	Exposure route and type[a,b,c]	U-NMF (mg/L)[d]	Contribution to U-NMF (%)[e]	Adjusted U-NMF (mg/L ppm^{-1})[f]	Contribution to adjusted U-NMF (%)[g]
High exposure group ($n = 2$)	Cskin-H	13.48 ± 3.69	41.3	0.77 ± 0.35	37.8
	Cinh-H	6.05 ± 10.87	18.5	0.44 ± 0.83	21.5
	Cskin-L + Cinh-L	13.12 ± 3.27	40.2	0.83 ± 0.32	40.7
Mid exposure group ($n = 4$)	Cskin-H	4.96 ± 5.11	46.5	1.06 ± 1.34	38.6
	Cinh-H	−1.27 ± 5.12	−11.9	0.10 ± 1.35	3.6
	Cskin-L + Cinh-L	6.97 ± 2.19	65.4	1.59 ± 0.66	57.8
Low exposure group ($n = 4$)	Cskin-H	0.56 ± 0.72	18.9	3.97 ± 0.76	60.2
	Cinh-H	−1.50 ± 3.89	−50.5	1.03 ± 2.11	15.6
	Cskin-L + Cinh-L	3.91 ± 3.20	131.6	1.60 ± 0.30	24.2

[a] Cskin-H: the contribution of U-NMF in the body from skin DMF exposure in high exposure tasks.
[b] Cinh-H: the contribution of U-NMF in the body from respiratory DMF exposure in high exposure tasks.
[c] Cskin-L + Cinh-L: the contribution of U-NMF in the body from both skin and respiratory DMF exposures in low exposure tasks. Adjusted U-NMF, equations for contribution to adjusted U-NMF.
[d] For Cskin-H: U-NMF in day 1 − U-NMF in day 3; for Cinh-H: U-NMF in day 3 − U-NMF in day 4; for Cskin-L + Cinh-L: U-NMF in day 4.
[e] Contribution to U-NMF (%) = the proportion of Cskin-H or Cinh-H or (Cskin-L + Cinh-L) among the sum of Cskin-H + Cinh-H + (Cskin-L + Cinh-L).
[f] Adjusted U-NMF for Cskin-H: (U-NMF in day 1/airborne DMF in day 1) − (U-NMF in day 3/airborne DMF in day 3); for Cinh-H: (U-NMF in day 3/airborne DMF in day 3) − (U-NMF in day 4 /airborne DMF in day 4); for Cskin-L + Cinh-L: (U-NMF in day 4/ airborne DMF in day 4).
[g] Adjusted contribution to U-NMF (%) = the proportion of adjusted Cskin-H or Cinh-H or (Cskin-L + Cinh-L) from column 3 among the sum of adjusted Cskin-H + adjusted Cinh-H + adjusted (Cskin-L + Cinh-L).

20% and −30%, respectively. This suggested that applying barrier cream could provide highest protection from DMF exposure when the DMF exposure was high (i.e., A-DMF > PEL) or low (i.e., A-DMF < 2 ppm) and the protection effectiveness could be even better than the wearing of rubber gloves, almost equivalent to the impermeable gloves plus respirator. When the DMF exposure at intermediate levels (i.e., A-DMF about 5 ppm), wearing rubber gloves would be the most effective measure to reduce the exposure.

