

Environmental monitoring of occupational exposure to *N,N*-dimethylformamide: comparison between active and diffusive sampling

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Abstract

Objectives The objective of this study is to optimize the evaluation of the exposure to *N,N*-dimethylformamide (DMF) in synthetic leather factories by diffusive samplers. The DMF exposure was monitored in synthetic leather factories by two sampler types: active and diffusive.

Methods Air measurements were carried out using two different personal air samplers, a diffusive and an active one. The diffusive sampling method, TK200 with charcoal filters, was examined in comparison with pumping through NIOSH silica gel tubes workplace air as with the currently available “gold standard”. The evaluation was carried out, in two different years but in the same season, for all the duration of the shift, i.e. 8 h on workers employed in five different factories in the district of Florence and Prato (Italy).

Results The statistical and graphical analysis of data show a good correlation between active and passive samplers ($r = 0.96$, $P < 0.001$, $n = 91$), a good linear regression ($\text{DMF}_{\text{diffusive}} = 0.95 \text{ DMF}_{\text{active}} + 0.15$, $R^2 = 0.92$), a not statistically significant difference between data (tested by paired t test and non-parametric Wilcoxon test). Moreover, all these results are confirmed for data lower and

higher than TLV-TWA, in particular we found a significant Pearson correlation ($r = 0.92$, $P < 0.001$, $n = 83$; $r = 0.92$, $P < 0.05$, $n = 8$, respectively) and a significant linear regression ($\text{DMF}_{\text{diffusive}} = 0.88 \text{ DMF}_{\text{active}} + 0.73$, $R^2 = 0.86$; $\text{DMF}_{\text{diffusive}} = 0.90 \text{ DMF}_{\text{active}} + 3.76$, $R^2 = 0.85$). Besides, the analysis of graphical representations confirmed the previous evidences. Finally, we can not find a significant difference between different types of job.

Conclusions Due to the good agreement between the two groups of data, the TK200 samplers can be considered as a simpler approach than the pump for screening worker exposures to DMF.

Keywords *N,N*-dimethylformamide · Active sampling · Diffusive sampling · Occupational hygiene

Introduction

N,N-dimethylformamide (DMF) is an organic solvent used extensively in industry, for its high miscibility with water and various organic compounds. It was defined the universal organic solvent especially when a low rate of evaporation is required. Owing to its qualities, the search for alternative solvents to employ in industrial processes is not a simple task without loss of product quality. Due to the low vapour pressure (2.7 mmHg at 20°C) and the high boiling point (153°C at 1 atm.) the DMF air concentration is generally low (Minoia and Perbellini 2001). Otherwise, a heating process (40–50°C) of DMF solutions may cause an increase of DMF air level. Occupational exposure normally results from inhalation or skin absorption and the toxicity, after excessive exposure, is prevalently in the liver; accordingly, the

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occupational exposure limit is set at 10 ppm (30 mg/m³) (ACGIH 2004). The methods to measure the time-weighted average (TWA) concentration in breathing zone air vary from pumping air through charcoal or silica gel tubes (OSHA Method n. 66 1990; NIOSH 1994; Yang et al. 2000). All these methods are rather inconvenient for personal sampling due to the heavy weight of the pumping equipment. Since the TLV-TWA was set at 30 mg/m³ by ACGIH the interest for industrial hygienists is focused on a wide range of environmental DMF concentrations. Various diffusive sampling methods were studied with different adsorbent substrates, such as water (Yasugi et al. 1992; Tanaka et al. 2002), or charcoal (Wrbitzky and Angerer 1998), since diffusive samplers were lightweight, small volume, low initial cost, ease of operation and a little maintenance and calibration needed (Tung-Sheng et al. 2004). The aim of the present study was to compare an active sampling method with a diffusive one to monitor DMF in the workplace air. The exposure level for workers handling DMF in the process of manufacturing spandex fibres and polyurethane products was determined both by the active method of NIOSH (1994) and by the diffusive samplers with charcoal filters, the first was adopted as a reference method to validate the diffusive samplers. The five factories involved in the study were located in the district of Florence and Prato (Italy) where there was about 15% of the national production of synthetic leather with a large use of DMF.

