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# **Novel Technique for Analysing Volatile Compounds in Indoor Dust**

**Application of Gas Chromatography - UV Spectrometry  
to the Study of Building-Related Illness**

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*Perfect as the wing of a bird may be, it will never enable the bird to fly if unsupported by the air.  
Facts are the air of science. Without them a man of science can never rise.*

*Ivan Pavlov (1849 - 1936)*



## ABSTRACT

It is now generally acknowledged that particulate air pollution can cause respiratory symptoms and that indoor dust particles may be associated with mucous membrane irritation and odour annoyance. One reason for this may be that dust particles adsorb large quantities of gases and other volatile compounds. It is therefore important to be able to determine the chemical compounds adsorbed onto indoor dust particles. In this thesis, a new technique was developed that can analyse chemical compounds in indoor dust particles in a simple yet accurate way. In its basic configuration, it comprises a one stage thermal desorption oven, a gas flow cell with a miniaturized GC column, and a nitrogen-flushed photo diode array (PDA) detector for fast UV spectra recording. The dust sample is thermally desorbed in the oven and the released compounds are flushed onto the GC column by means of a carrier gas stream; the separated compounds are then registered by the PDA detector and identified by their characteristic gas-phase UV spectra. Using this set-up, a number of volatile organic as well as inorganic compounds were identified in indoor dust particles, e.g. nitric oxide, ammonia, hydrogen sulphide, pyridine, 2-furaldehyde, 2-methylfuran, and isoprene. Moreover, acrylate monomers were identified in dust samples from a secondary school with problems due to powdering floor polish. An instrumental set-up with higher performance was achieved by interfacing the gas flow cell to a capillary GC column. When airborne indoor dust samples were analysed by this system and by GC-MS under similar conditions of thermal desorption (150 °C) and GC separation, the two analytical systems were found to be complementary. GC-UV together with GC-MS was thus demonstrated to be considerably more powerful than GC-MS alone for the analysis of volatile organic compounds (VOC) in indoor dust. When airborne dust samples from damp (n=9) and control (n=9) residences were analysed for VOC and microorganisms, identifications made by culture and microscopy of the major moulds found, i.e. *Aspergillus*, *Cladosporium* and *Penicillium*, coincided with the identification of VOC known to be produced by these species. A number of additional VOC were also found, some of which may be irritating to the skin, eyes or respiratory tract if present at higher concentrations. Quantitative GC-UV analysis of indoor dust from 389 residences in Sweden showed that the VOC found at the highest concentrations were saturated aldehydes (C<sub>5</sub>-C<sub>10</sub>), furfuryl alcohol, 2,6-di-*tert*-butyl-4-methylphenol, 2-furaldehyde, and benzaldehyde. Alkenals were also found, notably 2-butenal (crotonaldehyde), 2-methyl-propenal (methacrolein), hexenal, heptenal, octenal, and nonenal. GC-UV was also applied (together with GC-MS) to determine VOC in dust from residences of 198 children with symptoms of asthma and/or allergy (cases) and from residences of 202 children without symptoms (controls). The mean concentration of nicotine was found to be significantly higher in dust from case residences, while the mean concentrations of hexane, nonanal, octane, 2-pentylfuran and tridecanol were significantly higher in dust from control residences. In a stepwise logistic regression model, nicotine, hexanal, furfuryl alcohol, nonane, butanol, and octenal showed increased relative risks, expressed as odds ratios comparing cases with controls. By contrast, benzaldehyde, nonanal, butenal, hexane, tridecanol, and pentylfuran showed decreased relative risks. These findings point to the possibility that not only environmental tobacco smoke but also other emissions in the indoor environment may be linked to the increased prevalence of asthma and/or allergy in children. It is concluded that GC-UV may be used as an alternative or complement to GC-MS for measuring chemicals in indoor dust, thus improving the survey and control of human exposure to particle-bound toxicants and other chemicals.

## ABBREVIATIONS

|                   |   |
|-------------------|---|
| ETS               | Environmental Tobacco Smoke                           |
| FTIR              | Fourier Transform Infra Red Spectrometry              |
| GC                | Gas Chromatography                                    |
| GC-MS             | Gas Chromatography Mass Spectrometry                  |
| GC-UV             | Gas Chromatography Ultraviolet Spectrometry           |
| HPLC              | High Performance Liquid Chromatography                |
| HVAC              | Heating, Ventilating and Air Conditioning             |
| IAQ               | Indoor Air Quality                                    |
| LC                | Liquid Chromatography                                 |
| LPS               | Lipopolysaccharide                                    |
| MS                | Mass Spectrometry                                     |
| MVOC              | Microbial Volatile Organic Compounds                  |
| NOEL              | No Observed Effect Level                              |
| PDA               | Photo Diode Array                                     |
| PGE <sub>2</sub>  | Prostaglandin E <sub>2</sub>                          |
| PM <sub>2.5</sub> | Particulate Matter with < 2.5 µm aerodynamic diameter |
| PM <sub>10</sub>  | Particulate Matter with < 10 µm aerodynamic diameter  |
| SBS               | Sick Building Syndrome                                |
| SPME              | Solid Phase Micro Extraction                          |
| TVOC              | Total Volatile Organic Compounds                      |
| UV                | Ultraviolet Spectrometry                              |
| VOC               | Volatile Organic Compounds                            |

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## LIST OF PAPERS

This thesis is based on the following papers, which are referred to in the text by their Roman numerals:

- I. Novel technique for measuring low molecular weight chemicals in indoor dust. Nilsson A, Nosratabadi AR, Lagesson V, Murgia N, Leanderson P, and Tagesson C. Indoor + Built Environment 2002; 11: 153-161
- II. Powdering floor polish and mucous membrane irritation in secondary school pupils. Malmberg B, Leanderson P, Nilsson A, and Flodin U. International Archives of Occupational Environmental Health 2000; 73: 498-502
- III. Qualitative determination of compounds adsorbed on indoor dust particles using GC-UV and GC-MS after thermal desorption. Lagesson V, Nilsson A and Tagesson C. Chromatographia 2000; 52: 621-624
- IV. Microorganisms and volatile organic compounds in airborne dust from damp residences. Nilsson A, Kihlström E, Lagesson V, Wessén B, Szponar B, Larsson L and Tagesson C. Indoor Air 2004; 14: 74-82
- V. Quantitative determination of volatile organic compounds in indoor dust using Gas Chromatography - UV spectrometry. Nilsson A, Lagesson V, Bornehag C-G, Sundell J and Tagesson C. (Submitted.)
- VI. Volatile organic compounds in indoor dust from residences of children with symptoms of asthma and/or allergy; a case-control study. Nilsson A, Fredrikson M, Lagesson V and Tagesson C. (Manuscript.)

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## BACKGROUND

### *Indoor environment and health*

The concept of an association between indoor environment and health is old. A passage in the Old Testament refers to the remedy for buildings affected by leprosy (visible mould growth); it gives detailed instructions on how to proceed with this remedy and concludes by directing that buildings must be demolished if they cannot be restored (Leviticus 14:45). In ancient times, exposure to high levels of indoor pollution was evident from soot deposits on the ceilings of caves and houses where open fires were used for heating and cooking and the fumes from the fires were ventilated by an opening in the roof (Jones 1999).

During the 19<sup>th</sup> century it was widely believed that the cause of disease was miasmas (noxious odours) (Halliday 2001). In attempts to remove odours, sewers were constructed and improved, and garbage was handled in such a way as to prevent foul odours. As understanding and awareness increased regarding the serious threat epidemics posed to public health, as well as regarding how infectious diseases can be prevented, public health continued to improve. Subsequently, more interest was then focused on the working environment of heavy industry and on outdoor air pollution (Sundell and Kjellman 1994). It is only recently that interest has been directed toward non-industrial indoor environments. This focus was initially triggered by reports of occupants of various indoor environments who complained about a variety of unspecific symptoms such as irritation or dryness of mucous membranes, burning eyes, headaches and fatigue. Although in some cases elevated concentrations of specific air pollutants such as formaldehyde could be related to symptoms, it rapidly became clear that acute reactions to specific chemicals in the indoor air were not the only concern (Maroni et al., 1995). Estimates of population exposure to air pollutants had been based exclusively on data from outdoor air monitoring, and thus the estimates of exposure to indoor pollutants were most likely misjudged (Maroni et al., 1995). Although indoor pollution is not per se more dangerous than outdoor pollution, concentrations of indoor contaminants are often higher than those encountered outside. Moreover, since people today spend a large proportion of their time indoors, for many individuals indoor air is more important than outdoor air in terms of exposure (Jones 1999).