3.3. Total body contribution via skin and inhalation exposure

The U-NMF concentrations in day 1 (without wearing any PPE) subtracting day 3 (only wearing rubber gloves) for the same individual were used to evaluate the contribution of U-NMF in the body from skin DMF exposure in high exposure tasks (Cskin-H). In the same analogue, the U-NMF in day 3 subtracting day 4 (wearing rubber gloves + respirator) were used to evaluate the contribution of U-NMF in the body from respiratory DMF exposure in high exposure tasks (Cskin-H). Finally, U-NMF concentrations on day 4 were used to evaluate the contribution from both skin and respiratory DMF exposures in low exposure tasks (Ckin-L + Cinh-L). For high exposure group, the contribution to individual U-NMF for skin exposure in high exposure tasks of 41%, was similar to that from both skin and inhalation exposures in the low exposure tasks (40%), higher than that inhalation in high exposure tasks (18%) (Table 4). Due to the U-NMF in day 3 lower than day 4 in both intermediate and low exposure groups, negative contributions in the calculation of inhalation in high exposure tasks were found. When further examining the data carefully, we found the airborne DMF concentrations in day 3 were lower than that in day 4 and possibly causing the misleading outcome. To correct the possible unequal airborne concentration between days, adjusted U-NMF and adjusted NMF contribution (%) were used to evaluate the actual contribution percentage, as shown in Table 4. Using the adjusted indices, we found the skin exposure in high exposure tasks, the inhalation in high exposure tasks, and the skin and inhalation exposures in the low exposure tasks, and were 38%, 22%, and 41%, almost identical to those estimates prior to the adjustment. This suggested that the adjustment would not affect the actual estimates. Based on the adjusted approach, we found that for the intermediate exposure, the contribution from the skin and inhalation exposures in the low exposure tasks (58%) were highest, following by the skin exposure in high exposure tasks (39%), and lowest of the inhalation in high exposure tasks (4%). For the low exposure group, the high to low order were Cskin-H (60%), Cskin-L + Cinh-L (24%) and then Cinh-H (16%). Although the highest and second-highest contribution sources were somewhat different in the three groups, Cinh-H revealed the lowest contribution consistently among three groups. The above mentioned results suggested that the prevention from skin exposure for the potent skin penetrate like DMF could not be overlooked. Furthermore, the contribution from low exposure tasks were found about 41%, 58%, and 24%, for high, intermediate and low exposure groups, respectively. This implied that the exposure prevention for low exposure tasks should not be disregarded.

3.4. Evaluation of the adjusted PPE protective effectiveness index

To evaluate the protective effectiveness for various PPE, adjusted protective effectiveness index (PEI_{adj}) was used to

Table 5
Adjusted protective effectiveness index (PEI_{adj}, %) among different personal protective equipment

PEI (%)	BC[a]		RG[b]		RG + Res[c]	
	Mean	CV (%)	Mean	CV (%)	Mean	CV (%)
PEI_{adj-H}[d]	62	1	45	17	59	0.2
PEI_{adj-M}[e]	40	12	36	11	37	9
PEI_{adj-L}[f]	29	9	63	5	75	2
$PEI_{adj-total}$	40	4	49	3	57	3

[a] BC: barrier cream.
[b] RG: rubber gloves.
[c] Res: respirator.
[d] H: high exposure group.
[e] M: intermediate exposure group.
[f] L: low exposure group.

reduce the effect of different airborne DMF concentration during the experiment periods. Therefore the ratio of urinary NMF concentration to airborne DMF concentration was used to calculate the adjusted PEI.

The equation is shown below

$$PEI_{adj}\,(\%) = \{[(\text{U-NMF without PPE/A-DMF day 1}) - (\text{U-NMF with PPE/A-DMF day } i)]/(\text{U-NMF without PPE/A-DMF day 1})\} \times 100$$

The PEI results showed that applying barrier cream during the work shift could provide 40% effectiveness to prevent DMF exposure. Wearing rubber gloves and rubber gloves plus a respirator could provide 49% and 57% effectiveness to prevent DMF exposure, respectively. Because DMF exposure could vary depending on the different tasks in occupational settings, the PEI values were calculated in different DMF exposure scenarios including high, intermediate and low DMF exposure workers to evaluate the effectiveness of various PPE in different exposure groups. For the high exposure group, applying barrier cream during work shift could provide 62% effectiveness to prevent DMF exposure. Wearing rubber gloves and rubber gloves plus a respirator could provide 45% and 59% effectiveness to prevent DMF exposure, respectively. The variations in PEI values, however, were higher for the intermediate and low exposure groups. Applying barrier cream at work could provide 40% and 29% effectiveness. Wearing rubber gloves could provide 36% and 63% effectiveness. Wearing rubber gloves plus a respirator could provide 37% and 75% effectiveness for intermediate and low exposure group, respectively. The above-mentioned findings have shown that using PPE during the work could reduce DMF exposure to different degrees depending on exposure scenarios (Table 5).