Materials and methods

Material and chemicals

The DMF and methanol were purchased from J.T. Baker (Deventer, Holland). The water was purified by a Milli-Q system (Millipore, Bedford, MA, USA). The silica gel tubes were made by our laboratory as indicated in NIOSH method and the pumps Gilair 5 were from TCR Tecora (TCR TECORA S.r.l., Italy), TK200 samplers were purchased from Zambelli (Zambelli S.r.l., Italy). The instrumental apparatus was a gas chromatograph with a mass spectrometer (GC/MS Clarus 500, Perkin Elmer Instruments Life and Analytical Sciences, Inc., Boston, MA, USA) with a CP-PoraBOND Q (25 m × 0.25 mm) column.

Manufacturing processes and chemical used

In all five factories involved in the study, the polyurethane was dissolved in DMF and coated in at least three head and applied to a textile substrate by casting

a polymer film on a carrier paper. The solvents are then evaporated by passage through ovens. Every factory was characterized by a controlled relative humidity in the range of 75–80%.

Subjects

Forty-eight 8-full shift personal breathing zone active and diffusive samplers from exposed workers, randomly selected and employed in six different phases of the leather production, were collected in order to evaluate the agreement between the diffusive and active samplers. Everyone used personal protective equipments and in every factory there were well care work equipments. The people in group number 1 worked in the dissolving room and are responsible for mixing the raw materials and colours in DMF solvent; often this process is carried out in closed cycles so no direct contact with DMF occurs. The people in group 2 were not directly exposed to DMF. The group 3 people worked at coating line where they coated a textile substrate by casting a polymer film (DMF dissolved polyurethane PU) on a carrier paper. In group number 4, the workers stayed on the laboratory of the factory to test the colours and the right balance between PU and DMF. The number 5 considered the people employed on the printing tasks to impress a design to coated materials. In some cases, the printing material is chemically the same as coating material only thinned to a lower viscosity; finally the workers of group 6 are employed in the coagulation process, where the area of DMF evaporation is higher than in other production process. In the coagulation process, the fabric passes from the unwinding reel into an impregnation bath containing a solution of one-component polyurethane, in this case the evaporation area for DMF is higher than in other type of jobs.

DMF air monitoring

Personal air sampling was carried out at the workplace in all subjects for the duration of a shift, i.e. 8 h by diffusion samplers TK200 and by silica gel tubes connected with pump. Both samplers were attached to the worker's collars during the sampling. TK200, with three charcoal filters, had the following dimension: diameter of 6.5 cm, height of 5.7 cm; diffusion chamber was high 0.8 cm, with an area of air contact of 7.065 cm² (Pozzoli and Maugeri 1986; Pozzoli and Capodoglio 1983). The active equipment consisted of a pump connected with silica gel tubes at a constant flow rate (1 l/min), the sampling flow rate was calibrated before and after each sampling. DMF was released

from the charcoal filters and silica gel by chemical desorption. Three charcoal filters were separately desorbed, the back one and the upper ones, with methanol and shaken for 1 h. The DMF was extracted separately from the back and the front sections of silica gel tubes with methanol after 1 h in an ultrasonic bath. The differential analysis of the back and the front sorbent sections was necessary, in both cases, in order to exclude the saturation of samplers with possible lack in linearity between DMF concentrations in the air and in the samplers due to the sample loss.

DMF analysis and calculations

The analytical method was characterized by an intra-day precision, expressed as % variation coefficient (CV%), of 7, a day-to-day precision of 15 (CV%), the limit of detection (LOD) was 1 µg/l and the concentration range of the standard curve was 4–100 µg/l. The extraction solutions were directly injected into GC/MS set as shown in Table 1. The quantification was carried out by the standard curve in methanol prepared freshly. The DMF concentrations were calculated for both samplers by the following procedures. In case of diffusive sampling experiments we used the formula from Pozzoli, $C \text{ (mg/m}^3\text{)} = (Q1.9)/(tD)$ where Q is the amount of DMF (µg), 1.9 is TK200 constant, t is the time of sampling (minutes) and D is DMF diffusion coefficient (Lugg 1968). The DMF calculations in active samples followed the descriptions in analytical method of NIOSH (1994).

