

Assessment of airborne and dermal exposure to 2-ethoxyethyl acetate in an occupational environment

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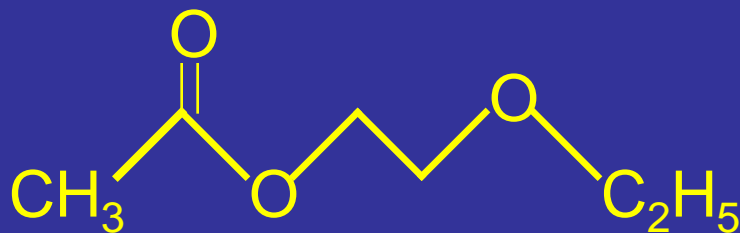
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The properties of EEAc

2-ethoxyethyl acetate (EEAc)

- Ethylene glycol ethers : high boiling-point, low vapor pressure
- Two functions : ether and ester
- Used as organic solvent mixtures, ink diluents and cleaners

| EEAc | |
|---------------------------------|------------------|
| Phase | Colorless liquid |
| MW | 132.2 |
| Boiling point(°C) | 156.3 |
| Freezing point (°C) | 61.7 |
| Vapor pressure (mm Hg 25 °C) | 2.8 |
| Water solubility(%) | 23 |
| Kow | 1.27 |



[Johanson et al., 1988; NIOSH, 1991;
lin et al., 1993]

Occupational exposure standards of EEAc

| OELs | | | Reference |
|-----------------|---------|------|-------------|
| OSHA PEL (TWA) | 100 ppm | Skin | OSHA, 1998 |
| NIOSH REL (TWA) | 0.5 ppm | Skin | NIOSH, 1997 |
| ACGIH TLV (TWA) | 5.0 ppm | Skin | ACGIH, 2008 |
| CAL PEL(TWA) | 5.0 ppm | Skin | CAL, 1995 |



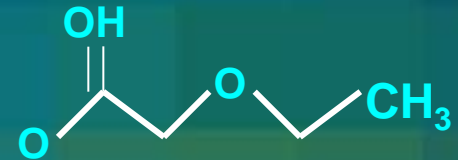
2-ethoxyethyl acetate



2-ethoxyethanol



2-ethoxyacetic aldehyde



EAA



Metabolic pathway for EEAc exposure

2-ethoxyacetic acid (EAA)

ADH: Alcohol dehydrogenase

ALDH: Aldehyde dehydrogenase

Health effects for EEAc exposure

Toxic metabolite (EAA) responsible for the adverse effects

- **Hematological toxicity**
Hb, Hct, RBCs, WBCs, and MCV ↓
- **Male reproductive toxicity**
testicular atrophy, germ cell depletion, and sperm motility ↓
- **Female reproductive toxicity**
body weight ↓ , prolonged gestation, and embryoletality

[Welch et al., 1988; NIOSH, 1991; Kim et al., 1999; Loh et al., 2003]

Dermal absorption of EEAc

| Glycol ethers | EGBE | EEAc |
|--|------|------|
| Absorption rate (mg/cm ² per hr) | 0.2 | 0.8 |
| Relative rate | 1.0 | 4.0 |

[Dugard et al., 1984]

- Dermal uptake of BE accounts for about 75% of the total uptake during whole body exposure to BE vapor. *[Johanson et al., 1991]*
- We suppose the **dermal uptake of EEAc** could account for about **>75%** of the total uptake during whole body exposure to EEAc vapor.

Absorption routes of EEAc

◆ Inhalation
vapor

◆ Skin
vapor and liquid

◆ Ingestion

**The main routes of
occupational exposure**

[Kezic et al., 1997; NIOSH, 1991]

Literature review regarding EEAc exposure

| Study type | Conclusion | Disadvantage |
|--|---|-----------------------------------|
| human skin <i>in vitro</i> ¹ | Glycol ethers are easily dermally absorbed | Non-occupational exposure |
| field study ² | Almost glycol ethers are dermally absorbed | Lack of skin exposure measurement |
| field study ³ | Dermal absorption is a main exposure route | Lack of skin exposure measurement |

Reference : 1.Dugard et al., 1984; 2. Angerer et al., 1990; 3. Vincent et al., 1994

Objective

To determine the actual dermal exposure on various anatomical sites and to explore the relation between EEAc skin exposure concentrations and that from inhalation

Study workplaces and population

The company is manufacturing logos or packing for commercial products, and organic solvents are used as ink detergents or cleaners.