4. Discussion

The protective effectiveness for various personal protective equipment have been evaluated using biological monitoring results, e.g., contaminant levels in urine or in blood for the studies using human subjects. The biological monitoring assessment methodology, however, has inevitable limitations from the wide inter-individual variability. Therefore, these findings are easily undermined by the substantial noise subsequently toward the null or raising the criticism in comparability in the study subjects. In this study, the protective effectiveness among various scenarios was evaluated based on urinary biomarkers collected from the identical individuals with repeated measurement. The incomparability of the subject and the consideration in the wide inter-individual variability could be eliminated to an acceptable degree.

Given A-DMF concentrations were quite constant and stable across four consecutive days for high and intermediate exposure groups (Fig. 1), U-NMF concentrations consistently showed decreases to different degrees on day 2 (barrier cream), day 3 (impermeable gloves) and day 4 (impermeable gloves plus respirator) compared with the day 1 (without any PPE)(Table 3 and Fig. 2,). This suggested that wearing any kind of personal protective equipment would reduce 25–60% of the DMF body burden exposure for the high and intermediate exposure groups in the occupational settings. For the low exposure group wearing rubber gloves plus a respirator seem to increase the total body burden of U-NMF (130%; Fig. 2), possibly due to an apparently high A-DMF concentration in day 4. In general, the PPE against dermal exposure, including applying barrier cream and wearing rubber gloves, were found to be seemingly more effective than the respiratory exposure for the chemical hazards with strong skin penetration capability like DMF.

A study exposing human volunteers to DMF vapor at 50 mg/m^3 for 4 h concluded that the absorbed dose through the skin tract was only 13–36% of that absorbed via inhalation tract [13]. Another human volunteer study revealed a similar finding of about 40% of absorbed DMF through skin compared with that of 60% through inhalation [11]. Our study found much more contribution from skin exposure than from respiratory exposure, possibly due to the discrepancy in the exposure conditions. From the field study observation, the major source of the dermal exposure in our case was the direct contact to DMF rather than only skin vapor exposure. Our findings are, therefore, more consistent with another human study conducted by Mraz and Nohova (1992). In their study, they found that the number of urinary biomarkers of DMF after immersing the sole of one hand into pure DMF solution for only 15 min was equivalent to that after respiratory exposure to 60 mg/m^3 (=two-fold concentration of allowable DMF exposure recommended by US-NIOSH) of DMF via inhalation route for 8 h [13]. Moreover in this study the major U-NMF contributions were found from high exposure tasks for high and low exposure group, they contributed about 60% and 75%, respectively, to U-NMF and about 2/3 and 4/5 were from skin (Table 4). Our study demonstrated that, in the actual occupational environment, direct skin contact to the chemical hazards could be a more significant exposure source than the respiratory exposure.

The rubber gloves were found to have higher protective effectiveness than other skin protective equipment. In this study, however, barrier cream could reduce about 40% of the DMF exposure, and about 62% and 40% of DMF exposure for high and intermediate exposure groups respectively. This is more effective than rubber gloves. Chang and colleagues investigated the effectiveness of rubber gloves and cotton gloves to prevent 2-methoxyethanol (2-ME) exposure. In that study the protective effectiveness indices (PEI) for the biomarkers of 2-ME in plasma and urine were measured and the result indicated that rubber gloves could provide the best protective effectiveness. They could reduce about 75% and 69%, for urine and plasma PEI respectively, of 2-methoxyethanol exposure [14]. This was higher than the results of this study. Due to inconvenience and uncomfortable properties of rubber gloves, they are usually used only during some specific task and provide limited effectiveness. The results from Table 4 also demonstrated that the exposure from low exposure tasks in this study accounted for 40–58% in high and intermediate exposure groups. This is the reason why barrier cream could be more effective than wearing rubber gloves plus a respirator because rubber gloves and respirator are only worn during high exposure tasks. Once the barrier cream is applied, it can build up a diffusion barrier against hazardous agents for both high and low exposure situations. This could at least partially explain why protective cream in this case could provide more PEI than gloves. Therefore applying barrier cream before work could be an alternative method to reduce DMF exposure in occupational settings.