Statistical analysis

SPSS® 10.0 for Windows was used for statistical calculations. In order to test the normality of the airborne concentration, Kolmogorov–Smirnov test was carried out. Paired t test, Wilcoxon test, linear regression, Pearson correlation coefficients and concentration difference (diffusive–active) versus the active and diffusive plot (Bland and Altman 1986) were used to assess the agreement between diffusive and active sampling methods. ANOVA analysis, with Bonferroni post hoc

test, was carried out to underlie possible difference between job types.

Results

Solvent blanks, medium blanks and fields blanks show no sample contamination during sample shipping and storage processes, all the back sections of samplers show a DMF amount less than 10% of in the front sections, in the differential analysis. Both active and diffusive sampler data appear to be approximately log-normally distributed (Fig. 1a–d). Moreover, they cover all the range of interest in industrial hygiene as shown in Table 2. In accordance with guidelines for the combined graphical/statistical interpretation of method-comparison studies (NCCLS 1995) we test our data with three different statistical analyses: a scatter plot combined with correlation and regression analysis, a difference plot and finally the paired sampled test for mean or median (the parametric t test and the non-parametric Wilcoxon test). DMF concentrations in TK200 show a significant correlation with DMF in silica gel tubes and a significant regression as shown in Table 3. In particular, the slope of the regression equation is not different from 1 but it is significantly different from 0 since its 95% confidence intervals are from 0.89 to 1.01 (Table 3). Moreover, at environmental DMF concentrations lower and higher than threshold limit value (TLV-TWA), revealed by active samplers, the two methods have a good Pearson correlation coefficient and in both cases the regression analysis shows a slope of the regression significantly different from 0 but not from 1 (Table 3). The plot with line of identity is shown in Fig. 2, the data are well scattered along the line. The concentration difference, between active and diffusive, is plotted versus the mean concentration of paired active and diffusive samples, the plot reveals that most of the points are within the 95% confidence limits and that there is not a evident trend in difference points with the magnitude of measurements (Fig. 3). Moreover, the concentration difference is analysed in relation to the job type, in the plot it is possible to note that there is not any significant difference between job type but most of the extreme values are concentrated on job number 5 and 6 (Fig. 4). The difference between active and diffusive results is tested by t test on log-transformed data, and by non-parametric Wilcoxon test on not transformed data, both statistical analyses support the concept that the two groups of data can be considered not significantly different, as for the data sorted by job type. In particular, the same analysis, conducted for the data lower and higher than

Table 1 Instrumental parameters of GC/MS for DMF analysis

Carrier gas	Helium
Flow rate	1 ml/min
Column temperature	190°C
Injection temperature	300°C
Column	CP-PoraBOND Q (25 m × 0.25 mm)
Split ratio	10
Ions	73 → 44