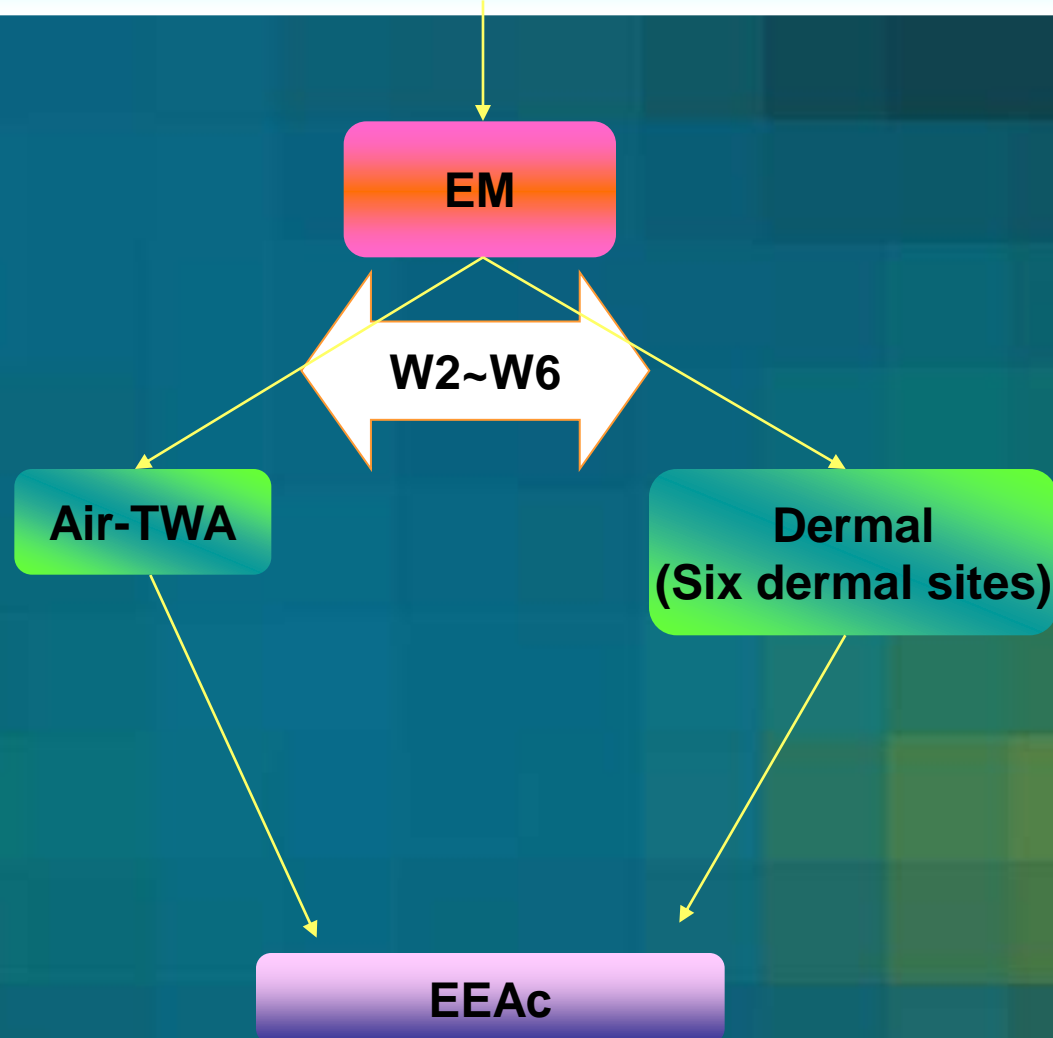
20 participants were recruited from the printing department

- ✓ Automatic printing lines (Auto) :
drying process is automatic (n=3)
- ✓ Semi-automatic printing lines (Semi-auto) :
drying process is manual (n=13)
- ✓ On-line inspection (QA/QC) :
quality assurance and control in the field (n=4)