Faced with hazardous materials with substantial skin absorption potential in the occupational environment, wearing gloves as the personal protective equipment (PPE) is a popular measure for the workers to seek protection from hazards. The effectiveness evaluation among various PPE has been investigated in the previous studies. Various components in the manufacturing gloves have been investigated for their protection effects in literature. For instance, Que Hee and colleagues used a disposable nitrile glove material to evaluate the permeation of an aqueous emulsion of the captan by adopting the test cell method of the American Society for Testing and Materials (ASTM). They found the disposable nitrile glove showed excellent resistance to a highly concentrated aqueous emulsion of captan [20]. They further assessed if nitrile and multi-layer gloves provide adequate protection against Telone ECTM formulation. They found the laminated gloves offered limited protection and Silver Shield™ afforded about 2.5 times more protection for 8 h and recommended that Viton gloves should still be worn for protection [21]. Chao and colleagues explored the permeation of several organic solvents through nitrile gloves also using the ASTM method on benzene, toluene, ethyl benzene, xylene, and styrene. They found the effective diffusion coefficients were inversely correlated to the molecular weight of the compounds [22]. These findings, however, were all merely based on the experimental settings without any actual humans involved. The gap between the experimental settings and the actual human exposure needs to be bridged. Although Chang and colleagues demonstrated that wearing impermeable rubber gloves could provide about 2/3 protective effectiveness from 2-ethoxyethanol exposure for the workers [14], rubber gloves, however, have been challenged with discomfort, failure to resist the penetration of low molecular weight chemicals [23], and chances to induce severe dermatitis [24]. Barrier creams, theoretically, could form a physical barrier on the skin to prevent or reduce penetration from chemical hazards [17–19]. More importantly, the cream is less uncomfortable and more acceptable for workers. This study has demonstrated that the application of barrier cream could be as effective as wearing impermeable rubber gloves in the prevention from the skin penetrates like DMF in the occupational settings (Table 5). The success of using barrier creams in this case does not, however, warrant the recommendation of the general application of the barrier creams in reducing the skin penetrates in the worksite. The effectiveness of a barrier cream depends on the basis of the skin barrier formulation, the chemical penetrates, as well as the skin conditions [23]. Further studies incorporating more thorough considerations to reach a more conclusive finding were warranted.

5. Conclusion

In summary, we found the respective contribution of total body burden from skin and inhalation exposure route and identified that prevention of skin exposure in high exposure task could reduce major DMF exposure. We also demonstrated that the barrier cream can serve as a good measure to effectively diminish the skin-absorption chemicals like DMF in the occupational setting given it is more convenient to the workers. Further studies incorporating more thorough considerations to reach a more conclusive finding are warranted.

Disclosure

There are no relevant financial interests to disclose.

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References

[1] W.J. Moorman, H.W. Ahlers, R.E. Chapin, G.P. Daston, P.M. Foster, R.J. Kavlock, J.S. Morawetz, T.M. Schnorr, S.M. Schrader, Prioritization of

NTP reproductive toxicants for field studies, Reprod. Toxicol. 14 (2000) 293–301.

[2] C.P. Chivers, Disulfiram effect from inhalation of dimethylformamide, Lancet 1 (1978) 331.

[3] N.H. Cox, C.P. Mustchin, Prolonged spontaneous and alcohol-induced flushing due to the solvent dimethylformamide, Contact Dermat. 24 (1991) 69–70.

[4] W.H. Lyle, T.W. Spence, W.M. McKinneley, K. Duckers, Dimethylformamide and alcohol intolerance, Br. J. Ind. Med. 36 (1979) 63–66.

[5] A. Fiorito, F. Larese, S. Molinari, T. Zanin, Liver function alterations in synthetic leather workers exposed to dimethylformamide, Am. J. Ind. Med. 32 (1997) 255–260.

[6] R. Wrbitzky, Liver function in workers exposed to *N*,*N*-dimethylformamide during the production of synthetic textiles, Int. Arch. Occup. Environ. Health 72 (1999) 19–25.