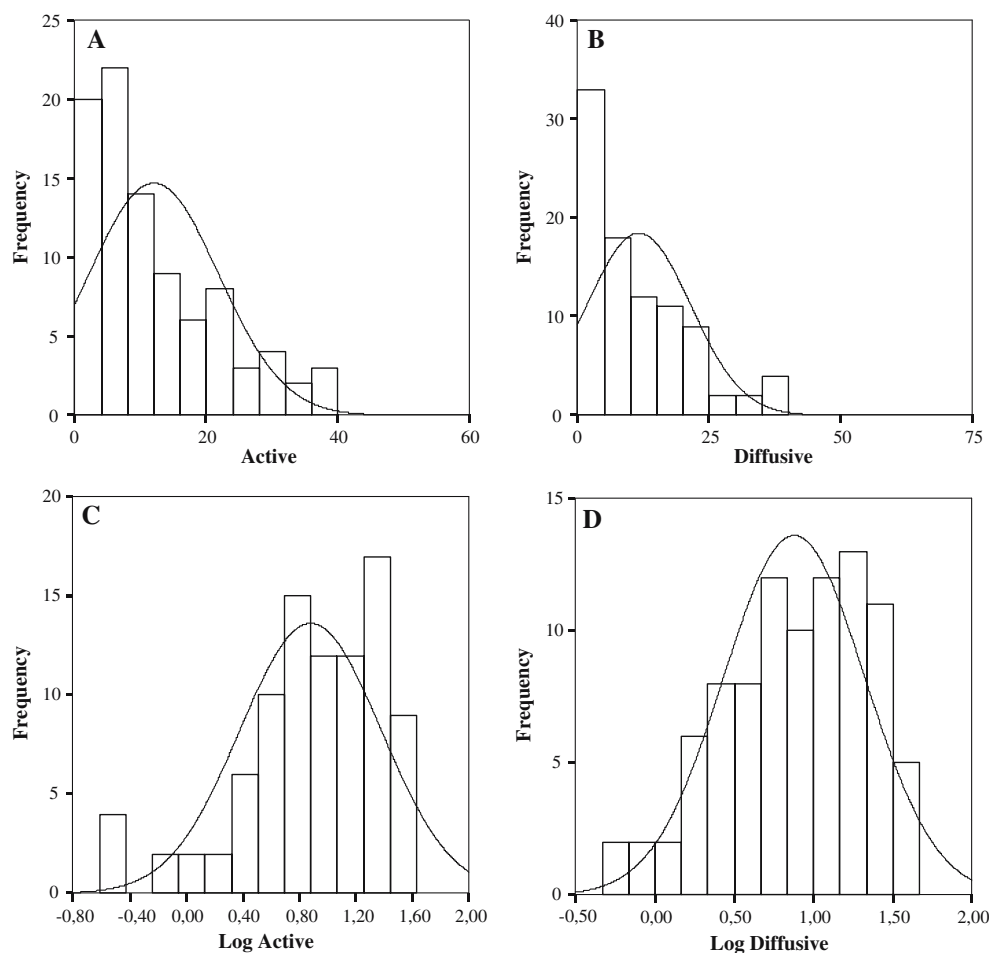


Fig. 1 Distribution of raw active (a), diffusive (b), log active (c) and log diffusive (d) data compared with Gaussian distribution. Kolmogorov–Smirnov coefficient (Z) and its relative P value are (Z/p) 1.63/0.01, 1.51/0.02, 0.84/0.48, 0.75/0.62

Table 2 Sample descriptive statistics for environmental DMF revealed by active and diffusive samplers

	N	Mean	SD	Minimum	Maximum	Percentiles		
						25th	50th	75th
Active (mg/m^3)	91	11.97	9.88	0.30	37.60	4.20	8.51	18.90
Diffusive (mg/m^3)	91	11.57	9.83	0.60	39.01	3.42	8.60	18.12
Log active	91	0.88	0.50	−0.52	1.58	0.62	0.93	1.28
Log diffusive	91	0.88	0.44	−0.22	1.59	0.53	0.93	1.26

the TLV-TWA, reveals a non-significant difference between the two compared set of data. ANOVA analysis, applied on diffusive and active data, shows that job number 5 and 6 are characterized by a significant higher environmental DMF concentration than other types of job.

Discussion

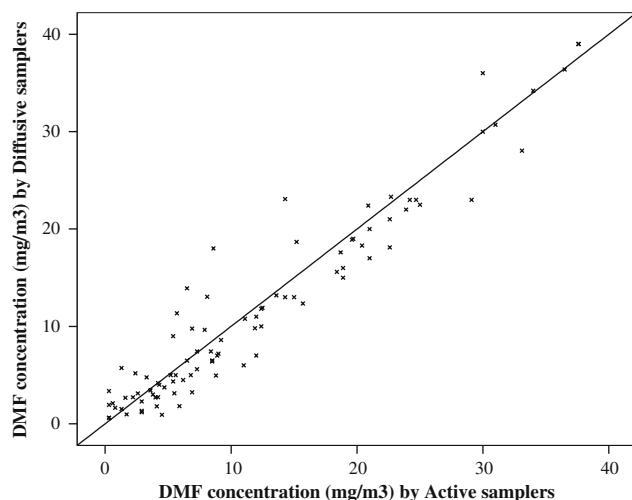
In order to evaluate DMF exposure during synthetic leather production it is essential to use the personal