Today, there is increasing concern about the health effects of poor quality indoor air. The importance of the indoor air environment is further augmented by new building techniques to conserve energy, since this has resulted in reduced ventilation rates (rates as low as 0.2 to 0.3 air exchanges per hour can now be found). Reduced ventilation enables the build-up of concentrations of indoor pollutants that are higher than those found outdoors (Jones 1999). Various indoor

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exposures have been associated with asthma, such as allergens from dust mites, pets, and microorganisms and irritants such as sulphur dioxide and nitrogen dioxide (Jones 2000). During the past few decades a large number of new materials have also been introduced, such as fiber board and plastic carpeting, resulting in new emission sources of exposure that have not previously been encountered. The long-term health implications of these emissions and exposures are presently unknown.

### ***Sick Building Syndrome***

The characteristics of SBS are non-specific symptoms that occur in non-industrial environments. Common symptoms are headache, fatigue, lack of concentration, eye, skin and throat irritation, and cough (Redlich et al., 1997). Accordingly, 24 % of the residents of multi-family buildings in Sweden reported tiredness (Engvall et al., 2001). SBS has been an increasingly common problem over the past few decades, as older, naturally ventilated buildings have been replaced by buildings with more energy-efficient mechanical ventilation (Redlich et al., 1997). Thus, 30.6 % of workers in an air-conditioned building reported a lack of comfort as compared to 18.9 % of workers in naturally ventilated buildings (Muzi et al., 1998).

Thus far there are no clues as to the mechanism behind SBS. In general, exposure to chemical, physical, and biological hazards occurs at low levels, since mainly non-industrial environments are affected. However, unlike industrial or accidental exposures, such low-level indoor exposures are very common and a much larger number of people are exposed on a daily basis throughout the year. Levels of exposure estimated to be safe in occupational environments may thus pose a risk if they are also present in the home, since the exposure takes place during a much longer period. Also, the people who are exposed may represent a more diverse group than can be expected in an industrial environment and may include more sensitive individuals, e.g. children and the elderly, who may react to levels of exposure that would go unnoticed by others.

There is no clear distinction between “healthy” and “sick” buildings. In all buildings, people experience symptoms of SBS to varying degrees. SBS is a term used to describe the reduced comfort and health status of a larger number of subjects. The prevalence of symptoms can vary between buildings, as can the severity of symptoms. Some residents in a sick building may be free of symptoms, whereas others have severe although not life-threatening respiratory or skin disorders that can be unpleasant and disruptive.

Thus far there is no universally accepted clinical definition of SBS, no single factor or group of factors has been established as the single cause of SBS, and it is best viewed as multifactorial in origin (Redlich et al., 1997). Interventions in offices that increase ventilation and reduce VOC levels may have a positive effect in reducing

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SBS symptoms. In one intervention study (Pejtersen et al., 2001), ventilation was increased in effectiveness and the heating system redesigned. A linoleum carpet had been identified as a cause of dissatisfaction and it was replaced with a low emitting vinyl carpet at the same time. The study involved two offices, and both received the intervention regarding ventilation and heating, while the floor material was changed in only one of the offices. It could be shown that perceptions of thermal discomfort and poor air quality, as well as symptoms of irritation in the nose and throat, itchy hands, dizziness and concentration difficulties, were reduced by the intervention when compared to a control office (Pejtersen et al., 2001). Both offices that received the intervention showed reduced complaints and symptoms, but the office where the ventilation and heating as well as the floor material were changed had the most pronounced improvement. This study indicates that intervention may have a positive effect on the comfort and health of occupants. Ventilation rates alone may also have an effect; in an exposure chamber modelled as a normal office room, ventilation rates were changed between 3, 10 and 30 L/s per person while subjects performed simulated office tasks. Increasing the ventilation rate had significant positive impact on perceived air quality while productivity increased (Wargocki et al., 2000).

### ***The increased prevalence of allergy and hypersensitivity***

In 1873 Charles Blackley provided clear evidence that pollen grains are the causative agents of hay fever and that farmers were less inclined to suffer from hay fever than were educated people. He also made the prediction that “as civilisation and education advance, the disorder will become more common than it is at the present time” (Blackley 1873). Today, a number of epidemiological studies have shown that the prevalence of allergic and other hypersensitivity conditions in children has increased, particularly in industrialised countries. In Melbourne, Australia, the 12-month prevalence of wheeze in 7-year-old children increased from 19.1 % in 1964 to 46 % in 1990 (Robertson et al., 1991). A similar study was performed in Aberdeen, Scotland, showing that the prevalence of wheeze increased from 10.4 % in 1964 to 19.8 % in 1989 in children aged 8 - 13 years. (Ninan and Russell 1992). A follow-up study in 1994 demonstrated a further increase to 25.4 % (Omran and Russel 1996). Similar results were found in Singapore, with an increased prevalence of childhood asthma from 5.5 % in 1967 to 13.7 % in 1987 and 19.5 % in 1994 (Lai et al., 1996). The prevalence of asthma increased from 6.8 % in 1980 to 11.0 % in 1996 in the USA (national data) in children up to 14 years of age (Mannino et al., 2002). Further, in Münster, Germany, the 12-month prevalence of wheeze in girls aged 6-7 years increased from 7.5 % in 1994/1995 to 12.7 % in 1999/2000 (Maziak et al., 2003). In the United Kingdom, the prevalence of doctor-diagnosed asthma had increased to 20 % for children aged 2-15 years in 1996 (Primates et al., 1996).

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In Sweden, the prevalence of asthma in 7-year-old school children increased from 2.3% to 5.1 % in Gothenburg and from 4.0 % to 6.8 % in Kiruna between 1979 and 1991 (Åberg et al., 1995). In the county of Östergötland, the prevalence of asthma in 7-year-old children increased from 5.3 % in 1989 to 10.9 % in 1997 (Faresjö et al., 1999). The prevalence of doctor-diagnosed asthma increased from 5.7 % in 1996 to 7.1 % in 1998 in children aged 7-8 years in Kiruna, Luleå and Piteå, while the 12-month prevalence of wheeze was reduced from 11.7 % to 10.2 % (Rönmark et al., 2002). The prevalence of asthma increased from 2.0 % for men in Sweden aged 17-20 years and liable for military service who were born in 1952-1956, to 7.2 % for those born in 1977-1981 (Bråbäck et al., 2004). In the county of Värmland, Sweden, 4.5 % of all children under 7 years of age had been diagnosed as having asthma during 1998 (Hederos et al., 2002). The Swedish part of the ISAAC study found a 12-month prevalence of wheeze of 10.2 % in Östersund and 7.9% in Linköping for children aged 10-11 years in 1997 (Annus et al., 2001).

It is not entirely clear whether or not the prevalence of allergic disease has further increased during the past few years. In Ankara, Turkey, the prevalence of asthma, wheeze, allergic rhinoconjunctivitis and allergic dermatitis in children 6-13 years did not change between 1992 and 1997 (Kalyoncu et al., 1999). In the UK, data on incidences of asthma episodes in children were collected during 1989 through 1998, and a gradual decrease was evident for all age groups after 1993 (Fleming et al., 2000). In Australia, on the other hand, an increase in the prevalence of asthma and atopy in children aged 8-11 years was found between 1992 and 1997; the 12-month prevalence of wheeze increased from 22.1 % to 27.2 % while doctor-diagnosed asthma increased from 30.5 % to 38.6 % (Downs et al., 2001). In the United States, asthma hospitalisation and mortality in children 0-17 years of age were found to have plateaued since 1995, suggesting that intervention and prevention may have reduced hospitalisation and mortality (Akinbami and Schoendorf 2002). It should be borne in mind that minor increases in the prevalence of asthma and allergy in recent years may be due to treatment of mild symptoms (Kwong et al., 2001).

In all, respiratory diseases represent a major health burden for children today. Among children under 15 years of age, respiratory diseases (ICD 460-519) accounted for 7 of the top 15 diagnoses emanating from physicians' offices in the United States in 1995-1996 (Schappert and Nelson 1999). The economic costs of asthma on a national scale are thus substantial. For example, it was estimated that in 2000 approximately 9.3 billion dollars were spent on hospital and emergency departments and pharmaceuticals in the United States (Redd 2002).

Allergy is associated with increased IgE-production and an imbalance between different types of T-helper cells (Th-cells) (Strannegård and Strannegård 2001). The two major categories of Th-cells (Th1 and Th2) are characterized by production of different cytokines such as IFN- $\gamma$  (a Th1 cytokine) and IL-4 (a Th2 cytokine)

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(Chung 2001). Th1 cells stimulate cell-mediated inflammatory reactions, while Th2 cells stimulate the production of IgE antibodies. Allergic disease is characterized by an increased expression of Th2 cytokines relative to Th1 cytokines (Benson et al., 2001).