The main component of the screen-cleaning solvent is **EEAc**

Structure of study design

20 EEAc-exposed workers in a silk-screening shop



Respiratory exposure

- Personal passive-sampler (3M 3500)
- Sampling flow rate: 26.6 ± 0.4 ml/min
- Sampling days: $W_2 \sim W_6$ (08 : 30~15 : 30)
- Recording relative humidity and temperature



Dermal exposure-tape stripping

Skin location:

Palm × 2

Dorsum × 2

Forearm-interior (arm-in) × 2

Forearm-exterior (arm-ex) × 2

Forehead × 1

Neck × 1



2 ml CS₂



TDEM (Total dermal exposure mass)

TDEM =

$$\begin{aligned} & (\text{Palm conc.} + \text{Dorsum conc.}) / 2 * \text{Skin area}_{\text{hand}} + \\ & (\text{Forearm-in conc.} + \text{Forearm-ex conc.}) / 2 * \text{Skin area}_{\text{forearm}} + \\ & (\text{Forehead conc.}) * \text{Skin area}_{\text{forehead}} + \\ & (\text{Back neck conc.}) * \text{Skin area}_{\text{back neck}} \end{aligned}$$

Skin area:

Hand: 730 cm²

Forearm: 1077 cm²

Forehead: 100 cm²

Back neck: 97.9 cm²

[EPA, 1987]

Questionnaire interview

- **Demographic data**
name, gender, birth date, working duration, smoking- and alcohol-drinking habits
- **Disease history**
Liver disease and skin diseases on hands
- **Personal protective equipment**
materials, frequency, duration, etc.
- **Solvent use**
substances and contact location

Table 1. Demographic characteristics of study subjects for three job titles in silk-screening printing shop

| | | Semi-auto (n=13) | Auto (n=3) | QA/QC (n=4) | Total (n=20) | p-value |
|---|-----|---------------------|---------------|----------------|-----------------|-------------------|
| Age(y/o) | | 28.7±3.5 | 26.7±4.0 | 28.0±2.8 | 28.2±3.3 | 0.67 ^b |
| Working duration(y) | | 6.4±4.4 | 3.8±5.3 | 3.6±2.9 | 5.3±4.2 | 0.46 ^b |
| Gender | M | 7 | 3 | 2 | 12 | 0.31 ^c |
| | F | 6 | 0 | 2 | 8 | |
| Skin diseases (hands) | No | 10 | 2 | 3 | 15 | 0.93 ^c |
| No significant difference for demographic data among three job titles | | | | | | |
| Alcohol drinking | No | 10 | 3 | 4 | 17 | 0.39 ^c |
| | Yes | 3 | 0 | 0 | 3 | |
| Cigarette smoking | No | 9 | 3 | 4 | 16 | 0.26 ^c |
| | Yes | 4 | 0 | 0 | 4 | |
| Glove use ^a | No | 9 | 2 | 4 | 15 | 0.43 ^c |
| | Yes | 4 | 1 | 0 | 5 | |

^aonly used when washing screening;

^btested by one-way ANOVA; ^ctested by Chi-square

All 20 workers didn't wear any respiratory protection equipment

Table 2. Airborne concentrations (ppm) of EEAc across five consecutive workdays

| Workday | n | AM±SD (ppm) | Median (ppm) | Range (ppm) | >PEL(%) |
|----------------|-----------|--------------------|---------------------|--------------------|-------------------|
| W2 | 18 | 25.40±13.09 | 28.68 | 3.97-46.56 | 94.4 |
| W3 | 20 | 22.40±11.46 | 21.99 | 3.61-40.23 | 95.0 |
| W4 | 19 | 27.53±15.66 | 33.99 | 5.56-49.39 | 100.0 |
| W5 | 18 | 28.17±15.68 | 30.85 | 5.19-54.89 | 100.0 |
| W6 | 19 | 20.56±13.25 | 23.33 | 2.95-39.39 | 89.5 |
| W2-W6 | 94 | 24.75±13.90 | 26.48 | 2.95-54.89 | 95.7 |