[7] Anonymous, Reproductive toxicology *N*,*N*-dimethylformamide, Environ. Health Perspect. 1 (1997) 305–307.

[8] P.A. Fail, J.D. George, T.B. Grizzle, J.J. Heindel, Formamide and dimethylformamide: reproductive assessment by continuous breeding in mice, Reprod. Toxicol. 12 (1998) 317–332.

[9] E. Hansen, O. Meyer, Embryotoxicity and teratogenicity study in rats dosed epicutaneously with dimethylformamide (DMF), J. Appl. Toxicol. 10 (1990) 333–338.

[10] H.-Y. Chang, T.-S. Shih, Y.L. Guo, C.Y. Tsai, P.C. Hsu, Sperm function in workers exposed to *N*,*N*-dimethylformamide in the synthetic leather industry, Fertil. Steril. 81 (2004) 1589–1594.

[11] T. Nomiyama, H. Nakashima, L.L. Chen, S. Tanaka, H. Miyauchi, T. Yamauchi, H. Sakurai, K. Omae, *N*,*N*-dimethylformamide: significance of dermal absorption and adjustment method for urinary *N*-methylformamide concentration as a biological exposure item, Int. Arch. Occup. Environ. Health 74 (2001) 224–228.

[12] H.-Y. Chang, C.Y. Tsai, Y.Q. Lin, T.-S. Shih, Y.C. Lin, Urinary biomarkers of occupational *N*,*N*-dimethylformamide (DMF) exposure attributed to the dermal exposure, J. Expo. Anal. Environ. Epidemiol. 14 (2004) 214–221.

[13] J. Mraz, H. Nohova, Percutaneous absorption of *N*,*N*-dimethylformamide in humans, Int. Arch. Occup. Environ. Health 64 (1992) 79–83.

[14] H.-Y. Chang, C.C. Lin, T.-S. Shih, H. Chan, J.-S. Chou, Y.-S. Huang, Evaluation of the protective effectiveness of gloves from occupational exposure to 2-methoxyethanol using the biomarkers of 2-methoxyacetic acid levels in the urine and plasma, Occup. Environ. Med. 61 (2004) 697–702.

[15] B. Kutting, H. Drexler, Effectiveness of skin protection creams as a preventive measure in occupational dermatitis: a critical update according to criteria of evidence-based medicine, Int. Arch. Occup. Environ. Health 76 (2003) 253–259.

[16] U. Berndt, W. Wigger-Alberti, B. Gabard, P. Elsner, Efficacy of a barrier cream and its vehicle as protective measures against occupational irritant contact dermatitis, Contact Dermat. 42 (2000) 77–80.

[17] A. zur Muhlen, A. Klotz, S. Weimans, M. Veeger, B. Thorner, B. Diener, M. Hermann, Using skin models to assess the effects of a protection cream on skin barrier function, Skin Pharmacol. 17 (2004) 167–175.

[18] J. Kresken, A. Klotz, Occupational skin-protection products—a review, Int. Arch. Occup. Environ. Health 76 (2003) 355–358.

[19] H. Zhai, H.I. Maibach, Effect of barrier creams: human skin in vivo, Contact Dermat. 35 (1996) 92–96.

[20] R.N. Phalen, S.S. Que Hee, Permeation of captan through disposable nitrile glove, J. Hazard. Mater. B 100 (2003) 95–107.

[21] H. Zainal, S.S. Que Hee, Permeation of Telone ECTM through protective gloves, J. Hazard. Mater. B 124 (2005) 81–87.

[22] K.P. Chao, P.H. Lee, M.J. Wu, Organic solvents permeation through protective nitrile gloves, J. Hazard. Mater. B 99 (2003) 191–201.

[23] A. Teichmann, U. Jacobi, E. Waibler, W. Sterry, J. Lademann, An in vivo model to evaluate the efficacy of barrier creams on the level of skin penetration of chemicals, Contact Dermat. 54 (2006) 5–13.

[24] W. Wigger-Alberti, P. Elsner, Do barrier creams and gloves prevent or provoke contact dermatitis? Am. J. Contact Dermat. 9 (1998) 100–106.