The major hypothesis proposed to explain the increase in allergy and hypersensitivity has been the hygiene hypothesis. This involves the idea that newborn infants (who are skewed towards a spontaneous Th2-cell activation because Th1-cells are suppressed during pregnancy (Raghupathy 1997)) do not receive enough activation of the Th1-cell immune system after birth to overcome the imbalance (Chung 2001). Normally, infants have an increased Th1 expression as they mature that overcomes the Th2 imbalance, and delay or failure of this Th1 response may result in Th2 persistence and a later development of allergy and other hypersensitivity (Chung 2001).

For an environmental factor to cause an increased prevalence of allergy, it should be able to polarize the cytokine balance towards Th2 immunity. Furthermore, its occurrence in nature should help to explain the difference in allergy and hypersensitivity between different geographical areas (Strannegård and Strannegård 2001). Children with many older siblings have a reduced risk for allergy and hypersensitivity (Strachan et al., 1997); the more children in a family, the more infections they encounter. This has led to the hypothesis that a high load of infections early in life may help to prevent allergy and hypersensitivity. (Strannegård and Strannegård 2001). Many infections are caused by viruses, and viruses such as enterovirus that stimulate IFN- $\gamma$  production are indeed common in countries with a low prevalence of allergy and hypersensitivity (Strannegård and Strannegård 2001). Although other viruses such as the respiratory syncytial virus and the Epstein-Barr virus instead stimulate IgE production, viral infections seem to be protective overall (Strannegård and Strannegård 2001). The hygiene hypothesis has not been scientifically verified however (Strannegård and Strannegård 2001). In fact, strong support in epidemiological studies for an early life Th1 activation as a critical factor in preventing the development of allergic disease is still lacking (Kemp and Bjorksten 2003).

In earlier times, healthy newborn infants were quickly colonized by *E. coli* or other enterobacteria during their first days of life, but in countries characterized by a Western lifestyle this colonization now occurs more slowly (Strannegård and Strannegård 2001). The delayed colonization is due at least in part to improved hygienic conditions and is thus consistent with the hygiene hypothesis. A late colonization of Gram-negative bacteria causes reduced LPS levels in the gut and reduced oral tolerance for substances introduced perorally (Strannegård and Strannegård 2001). It also leaves the field open to other bacteria. Accordingly, early colonization by *Staphylococcus aureus* seems to be increasingly common in

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developed countries (Strannegård and Strannegård 2001). This altered bacterial colonization might lead to a persistent Th2-type immunity and, later, to the development of allergic disease (Strannegård and Strannegård 2001).

In recent decades, changes have occurred in the dietary consumption of fatty acids. The consumption of linoleic acid in margarines has increased, while the consumption of omega-3 fatty acids (found in large quantities in fat fish and fish oil) has decreased (Black and Sharpe 1997). It is known that atopic individuals have a different composition of fatty acids in their blood compared to healthy individuals with higher levels of linoleic acid. One theory is that linoleic acid promotes the formation of PGE<sub>2</sub>, because linoleic acid is a precursor of arachidonic acid which in turn is a precursor of PGE<sub>2</sub>. Interestingly, PGE<sub>2</sub> inhibits the formation of IFN- $\gamma$  (Black and Sharpe 1997) and thus linoleic acid would promote a Th2-type immunity. Some epidemiological data support the idea that dietary factors may contribute to the increased prevalence of allergy and hypersensitivity. Thus, high intake of fish oil and fatty fish has been shown to be a protective factor against allergy and hypersensitivity in several parts of the world (Strannegård and Strannegård 2001).

The increased prevalence of allergy and hypersensitivity has also coincided with the increased use of fossil fuels. Diesel exhaust particles have been found to stimulate formation of IgE both *in vitro* and *in vivo* (Peterson and Saxon 1996). However, epidemiological data that fully support the idea that diesel exhaust particles may cause allergy and/or hypersensitivity are still lacking (Strannegård and Strannegård 2001).

Regarding ETS, this is a well known trigger for symptoms if asthma is already present. The precise role of ETS in asthma development is less well understood (Gold 2000). Although children exposed to maternal smoking have been found to have increased serum IgE levels, there is little evidence to support the idea that the general increase in allergy and hypersensitivity is due to ETS (Gold 2000). However, ETS is a risk factor for wheezing among non-atopic children and for severe respiratory disease in children with established asthma (Strachan and Cook 1998).

Ambient outdoor air pollution has been suggested as a cause of the increase in allergy and hypersensitivity. The International Study of Asthma and Allergies in Childhood (ISAAC) study describes the worldwide prevalence of asthma, allergic rhinoconjunctivitis and atopic eczema in children aged 13-14 years (Beasley et al., 1998). The highest prevalences of asthma were found in the UK, Australia, New Zealand and the Republic of Ireland, while the lowest were found in Eastern Europe, Greece and several developing countries. Low prevalences of allergic rhinoconjunctivitis and atopic eczema were found in countries with low prevalences

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of asthma, while high prevalences were scattered across the world without a clear connection to high prevalences of asthma. The finding that countries with elevated ambient air pollution had low prevalences of asthma indicates that outdoor air pollution is not a major risk factor for the development of asthma, although it may exacerbate existing asthma in affected individuals (Beasley et al., 1998).

In summary, the prevalence of allergy and hypersensitivity has increased during the past few decades in several parts of the world. However, the reason(s) for this increase remain unclear. Since the increase has been too rapid to be explained by changes in genetic predisposition, one or several environmental factors are thought to underlie the increase. It is possible that combinations of physical, chemical and biological factors play important roles in the development of allergy. There might be changes in adjuvant or enhancing factors, or loss of protective factors (Ring et al., 2001). Therefore, continuing research is needed regarding different environmental factors and tools and techniques that expand our knowledge of different environmental factors.

### *Indoor Air Quality*

The role of the indoor environment in the increased prevalence of allergy and hypersensitivity is receiving increasing attention. Accordingly, a number of indoor environmental factors such as low air quality, mould growth, and dampness have been connected to respiratory symptoms and to asthma and allergy (Davies et al., 1998; Garrett et al., 1998; Peat et al., 1998; Koskinen et al., 1999; Gent et al., 2002; Jacob et al., 2002; Zock et al., 2002). The association between dampness in buildings and health effects was recently confirmed in an extensive review of available epidemiological data (Bornehag et al., 2001). A previous review also found cough and wheezing in children to be connected to damp and mouldy residences (Peat et al., 1998). However, the agents in the damp residences that are responsible for the health effects remain to be demonstrated. Moreover, it has not yet been shown whether a poor indoor climate plays a causal role in the increased prevalence or if this association is due to a precipitation of symptoms in already sensitized individuals (Strannegård and Strannegård 2001). It is a common belief that a cleaner indoor environment with fewer allergens and chemicals will result in fewer cases of allergy and hypersensitivity, but this is not supported by scientific data. Nor do scientific data support the idea that the introduction of new allergens and chemicals in the environment is the cause of the increased prevalence of allergy and hypersensitivity.

The relation between indoor air quality (IAQ) and perceived health is complex. It is difficult to simply define and measure good IAQ, and the meaning of the concept of good IAQ may differ depending on the observer. The building engineer determines IAQ based on ventilation rates, the chemist based on the presence of chemical pollutants in the air, the microbiologist based on the presence of

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microorganisms, and the physician based on medical examinations. There are at least three different categories of factors that affect the IAQ: thermal comfort, physical stressors such as noise and lightning, and air concentrations of chemical and biological pollutants and (Levin 1995).

Among the factors that affect indoor thermal comfort, air temperature, humidity and air velocity are vital. The optimal air temperature in an indoor environment depends on type of work, climate and clothing. For light office work during the winter period and clothing with high thermal resistance, the optimal temperature range has been calculated at 21-23 °C (Höppe and Martinac 1998). This temperature range is estimated to satisfy 80 % of occupants. During the summer period the optimal temperature interval is 23-26 °C as clothes with low thermal resistance are used (Levin 1995). Humidity might appear to be too low in buildings with poor indoor quality, but this is often a symptom of chemical contaminants rather than dry air. Instead, humidifying the air can lead to unwanted bacterial growth (Sundell and Kjellman 1994). At high humidity levels, residents tend to describe the air as stale, while low levels of humidity can promote unpleasant electrostatic discharges. The acceptable relative humidity range for an air temperature of 20 °C has been described as 30-81%, although there is little scientific evidence to support a need to regulate humidity (Höppe and Martinac 1998). Air velocity is important for heat exchange between the human body and the ambient air, and small changes in air velocity can have a large effect on heat transfer (Höppe and Martinac 1998). It is also important to design the ventilation system so that it does not cause draughts as air moves along cold surfaces (Höppe and Martinac 1998). Among physical stressors that may reduce IAQ and cause discomfort are: heat or glare from sunlight, glare from indoor lighting (which may also cause glare on monitor screens), noise, vibrations and crowding at the workplace.