*No significant day-to-day differences of airborne EEAc conc. tested by one-way ANOVA (p=0.39). Permissible exposure limit of EEAc in Taiwan is 5 ppm

Table 3. Correlation matrix of daily air conc. of EEAc across five consecutive workdays

| Workday | | W3 | W4 | W5 | W6 |
|----------------|----------|---------------|---------------|---------------|---------------|
| W2 | n | 18 | 17 | 16 | 17 |
| | r | 0.89** | 0.92** | 0.96** | 0.94** |
| W3 | n | | 19 | 18 | 19 |
| | r | | 0.92** | 0.94** | 0.92** |
| W4 | n | | | 18 | 19 |
| | r | | | 0.92** | 0.97** |
| W5 | n | | | | 18 |
| | r | | | | 0.93** |

Tested by Pearson Correlation;

n: sample size; r: correlation coefficient; p: p-value; **p<0.01

Both intra- and inter- variability of personal air conc. of EEAc for 20 workers across 5 workdays were not significant

Table 4. Dermal exposure levels ($\mu\text{g}/\text{cm}^2$) of EEAc across five consecutive workdays

| Workday | n | GM(GSD) | Median | Range | ND% |
|----------------|------------|-------------------|---------------|-----------------|-------------|
| W2 | 105 | 0.37(2.26) | 0.47 | 0.1-1.47 | 22.0 |
| W3 | 117 | 0.55(1.75) | 0.58 | 0.1-1.76 | 4.3 |
| W4 | 112 | 0.57(2.33) | 0.59 | 0.1-3.28 | 7.1 |
| W5 | 102 | 0.66(2.23) | 0.70 | 0.1-3.15 | 4.9 |
| W6 | 110 | 0.44(2.13) | 0.49 | 0.1-1.98 | 10.9 |
| W2-W6 | 546 | 0.51(2.19) | 0.54 | 0.1-3.28 | 9.5 |
| F-value | | 9.28*** | | | |

ND<LOD, LOD=0.20 $\mu\text{g}/\text{cm}^2$, ND=1/2*0.20=0.1

***p<0.01 tested by one-way ANOVA; *post hoc* by Tukey HSD for unequal N
Significant difference between W2 vs. W3, W2 vs. W4, W2 vs.W5 and W5 vs. W6

Table 5. Dermal exposure levels of EEAc ($\mu\text{g}/\text{cm}^2$) on six skin sites across five consecutive workdays

| Location | n | GM(GSD) | Median | Range | ND% |
|----------------|-----|-----------------|--------|----------|------|
| Palm | 90 | 0.79(2.12) | 0.82 | 0.1-3.28 | 4.4 |
| Dorsum | 91 | 0.56(2.03) | 0.59 | 0.1-2.72 | 5.5 |
| Arm-in | 92 | 0.52(2.04) | 0.57 | 0.1-2.32 | 7.6 |
| Arm-ex | 92 | 0.56(2.08) | 0.59 | 0.1-2.74 | 7.6 |
| Forehead | 89 | 0.41(2.06) | 0.46 | 0.1-2.18 | 11.2 |
| Neck | 92 | 0.32(2.17) | 0.35 | 0.1-1.83 | 20.7 |
| Total | 546 | 0.51(2.19) | 0.54 | 0.1-3.28 | 9.5 |
| F-value | | 16.08*** | | | |

ND<LOD, LOD=0.20 $\mu\text{g}/\text{cm}^2$, ND=1/2*0.20=0.1 $\mu\text{g}/\text{cm}^2$

***p<0.01 tested by one-way ANOVA; *post hoc* by Tukey HSD for unequal N

Table 6. Correlation matrix of airborne conc. (ppm) and dermal exposure levels ($\mu\text{g}/\text{cm}^2$) of EEAc on six different sites

| | Palm | Dorsum | Arm-in | Arm-ex | Forehead | Neck |
|--------------|--------|--------|--------|--------|----------|--------|
| Air n | 90 | 91 | 92 | 92 | 89 | 92 |
| r | 0.68 | 0.56 | 0.58 | 0.56 | 0.67 | 0.69 |
| p | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |

Tested by Pearson Correlation;
 n: sample size; r: correlation coefficient; p: p-value

Discussion-1

- Skin exposure levels of EEAc:
palm>dorsum~forearm-in~forearm-ex >forehead>neck
- The high-to-low pattern is consistent with the field observation that palms could contact with solvents directly.
- Vaporized EEAc could be an important source for dermal exposure as well as for respiratory exposure.