sampling method since stable samplers do not reflect the real exposure situation of workers (Takada et al. 1983; Ukai et al. 1986). Moreover, it is important to develop a personal sampling method very sensible and quantitative at concentrations either below or higher than TLV-TWA and which is not too heavy to wear during the shift. Some studies were published on the environmental DMF personal monitoring by diffusive samplers, each of these tested a different adsorption material (water, carbon). Some results are obtained in a laboratory study while others directly in the factory environment. Tanaka et al. (2002) found a linear rela-

Table 3 Statistical comparison of two methods

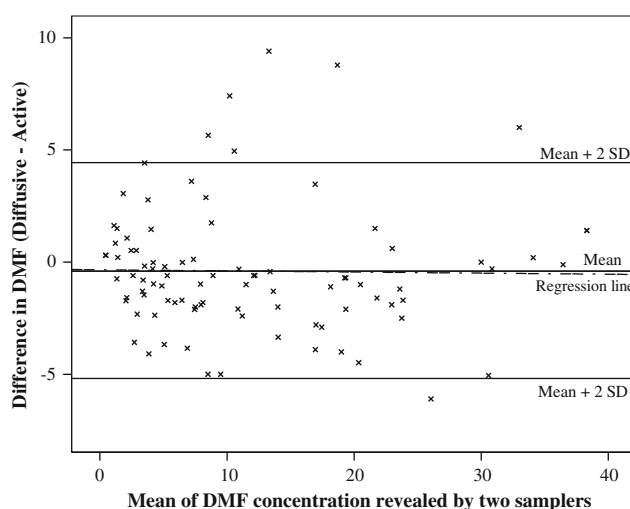
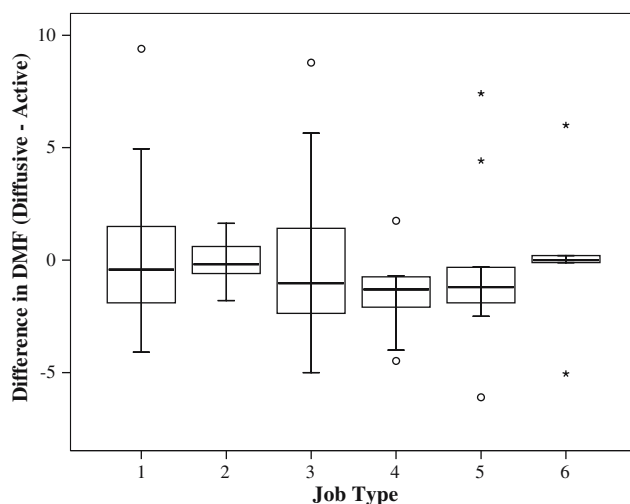
	N	R	Regression coefficients		R^2
			a	b	
All data	91	0.96	0.95 (0.89–1.01)	0.15 (–0.77–1.08)	0.92
< TLV-TWA	83	0.92	0.88 (0.80–1.01)	0.73 (–0.25–1.71)	0.86
≥ TLV-TWA	8	0.92	0.90 (0.56–1.24)	3.76 (–8.76–16.29)	0.85

Correlation (R is Pearson correlation coefficient) and regression analysis results ($Y = aX + b$; where y = DMF by diffusive samplers and x = DMF by active samplers). The estimated y intercept was tested for a statistically significant difference from 0; the estimate slope was tested for a statistically significant difference from 1