Inorganic air pollutants such as nitrogen dioxide, sulphur dioxide and carbon monoxide are primarily indicators of unventilated combustion, and if detected at elevated concentrations they should be dealt with promptly. Ozone indicates the presence of laser printers and copiers that are not properly ventilated, and it can lead to discomfort in cramped offices. Human effluents such as isoprene have been demonstrated to react with ozone, leading to odorous compounds, and this further underscores the importance of controlling indoor ozone emissions. Ozone may also be introduced purposely from air purifiers to improve the IAQ, possibly in combination with air fresheners that emit terpenes. In a mouse model experiment it has been shown that reaction mixtures of ozone and terpenes below NOEL levels can produce significant airway irritation (Wolkoff et al., 2000). The use of ozone generators as air fresheners was reviewed by Boeniger, who concluded that ozone generators are ineffective in improving IAQ and instead pose a serious potential health risk (Boeniger 1995). As early as 1858 it was shown that moderate levels of carbon dioxide (1000 ppm) lead to discomfort (Pettenkofer 1858), and thus carbon

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dioxide should be monitored so that it does not accumulate beyond the recommended threshold value of 800 ppm (Jones 2000). Elevated concentrations of carbon dioxide should result in an overhaul of the building's ventilation system. In general, concentrations of air contaminants must be kept at levels that do not cause adverse reactions, while physical parameters should be controlled in order to achieve comfort for the majority. A minority of individuals, however, may still have adverse reactions, since people differ regarding their tolerance for chemical contaminants and other stress factors. Sick and vulnerable individuals may be more sensitive and react to levels of exposure that would go unnoticed by others (Levin 1995).

Many factors that affect IAQ are complicated and interact with one another, and it is not easy to rank the different factors in terms of importance. Nevertheless, the operation and maintenance of the ventilation system are crucial, because ventilation cannot be expected to operate indefinitely at peak efficiency without maintenance, as fans cease to work and debris accumulates in ventilation shafts. Housekeeping and cleaning affect the amount of dirt and dust that is present on floors as well as particles in the indoor air. Occupants' activities and metabolism produce waste products, and equipment, materials and furnishings emit chemicals that may affect IAQ if the ventilation is not adequately designed. The outdoor climate and air quality may also pose particular problems. In addition, technological developments in recent decades have increased expectations regarding IAQ. When buildings relied on operable windows for ventilation, occupants had to choose between odours and stale air or ventilation with untempered outdoor air. This trade-off implied that occupants had control over the indoor environment while expectations of comfort were limited. Today occupants have little control over the indoor environment and in some buildings the windows may not even be opened if extra ventilation is desired. At the same time technology has made it possible to control fluctuating temperatures, unpleasant odours and other deviations from ideal conditions, and expectations regarding comfort have risen accordingly (Levin 1995).

Until now, research on the health effects of indoor air components has been directed towards a limited number of chemical and physical factors. Among these are volatile organic compounds, dampness, environmental tobacco smoke, microorganisms, and dust particles.

### **Volatile organic compounds**

Of the chemical contaminants present in the indoor air environment, formaldehyde is the VOC that has been studied most, and it has been shown to cause discomfort at low concentrations (Jones 2000). Since formaldehyde is off-gased from new furniture and building material, this is mostly a problem in new or newly

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renovated buildings. Formaldehyde has been shown to have effects at concentrations below 1 ppm (Koeck et al., 1997).

For other VOC commonly found in the indoor environment the situation is more complex. Experiments in which volunteers were exposed to VOC in exposure chambers were performed as early as 1984 (Mølhave et al., 1984) and 1987 (Kjærgaard et al., 1987). In these studies human subjects were exposed to VOC at levels that can be anticipated in normal residences, and a dose-response relation between concentrations of VOC and complaints could be established. In field studies, however, there has been considerably less success in connecting an individual VOC or groups of VOC to SBS symptoms. VOC have been used as markers of polluted indoor air in a number of studies and are frequently used by consultants in the IAQ business. Measurement of TVOC was originally designed as an *ad hoc* tool for screening and evaluation of odour irritation (Mølhave 2003). Its present use includes exposure assessment, source identification, and IAQ evaluation. It cannot be used alone as a tool to measure IAQ since it primarily measures the effectiveness of the ventilation (Mølhave 2003).

In addition to traditional VOC, cascade reactions that degrade chemicals emitted by building materials and chemicals introduced or emitted by humans add to the total chemical exposure in the indoor environment. Wolkoff and co-workers reviewed the literature on chemical reactions in the indoor environment and concluded that reactions between ozone and nitrogen oxides and VOC can produce significant amounts of irritants (Wolkoff et al., 1997). Reaction mixtures of  $\alpha$ -pinene, limonene or isoprene, and ozone were shown to adversely affect respiration rates in a mouse bioassay, while no individual NOEL value was reached for any of the reaction products (Wolkoff et al., 2000).

### **Dampness**

Although the causative agents responsible for the increased incidence of allergic diseases and the development of SBS have not been identified, several reviews have identified dampness in the indoor environment as a risk factor for respiratory health. Associations between dampness and respiratory symptoms in children (wheeze/cough) were thus demonstrated in a review of studies that investigated respiratory health outcomes in relation to housing characteristics (Peat et al., 1998). The association between dampness in buildings and health effects in airways, as well as other SBS symptoms such as tiredness and headache, was recently confirmed in an extensive review of available epidemiological data (Bornehag et al., 2001).

There are several ways a building may be damaged by moisture. Water from rain and snow may penetrate leaking roofs, and moisture from the ground may enter the building due to design flaws or carelessness on the part of builders. Water pipes

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can rupture or water may enter a building through heavy rains. Moisture-generating activities indoors may cause condensation on surfaces that is typically due to inadequate ventilation. Moisture is generated by perspiration and exhaled breath from humans and animals but also by plants. Shower and laundry rooms are other examples where moisture may be generated by the activities of residents. Condensation of moisture on indoor surfaces can lead to visible mould growth and increased presence of dust mites (Bornehag et al., 2001). In addition, moisture damage is characterized by a build-up of moisture in building materials, creating a reservoir of moisture that can allow growth of microorganisms to take place inside the building material. Such hidden growth of microorganisms is often noticeable due to a mouldy smell and odour (Bornehag et al., 2001). Condensation on the inside of windows, damp spots on indoor surfaces, flooding, water leakage, visible or smelly microorganisms, and building construction associated with increased risk for damage (such as a flat roof) have been used as indications of dampness and for characterizing houses as damp (Bornehag et al., 2001).

The association between dampness in buildings and health effects is convincing. Thus, Bornehag and co-workers identified four different categories of studies in the literature: self-reported “dampness” and self-reported health, self-reported “dampness” and clinical examinations, objective signs of “dampness” observed by investigators and self-reported health, and objective signs of “dampness” observed by investigators and clinical examinations (Bornehag et al., 2001). It was concluded that all categories of studies showed similar associations between health effects and “dampness”. Relative risks for respiratory symptoms such as cough, wheeze and asthma were in the range of 1.4-2.2 regardless of whether self-reported health or clinical examinations were used or self-reported “dampness” or objective investigations. Although there is strong evidence that the association between “dampness” and health effects is true, the humidity-related factor(s) that cause the health effects is not known.

### **Environmental tobacco smoke**

Environmental tobacco smoke (ETS) is an important and avoidable risk factor for respiratory diseases in children. Thus, ETS has been identified as a risk factor for asthma (and exacerbation of existing asthma) in children in a number of reviews. A pooled odds ratio of 1.46 for incidence or prevalence of asthma was reported in 17 studies (DiFranza and Lew 1996). Odds ratios of 1.21 for asthma and 1.24 for wheeze (Cook and Strachan 1997) have also been reported, as have odds ratios of 1.37 for asthma and 1.31 for wheezing illness (Strachan and Cook 1998). Exposure to ETS has usually been determined by questionnaires, and measures of exposure have included maternal or paternal smoking, number of household smokers, and number of cigarettes smoked. Urinary levels of cotinine have been included as an objective marker of ETS in a few studies (Strachan and Cook 1998). One study used urinary cotinine levels below or over 10 mg cotinine per mg creatine to classify

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children as non-exposed or exposed to ETS; this study demonstrated an odds ratio of 3.5 for respiratory morbidity in exposed children (Bakoula and Kafritsa 1995). It was also found that urinary cotinine levels were associated with peak expiratory flow rate variability and respiratory symptoms in 6-8-year-old boys, indicating that ETS exposure may be associated with bronchial responsiveness in children (Kuehr et al., 1998). When objective measures of ETS exposure were evaluated, it was concluded that markers such as urinary cotinine excretion or nicotine in air fail to take long-term ETS exposure into consideration (Woodward and Al-Delaimy 1999). Cotinine has a half-life of 20-24 hours in the body, i.e. only the last few days of exposure can be estimated, and nicotine in air measures only short-term exposure (Woodward and Al-Delaimy 1999). The potential use of a long-term sampler of nicotine in air is obvious. One such passive sampler is indoor dust. It was recently found that nicotine concentrations in indoor dust correlate strongly with the amount of tobacco smoked in the residence (Hein et al., 1991). Another study examined the amounts of nicotine in indoor air, on surfaces (typically the coffee table and the child's bedframe) and in indoor floor dust in relation to the urinary cotinine levels of infants. The concentrations of nicotine in indoor dust correlated well with urinary cotinine levels (Matt et al., 2004). In a similar study, a strong correlation between urinary cotinine and nicotine levels in house dust could be determined (Willers et al., 2004). Nicotine in indoor dust is therefore concluded to be a good measure of ETS exposure. Additional advantages are that dust sampling in a household can be done by the parents, which is a cost effective means of obtaining samples, and this is a non-invasive method as opposed to obtaining urine samples.