Table 7. Simple linear regression between ln(TDEM) and potential exposure variables

| Dependant var. | Independent var. | n | β_0 | β_1 | r |
|----------------|------------------|----|-----------|-----------|----------|
| Ln(TDEM) | Air | 94 | 6.28 | 0.03 | 0.64*** |
| | Job | 94 | 7.37 | -0.22 | -0.26* |
| | Glove | 94 | 6.96 | 0.29 | 0.19 |
| | Perspiration | 94 | 7.41 | -0.54 | -0.38*** |

Tested by Pearson Correlation; *p<0.05; ***p<0.001

TDEM=Total dermal-exposure-mass

Job titles: semi-auto (1), auto(2) and QA/QC (3)

Glove: no(0) and yes(1)

Perspiration: no(0) and yes(1)

Table 8. Airborne concentrations (ppm) and dermal exposure levels ($\mu\text{g}/\text{cm}^2$) of EEAc on six skin locations stratified by job classification

| | Semi-auto (n = 13) | | Auto (n = 3) | | QA/QC (n = 4) | | F-Value |
|----------|----------------------------------|---------|----------------------------------|---------|----------------------------------|--------|----------|
| | Central-tendency (Dispersion) | Median | Central-tendency (Dispersion) | Median | Central-tendency (Dispersion) | Median | |
| Air | 29.20(12.17) | 32.81 | 26.44(13.05) | 29.16 | 7.77(3.95) | 7.22 | 25.73*** |
| Palm | 0.90(2.13) | 0.92 | 0.91(1.74) | 0.80 | 0.46(1.81) | 0.46 | 6.10** |
| Dorsum | 0.61(2.04) | 0.61 | 0.59(1.87) | 0.66 | 0.42(1.94) | 0.43 | 2.04 |
| Arm-in | 0.57(2.05) | 0.61 | 0.48(1.86) | 0.57 | 0.40(1.98) | 0.38 | 1.91 |
| Arm-ex | 0.63(2.03) | 0.65 | 0.61(1.38) | 0.58 | 0.36(2.29) | 0.37 | 4.75* |
| Forehead | 0.46(2.09) | 0.54 | 0.36(1.48) | 0.42 | 0.28(1.93) | 0.29 | 3.78* |
| Neck | 0.37(2.13) | 0.40 | 0.34(1.69) | 0.31 | 0.19(2.04) | 0.14 | 6.47** |
| TDEM | 1255.46(1.97) | 1247.66 | 1188.72(1.60) | 1250.12 | 779.16(1.87) | 722.33 | 3.83* |

TDEM=Total dermal-exposure-mass

*tested by one-way ANOVA ;*post hoc* by Tukey HSD for unequal N

*** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$

Central-tendency and dispersion for air are AM&SD, for skin are GM&GSD

Discussion-2

- The relatively low exposure levels of EEAc for QA/QC workers could be explained by **neither solvent use nor directly dermal contact**.
- Due to the sophisticated pictures, semi-auto printing demands more cleaning tasks than auto printing.
 - *[Lon et al., 2003]*
- Respiratory and dermal exposure profiles significantly differ with job titles.

Conclusions

1. Evaporative EEAc could be an important source to both dermal EEAc exposure and respiratory exposure. Engineering control and/or wearing protective equipment should be performed at the priority to minimize the workers' EEAc exposure.
2. Direct contact to EEAc could also increase the EEAc dermal exposure on palms. Therefore, wearing impermeable gloves during high-exposure tasks might effectively reduce dermal exposure.
3. The exposures to EEAc via lungs and skin were both job-dependent, suggesting high-risk jobs should be identified in the first priority with respect to exposure reduction.

Acknowledgements

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Appreciate the cooperation of the workers and employers in the silk-screening shop

Thank you for your attention!!