**Fig. 2** Scatter plot between DMF concentration revealed by active and diffusive samplers, the line of identity is drawn

tionship with a high correlation coefficients between the amount of analyte collected and the exposure concentration; moreover, relative humidity, wind velocity and storage conditions had no significant effects in the studied range of concentrations (1–52 ppm, 3–156 mg/m³). Finally, they found a linear relationship between the results obtained by the NIOSH method and the method tested in their study ($Y = 0.912X$, $r = 0.932$, $P < 0.01$), in particular we found a accordance with our results as shown in Table 3. Yasugi et al. (1992) tested two different diffusive samplers with either water or carbon cloth in laboratory. They found a linear dose- and time-dependent absorption of DMF on samplers and they concluded supporting the validity of these diffusive samplers in the place of the silica gel tubes as recommended by NIOSH.

The main emphasis in method comparison studies clearly rests on a direct comparison of the results obtained by the alternative methods. The first step is to plot the data and draw the line of identity that is essen-

**Fig. 3** Plot of concentration differences versus mean concentrations of paired active and diffusive samples with mean and 95% limits of agreement (solid lines). Dotted lines indicate the regression line, its parameters are $y = -0.005x - 0.343$, the slope and the constant are not significantly different from zero, $R^2 = 0.00$ ($P > 0.05$), Pearson coefficient $R = 0.017$ ($P > 0.05$)**Fig. 4** Box-and-Whisker plot of concentration differences versus job type. Asterisk extreme values, open circle outlier values

tial to get a correct visual assessment of the relationship. Since the wide range of environmental DMF concentration evaluated in the plot shown a good agreement, in fact greater is the range and higher is the agreement. However, we can deduce that the linearity was hold along all the environmental DMF concentration studied. Therefore, it is preferable to plot the difference between the methods against the average. From this type of plot, it is much easier to assess the magnitude of disagreement and see whether there is a trend in the difference value, for example for high

value. From our scatter plot, we can deduce that the difference is well distributed around the mean and does not show a dose-dependent trend for low or high environmental DMF concentrations, as demonstrated by the regression line drawn on the plot (Fig. 3). Moreover, the magnitude of disagreement is acceptable in a field occupational exposure monitoring study, since the limits of agreement that we get from our data are (mean \pm 2SD, -0.4 ± 2.85). Thus, the diffusive samplers may measure ca. 6 mg/m³ below or 5.3 mg/m³ above the active samplers, which would be acceptable for occupational monitoring purpose. While these graphical approaches provide a visual impression of the agreement between the two methods, we also need a numerical estimation of errors. For comparison of our two different methods we applied the linear regression statistic that allows to estimate a hypothetic constant systematic error (CSE), intercept deviation from zero, and a proportional systematic error (PSE), slope deviation from unity, and a total systematic error (TSE). Our TSE at TLV-TWA is -1.35 mg/m³ which is acceptable for occupational hygiene purpose. Since the high value of Pearson coefficient, the correlation analysis shows us also a statistically significant association between the two methods and a little random error, about 4% (RE). Finally, we have the evidence that the mean of data from two methods is not significantly different by the paired *t* test, which is confirmed by the non-parametric Wilcoxon test. All these statistic considerations are right also for the data lower and higher than TLV-TWA and for all the job type DMF concentrations and for the data sorted by job type. The higher environmental DMF exposure in job number 5 and 6 can be due to the particularity of the two jobs, where the workers are more exposed to accidental spurts of polyurethane mix normally used at a lower viscosity than other types of job. Nevertheless, both sampling methods analysed in our study are able to reveal these eventuality since the ANOVA analysis, on difference between diffusive and active data, does not show a significant difference between job types (Fig. 4). These results are in accordance with Wrbitzky and Angerer (1998), they monitored the DMF exposure with diffusive personal samplers (ORSA 5) and they found the highest levels of DMF during the wet spinning. In conclusion, the TK200 samplers can be considered a simpler approach than the pump for screening workers' exposures to DMF and the two methods can be applied interchangeably in occupational exposure monitoring. The analytical method required instrumentations with

a high sensitivity since, in the last decades, exposure levels in numerous cases were decisively decreased by the use of protective work equipments.

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