### **Microorganisms**

Both bacteria and moulds have been linked to adverse health effects in several studies (Burrell 1991; Brunekreef 1992; Cooley et al., 1998; Garrett et al., 1998; Peat et al., 1998; Koskinen et al., 1999). For example, *Stachybotrys atra* (*chartarum*) in damp residences has been associated with SBS and even with life threatening conditions such as pulmonary haemorrhage and haemosiderosis (Smoragiewicz et al., 1993; Johanning et al., 1996; Etzel et al., 1998; Hodgson et al., 1998). *S. atra* is a somewhat extreme example, but more common moulds such as *Alternaria*, *Penicillium* and *Aspergillus* have also been linked to asthma and atopy (Garrett et al., 1998; Peat et al., 1998). Notably, a number of allergens have been characterized in several moulds commonly found in the indoor environment such as *Alternaria*, *Ulocladium*, *Stemphylium*, *Cladosporium* and *Aspergillus* (Larsen 1994; Kurup and Banerjee 2000).

*Bacterial cell wall components.* Endotoxin or LPS is the major component of the outer cell membrane of all Gram-negative bacteria, while peptidoglycan is the predominating macromolecular cell wall constituent of both Gram-positive and Gram-negative bacteria. Both these components are bioactive and pro-

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inflammatory: endotoxin can stimulate the immune system in amounts as small as 10 LPS molecules per cell (Liu 2002) , while the potency of peptidoglycan is magnitudes lower (Moreillon and Majcherczyk 2003). Exposure to endotoxin in early life has been suggested to protect against asthma and allergy. This is because endotoxin exposure is much higher in rural and farm homes than in nonfarm, metropolitan homes, and children growing up on farms have a lower incidence of asthma and allergy (Liu 2002). Moreover, both endotoxin and peptidoglycan stimulate a Th1 immune response and secondarily suppress Th2-type immunity. According to this mechanism, exposure to microbial air pollutants would be protective against allergy and asthma in young children, since microbial load changes the Th1/Th2 cytokine balance and protects against the development of allergic sensitization (Strannegård and Strannegård 2001).

Although exposure to endotoxin at an early age seems to protect against allergy and asthma, exposure to endotoxin later in life is a risk factor for developing asthma (Liu 2002; Rylander 2002). High endotoxin content in house dust of metropolitan homes is also a risk factor (Liu 2002). The reason endotoxin is a risk factor in one situation while it is a protective factor in another is thought to be due to timing, dose, environmental co-factors and genetic factors (Liu 2002). A rat model of atopic asthma in which rats were sensitized with ovalbumin (OVA) and then later challenged with OVA showed that: (1) If LPS was administered to the rats before or up to 4 days after sensitization with OVA, later exposure to OVA would result in reduced levels of OVA-specific IgE and increased serum IgG levels, along with decreased oedema and airway hyperresponsiveness compared to rats not treated with LPS. (2) If LPS was administered after 4 days had passed, a later challenge with OVA instead caused increased airway inflammation and oedema compared to rats not treated with LPS. Depending on the time of exposure, LPS was able to stimulate B cells to differentiate into IgG-producing plasma cells; however, if the isotype switch had already occurred, then LPS directly stimulated those B cells that had been primed to produce IgE (Tulic et al., 2000).

*Moulds.* Traditional measurements of moulds in indoor air used collection of air samples by impaction on agar surfaces. This method provides information on cultivable or viable microorganisms and enables identifications, but greatly underestimates the total amounts of spores in indoor air. Microorganisms do not have to be viable to have a biological effect, and therefore other techniques have been developed to measure the total amounts of microorganisms in air. Ergosterol is a robust measure of fungal biomass in air and has the advantage that it can be measured by well-established methods such as GC-MS (Miller and Young 1997; Sebastian and Larsson 2003). Another possibility is to measure airborne (1→3)-β-D-glucan, a polyglucose compound present in the cell wall of fungi that has also been demonstrated to have biological effects. Thus, (1→3)-β-D-glucan levels in indoor air have been shown to be associated with airway inflammation and other SBS

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symptoms such as fatigue, cough and wheeze (Rylander 1999). It has been suggested that (1→3)- $\beta$ -D-glucan is able to modulate the response to other agents including endotoxin (Rylander and Lin 2000).

*Microbial volatile organic compounds.* Microbiologically produced volatile organic compounds (MVOC) are emitted by microorganisms during all stages of growth (Sunesson 1995). Some of these compounds have sufficiently low odour thresholds to be detected by smell in a mouldy building (Wolkoff and Wilkins 1994; Wessén and Schoeps 1996). Even though MVOC analyses have been used commercially to investigate problem buildings, they remain difficult to use. This is at least partly due to the fact that the emission of MVOC is highly dependent on the substrate used by the mould, and by other growth conditions.

### **Indoor dust particles**

Most of the interest in the health effects of particle pollution has been focused on outdoor particles. In several studies, associations have been observed between outdoor particulate air pollution, mortality (Dockery et al., 1993), and respiratory symptoms (Dockery and Pope 1994; Neas et al., 1994; Pope et al., 1995). The focus has recently shifted somewhat to concern indoor environments as well. Non-occupational indoor exposure to dust particles has been shown to be low compared to that in occupational settings, although personal monitoring has revealed that exposure can be higher than stationary monitoring has indicated (Liu et al., 2003). Indoor particle concentrations may differ from outdoor concentrations depending on air exchange rates, filtration of outdoor air, and indoor sources of particles such as tobacco smoking, cooking and cleaning (Suh et al., 2000). The outdoor levels of particulate matter have been estimated to explain approximately 25% of the indoor levels in a general population, while smoking can add 30  $\mu\text{g}/\text{m}^3$  of  $\text{PM}_{2.5}$  to the indoor air (Wallace et al., 2003). Indoor sources of particles may increase indoor levels of  $\text{PM}_{2.5}$  to higher concentrations than outdoor levels even in non-smoking residences (Wallace et al., 2003).

Indoor dust exposure can lead to headache and other symptoms such as mucous membrane irritation and odour annoyance (Skov et al., 1990; Gyntelberg et al., 1994; Salvaggio 1994; Mølhavé et al., 2000a). One possible reason for this may be that dust particles adsorb large quantities of gases and other volatile compounds (Wolkoff et al., 1997) that may be irritating and cause odour annoyance. As early as 1880, Elias Heyman stressed, in a footnote regarding controlling dust in the indoor environment, the importance of cleaning in order to avoid problems with dust contamination, and pointed out that ventilation cannot in and of itself ensure a healthy indoor environment (Heyman 1880). More recently, Skov and co-workers investigated 14 town halls in the county of Copenhagen, Denmark, where 4369 people were employed. The employees answered questionnaires and a number of factors were investigated regarding the buildings. The results showed that among

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other things, the fleece and shelf factor (the area of fleecy materials divided by room volume and length of all open shelves and cupboards divided by room volume) was positively associated with mucous irritation, headache and fatigue (Skov et al., 1990).

Indoor dust is described as the dispersed distribution of solid material in indoor air (Butte and Heinzow 2002). It may consist of both inorganic and organic particles as well as fibres of different sizes and can be very heterogeneous with regard to quantity and composition. Indoor sources include smoking and combustion processes, fibers from paper, wood and textiles, the occupants themselves, their pets, and activities taking place in the residence. Outdoor sources include outdoor air polluted with particles and material tracked indoors from clothing and footwear. There is a large variation in particle size, shape, density and porosity (Butte and Heinzow 2002). Dust can be partitioned between fibrous and nonfibrous components. The relation between fibrous and nonfibrous components differs, not only between buildings but also between samples taken in different rooms in a building depending on the activities taking place in the room.

The dust particles consist of a relatively inert core with its surface covered by adsorbed compounds that can be biologically active (Wolkoff and Wilkins 1994; Mølhave et al., 2000b; Nilsson et al., 2004). Indoor dust adsorbs a large variety of gases and other volatile compounds from human activities and emissions from building and furnishing materials. In this way, indoor dust is a passive sampler of past emissions and can be regarded as an ideal screening material to obtain information about an indoor contamination (Butte and Heinzow 2002). Moreover, since analyses of indoor dust are an estimate of contamination of indoor pollution, they may provide valuable information regarding human exposure to indoor pollution (Butte and Heinzow 2002).

Indoor dust and compounds adsorbed onto indoor dust may enter the human body by inhalation of suspended or resuspended particles, through hand to mouth behaviour by toddlers, through ingestion of particles adhering to food or surfaces, and by absorption through the skin (Butte and Heinzow 2002). Particles in the range of 5-25  $\mu\text{m}$  may be resuspended by common activities such as walking on carpets and cleaning (Thatcher and Layton 1995). The determining factor when estimating the amount of indoor dust that is inhaled and deposited in various parts of the respiratory system is the aerodynamic diameter of the particle. Particles larger than 10  $\mu\text{m}$  are typically found in the stomach, since they are impacted in the nasal area due to inertial forces; the particles are then cleared by mucociliary transport and swallowed. Particles less than 10  $\mu\text{m}$  in aerodynamic diameter are known to be inhalable, and those less than 2.5  $\mu\text{m}$  are respirable. With nasal breathing, more than 90% of particles between 2 and 20  $\mu\text{m}$  in diameter are retained in the upper nasal airways. With mouth breathing, these particles are instead

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deposited to a large extent in the trachea and bronchi. Particles with irregular shapes can behave in unpredictable ways; asbestos fibres with lengths of 200  $\mu\text{m}$  and diameters of 0.5  $\mu\text{m}$  behave more like a spherical particle with a diameter of 0.5  $\mu\text{m}$  in terms of being able to travel to the alveolar parts of the lung (Salvaggio 1994).

It is reasonable to assume that particle size may influence the concentration of compounds adsorbed onto indoor dust particles. When pesticides and polycyclic aromatic hydrocarbons were quantified in size fractions of floor dust, the concentrations increased typically by a factor of 4 (median) between coarse dust (< 2mm) and respirable dust (< 4  $\mu\text{m}$ ) (Lewis et al., 1999). This increase was less than expected when only considering the increase in surface area, suggesting that other factors such as the porosity of the dust particles may also influence the contents of chemical compounds.

In this thesis (paper II), a relatively unexplored mechanism for SBS due to powdering floor polish is presented. In Sweden, the use of linoleum carpets has become common in public and private buildings. To maintain the carpet, a wax or polish is applied to its surface to create both a moisture barrier and a durable surface. If the polish is applied on too dry a carpet (which may be the case during the winter or if a cleaning agent is used with a pH that is greater than 8.0), the polish may decompose into a fine white powder (Follin 1995). Floor polish for linoleum carpets contains acrylate copolymers; acrylate monomers may have an irritating effect on mucous membranes and cause asthma (Savonius et al., 1993; Piirilä et al., 1998), and acrylic monomers are also known to cause allergic contact dermatitis (Björkner 1984; Kanerva et al., 1994).

### *Tools for indoor air quality assessment*

Traditional tools for investigation of IAQ are primarily:

- VOC or TVOC measurements with GC-MS. Despite lack of evidence for a relationship between TVOC and health, it continues to be a common measure of IAQ. Individual VOC such as 2-ethyl-hexanol are considered as markers for problem environments, but this is based on personal experience rather than scientific research.
- Air sampling for moulds and bacteria. This is regularly performed in IAQ investigations, although there are questions regarding its relevance to human health. Total number and number of colony forming units of moulds and bacteria are counted. If species are found that prefer high moisture conditions, this is considered an indicator of a damp environment. However, determinations of total and viable microorganisms in indoor air have not proven generally useful in showing their impact on human health (Husman 1996). At least some of these difficulties may be due to the problem of getting

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relevant samples for examination. Microorganisms may grow in building materials without any exposure to humans. Conversely, humans may be exposed to airborne microorganisms that are not demonstrated by examining building materials. It is possible that collecting and analysing airborne particles (as described in this thesis) is a better way of assessing human exposure to microorganisms than ordinary air sampling.

- Direct measurements of various inorganic gases such as carbon monoxide, carbon dioxide, nitrogen monoxide, nitrogen dioxide, sulphur dioxide and ozone. Results from measurements of inorganic gases can help the investigator determine ventilation effectiveness and whether unvented installations are polluting the indoor environment.

These methods have thus far been unsuccessful in determining the reasons why bad IAQ may lead to SBS. Statistically significant correlations between different IAQ parameters and symptoms of SBS have been reported in several studies. In practice, however, they are of less significance since in an individual case a healthy building may have more values indicating bad IAQ than a sick building.

In order to analyse the very complex samples from the indoor environment, combinations of analytical and spectrometric techniques are commonly used. The most widely used technique for the analysis of VOC is GC-MS. This is a powerful technique, but it has some limitations:

- MS spectra cannot readily be predicted for molecules with multiple fragmentation pathways. When a molecule has more than one starting point for fragmentation (which is the case in molecules with more than one functional group), the number of pathways for fragmentation grows exponentially and the ability to elucidate structures by predicting significant mass fragments diminishes accordingly.
- MS spectra for structural isomers are generally very similar, since the fragmentation pathways do not differ between the isomers. This makes it difficult to discriminate isomers from one another.
- In general, functional groups do not have characteristic spectra. This makes classifications of unknowns regarding functional groups difficult.
- Compounds containing oxygen can undergo catalytic dehydrogenation and dehydration reactions.
- For quantification in GC-MS to be accurate, standard curves for all compounds have to be generated from reference compounds.

## GC-UV

The principle of using UV-spectrometry as a detector for gas chromatography was first presented in several articles by Kaye in the early 1960s (Kaye 1961b; Kaye 1961a; Kaye 1962; Kaye and Waska 1964). Since then a series of papers have been published describing developments in this area, including a doctoral thesis (Lagesson 1992). Three research groups with different approaches regarding instrumental design have dealt with GC-UV (Novotny et al., 1980; Lagesson 1992; Vicente et al., 1996). The research group in Linköping, Sweden, originally designed a gas flow cell fitted for use in regular UV-spectrometers. It was later developed into a flow cell made of carbon-filled plastic material that can conduct electricity. Consequently, it can be operated at elevated temperatures of up to 200 °C with an external power source. The flow cell also contains a separation column, which can be compared in terms of efficiency with a traditional packed column used for GC. It is packed with support particles otherwise used to pack HPLC columns treated with a solid phase. Thus the column efficiency is comparable to a HPLC column with a length of 8 cm. The separation column is connected to an on-column injector for sample introduction, thereby turning the flow cell into a complete gas chromatograph (Figure 1). The gas flow cell can also be supplemented with a capillary GC column that bypasses the built-in separation column (not shown in figure).

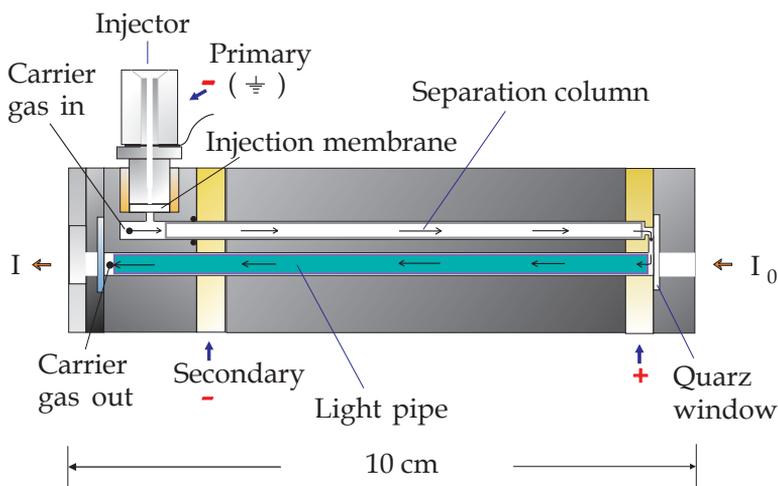


Figure 1. The GC-UV flow cell with a built-in micro gas chromatograph.

The flow cell is used in conjunction with a deuterium lamp and a PDA spectrometer to enable rapid scans of the effluent from the built-in separation column or the external capillary column in the UV-range.

A temperature control unit regulates the flow cell temperature as well as the supplemented one-stage desorption oven for sample introduction. The entire light path from the lens (this focuses the light from the deuterium lamp to the diodes on the PDA detector) is flushed with dry nitrogen in order to remove all oxygen and water vapour that would otherwise absorb UV-light (Figure 2).

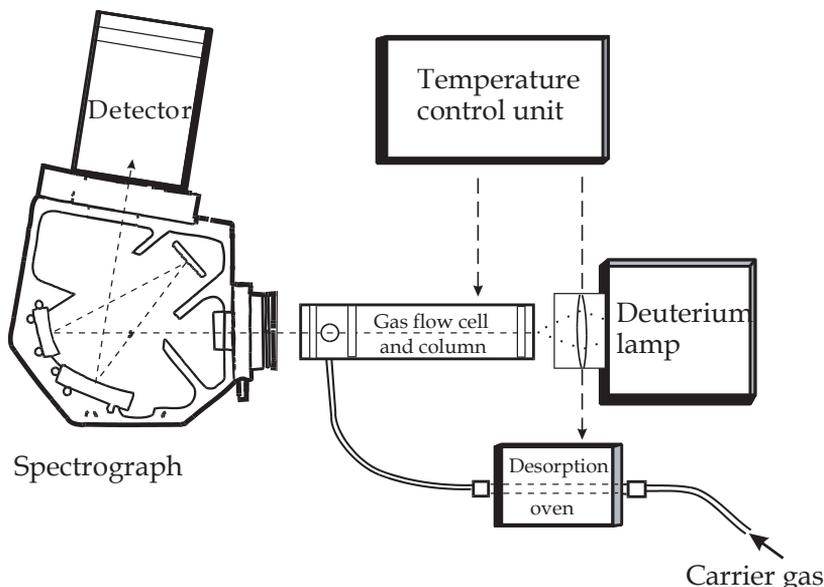


Figure 2. The GC-UV instrument supplemented with a one-stage desorption oven.

In comparison with UV-spectra taken in the liquid phase, the gas-phase spectra are not influenced by any solvent shift or interaction, and exhibit such details that libraries of spectra can be used for the identification of unknowns. Since dry nitrogen is used to flush the entire light path, it is possible to record spectra down to about 168 nm, and at these short wavelengths the highest absorptivities and the most pronounced spectral details are found. Furthermore, many groups of compounds not generally considered to be UV-absorbing can be determined at low concentrations at the short wavelengths below 190 nm. Also, groups of compounds that are generally considered as UV-absorbing in the context of liquid phase UV-spectra are magnitudes more UV-absorbing at shorter wavelengths. The benzene ring, for example, is approximately 300 times more UV-absorbing at the  $\lambda_{\max}$  in the gas-phase than at the wavelengths usually employed by HPLC-UV methods. In a library of about 1000 gas-phase UV spectra, about 70% of the compounds had absorption maxima below 190 nm (Lagesson-Andrasko 1997).

GC-UV is not limited to the analysis of organic compounds, since inorganic compounds with UV-absorption may also be analysed with high sensitivity. The

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GC-UV technique has previously been used for measuring ammonia in water (Lagesson and Newman 1986a), vinylchloride, carbon disulfide, terpenes and amines in air (Lagesson and Newman 1986b), and exhaled isoprene and acetone in children with diabetes (Nelson et al., 1998). Recently, GC-UV was also successfully applied for the determination of nitric oxide adsorbed onto different mineral fibres (Leanderson et al., 1997).

The use of complementary techniques to identify unknown compounds in environmental samples is sometimes overlooked. Conversely, confidence in the identification made by the type of mass spectrometer usually employed in environmental analyses, a quadrupole mass spectrometer with electronic ionisation, can sometimes be overestimated. In fact, to strictly follow the principles of how to identify a compound, two different detection methods that operate on different physical principles have to be used to independently identify the compound. In a GC-MS system this can be accomplished by analysing standards, since the retention time is dependent on the compound's volatility and polarity while the spectrum is dependent on the chemical structure. In environmental samples, however, it is often not practical to analyse standards of every suggested identity from a library search. An alternative method to confirm identities of unknown compounds is GC-FTIR. A recent example of how complementary techniques can identify compounds while a single technique fails was presented by Laniewski and co-workers. A combination of GC-FTIR (giving information on functional groups), GC-MS (providing information about molecular mass and mass of fragments), and GC with an atomic emission detector (supplying data on individual elements and enabling calculation of the empiric formula) was used to identify an unknown impurity (Laniewski et al., 2003). Because GC-UV is several magnitudes more sensitive than GC-FTIR, GC-UV may have an important advantage over GC-FTIR as a complement to GC-MS.

In summary, the GC-UV technique is a low cost and low maintenance system as compared to more complex systems such as GC-MS. The GC-UV system can easily be linked to an external capillary GC for sample introduction, whereby complex samples can be analysed. Other spectrographic methods such as FTIR have a long history of use as complements to GC-MS for structure elucidation (for review see Raganathan et al. (1999)), but are lacking in sensitivity. By contrast, UV-spectrometry has a high sensitivity for detection, identification and quantification of many compounds. Methods based on GC-UV might therefore be useful for the study of chemical compounds in indoor dust, since this is a complex sample matrix and reference compounds cannot be expected to be available for confirmation of all identities. These considerations encouraged the present work.

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## AIMS OF THE STUDY

- To develop a new technique for the sampling and GC-UV analysis of indoor dust.
- To apply GC-UV for the analysis of indoor dust from a secondary school in which pupils had health problems associated with powdering floor polish.
- To further develop the GC-UV technique for analysing chemical compounds in indoor dust using capillary GC, and to compare this technique with GC-MS.
- To compare airborne dust from damp and control residences with regard to microbial and chemical components using GC-UV and GC-MS for the analysis of VOC.
- To use GC-UV for the quantitative analysis of VOC in indoor dust from a large number of residences.
- To use GC-UV and GC-MS for the quantitative analysis of VOC in indoor dust from residences of children with symptoms of allergy and/or asthma and residences of healthy control children.

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## MATERIALS AND METHODS

### *Dust sampling*

Dust samples were collected for different purposes in the different papers. In paper I, the samples were obtained from 23 ordinary residences (13 apartments and 10 houses) and 4 offices. In paper II, samples were collected from a secondary school in which pupils and teachers reported frequently occurring mucous membrane irritation in the eyes, nose and throat as well as lower respiratory tract symptoms. In papers III and IV, samples were taken from nine damp and nine control residences. The damp residences were identified through co-operation with a local firm specialized in the detection and remedy of water-damaged residences, whereas control residences were ordinary residences with no problems or complaints from their occupants. In papers V and VI, a questionnaire was first sent to the families of 14 077 children aged 1-6 years in the county of Värmland, Sweden. Based on the responses to the questionnaires, 198 children with symptoms of allergy and/or asthma and 202 non-symptomatic children were selected. These children lived in 390 residences (since there were ten pairs of siblings). Samples were taken from all 390 residences.

As to the sampling technique, two different approaches were applied. To collect settled dust (papers I, II, III,V,andVI), a conventional vacuum cleaner and a dust filter system obtained from ALK Sverige AB (Kungsbacka, Sweden) were used. This system uses a standardized cellulose filter and is commercially available in one configuration only. The filter is mounted on a mouthpiece which can be fitted on the hose of any vacuum cleaner. The filter retains 74% of particles 0.3-0.5  $\mu\text{m}$ , 81% of particles 0.5-1.0  $\mu\text{m}$ , 95% of particles 1-10  $\mu\text{m}$  and  $\approx 100\%$  of particles  $> 10 \mu\text{m}$ . After sampling, the dust particles were put into gas-tight 4 ml glass vials and kept at  $-20^{\circ}\text{C}$  (papers I and III),  $+4^{\circ}\text{C}$  (paper II) or  $-70^{\circ}\text{C}$  (papers V and VI) until analysed.

To enable the analysis of airborne dust (papers I and III/IV), a new technique for dust sampling was designed. This technique uses a commercial electrostatic air cleaner modified to permit disassembling of the filter cassette and collection of dust from the metal plates (ALF-75, ELFI Elektrofilter AB, Lidköping, Sweden). This sampler can collect airborne dust at a rate of  $115 \text{ m}^3/\text{hour}$  with an efficiency of 99.5 % for particles 0.3  $\mu\text{m}$  and larger. During the sampling (1 to 7 days), the dust (5-60 mg) was collected onto 17 metal plates, each of which is about  $10 \times 13 \text{ cm}$  in size. The dust sampler was placed at a central location and at least 50 cm over the floor. In order to obtain the dust sample in a more handy form, a special vacuum-cleaning device was developed. The procedure for concentrating the dust sample onto a membrane filter is illustrated in Figure 3. After this procedure, the dust sample was

transferred from the membrane filter, weighed, and placed in gas-tight 4-ml glass vials and stored at -20°C until analysis.

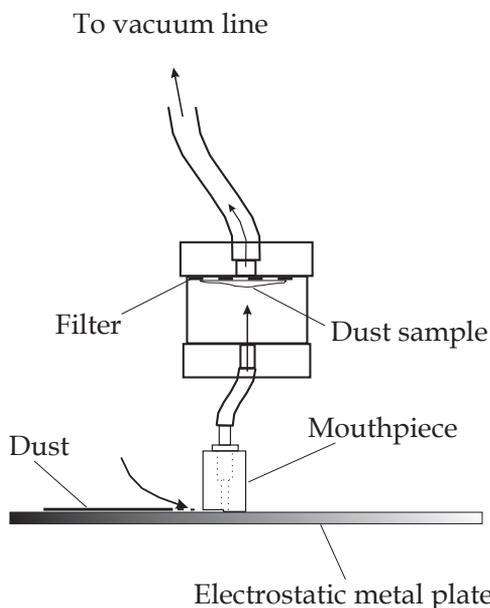


Figure 3. Device for collecting dust from electrostatic metal plates. The mouthpiece is slowly moved over the metal plate so as to collect the dust onto the filter. From paper I with permission.

When using this high capacity dust sampler for a longer period of time, the airborne dust concentration cannot be assumed to be constant over time. Therefore, figures indicating the amount of dust collected per volume of air sampled would give a falsely low exposure assessment. Thus comparisons between residences with respect to determinations of chemical compounds adsorbed on airborne dust are limited to qualitative comparisons. However, the applied sampling technique also has several advantages. The long sampling time eliminates temporary fluctuations, and airborne dust is likely to give a better measure of exposure than settled dust. The use of the electrostatic dust sampler also makes it possible to perform a wider range of different analyses on the dust, as is exemplified in this thesis, as compared to traditional dust sampling with low volume, short time sampling on filter cassettes.

### ***GC-UV equipment***

A novel GC-UV spectrophotometer was used (INSCAN GC-UV 175 Spectrophotometer, INSCAN AB, Stockholm, Sweden). The instrument comprises a

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gas flow cell with a built-in micro gas chromatograph, a one stage thermal desorption oven and a nitrogen (N<sub>2</sub>)-flushed PDA detector for fast UV spectra recording. PDA spectral sampling was performed by exposing the diodes for 0.14 seconds and collecting the average spectra every 4<sup>th</sup> second for packed column GC and every 2<sup>nd</sup> second for capillary column GC. A slit width of 0.3 mm (which gave a bandwidth of 1.7 nm) was used throughout the recordings. The wavelength scale was regularly calibrated using the spectral lines from a mercury/argon pen lamp. The whole light path was flushed with dried N<sub>2</sub>, thus enabling registration of UV spectra down to 168 nm, where many compounds show the highest absorptivities and the most important spectral details. Collection of raw data from the PDA-detector was performed with an Instaspec 2.25 program (Andor Technology, Belfast, Northern Ireland). Raw data were processed into chromatograms by a Grams 386 ver 3.02 program (Galactic Industries, Salem, NH, USA), which also handled identifications and quantifications in combination with the IR-search ver 3.18 program (Galactic Industries, Salem, NH, USA). Compounds were identified by using a reference library containing about 1000 reference spectra (Lagesson-Andrasko 1997).

#### ***GC-UV with packed column***

Dust particles (5-20 mg) were inserted into a small glass tube that was placed in the desorption oven and flushed with N<sub>2</sub>. The flow valve was then closed and the compounds desorbed at 150°C for 2 min in N<sub>2</sub>. The flow was then turned on and the desorbed compounds led into a 80 x 1.5 mm GC column packed with 10 µm Nucleosil NH and OV17 as a stationary phase (Alltech, Deerfield, IL, USA). To improve separation of basic compounds the column was treated with KOH. The GC was carried out using a carrier gas flow rate of 15 ml/min and a linear temperature ramp at 8°C/min from 40°C to 140°C.

#### ***GC-UV with capillary column***

For the analysis of less volatile organic compounds a capillary gas chromatograph was coupled to the gas flow cell, bypassing the built-in micro gas chromatograph. In this case the dust sample was desorbed at 150 °C, and the desorbed volatile chemicals were collected on a Carboxen/PDMS SPME fibre (Figure 4).

The SPME-fibre was then desorbed in the splitless mode (1min) in a split/splitless injector to the capillary column. The gas chromatograph used was initially a GC 6000 Vega series 2 from Carlo Erba Instrumentasone with an HP 5-MS column (30 m, 0.32 mm id, 1.0 µm); later, a Hewlett-Packard 5890A with an Elite-624 column (30 m, 0.32 mm id, 1.8 µm) was used.

#### ***GC-MS equipment***

For GC-MS analyses, samples were desorbed with the ATD400 from Perkin-Elmer and analysed with the Autosystem XL and Turbomass from Perkin-Elmer. A HP-

5MS column was used (30 m, 0.22 mm id, 1.0  $\mu\text{m}$ ). Dust samples were desorbed at 150  $^{\circ}\text{C}$  to a Tenax TA cold trap at + 10  $^{\circ}\text{C}$  and injected by heating the cold trap to 300  $^{\circ}\text{C}$ . The temperature program was 35  $^{\circ}\text{C}$  for 2 min, 10  $^{\circ}\text{C}/\text{min}$  to 290  $^{\circ}\text{C}$  with a 15 min conditioning.

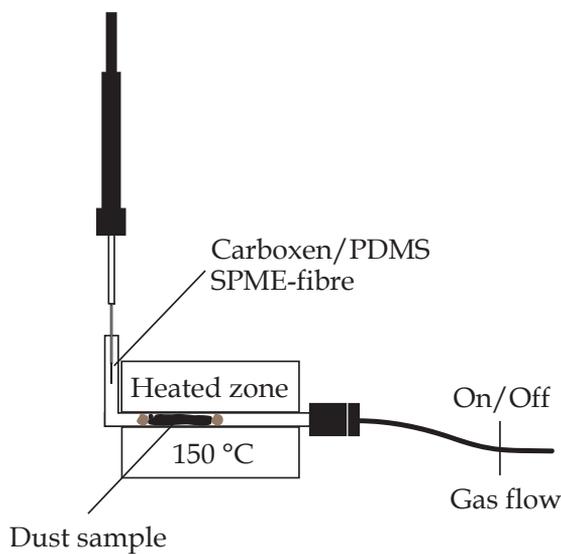


Figure 4. The procedure of desorbing adsorbed volatile compounds onto a SPME-fibre. The desorbed compounds diffuse to the SPME-fibre assisted by a 1 ml/min gas flow.

### ***Determination of microorganisms***

The dust samples were extracted with sterile particle-free (< 18 megohm/cm) 0.01 % Tween-80 solution for 3 minutes at 23  $^{\circ}\text{C}$ . The extract was then analysed for total, viable, and metabolically active (esterase-positive) microorganisms. The total bacterial and fungal biomass was determined as acridine orange-stained particles, while the viable fraction was determined as colony-forming units on malt extract agar for fungi and on tryptone glucose extract agar for bacteria (Ström et al., 1990). The esterase-positive fraction was determined as fluorescent cells after staining with fluorescein diacetate (Söderström 1977).

### ***Analysis of 3-hydroxy fatty acids and muramic acid***

3-Hydroxy fatty acids and muramic acid were used as marker substances for lipopolysaccharide (LPS) and peptidoglycan (PG), respectively, as described elsewhere (Saraf and Larsson 1996; Bal and Larsson 2000). In brief, 1-3 mg aliquots of dust samples were heated overnight in methanolic HCl. After cooling, penta-deuterated 3-OH C 14:0 methyl ester was added as an internal standard for 3-

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hydroxy fatty acids and a methanolysate of algal cells (containing C<sup>13</sup> - labelled muramic acid) was added as an internal standard for muramic acid. Samples were extracted with water and heptane; the organic phase was used for analysis of 3-hydroxy fatty acids and the aqueous phase was used for analysis of muramic acid. The organic (upper) phase was subjected to solid phase extraction in order to separate hydroxylated from non-hydroxylated fatty acid methyl esters, and trimethylsilyl derivatives of the hydroxy acids were then prepared (Saraf and Larsson 1996). The lower phase was evaporated, acetylated, and washed prior to analysis (Bal and Larsson 2000). The preparations were analysed by using gas chromatography-ion trap tandem mass spectrometry (GC-MS/MS) (Saraf et al., 1999).

### ***Statistical determinations***

In paper II the program EPI Info ver 6 (CDC, Atlanta, GA, USA) was used to calculate the prevalence rate ratios with 95 % confidence intervals for the different symptoms and to estimate the preventive effect of removing the polish. In paper IV the SigmaStat ver 2.03 program (SPSS Inc, Chicago, IL, USA) was applied. The t-test was used to determine if the concentrations of microorganisms, muramic acid and 3-OH fatty acids in airborne dust were different between damp and control residences. A two-tailed significance level of  $p < 0.05$  was used. To determine if the sample size was large enough the power was calculated for each test.

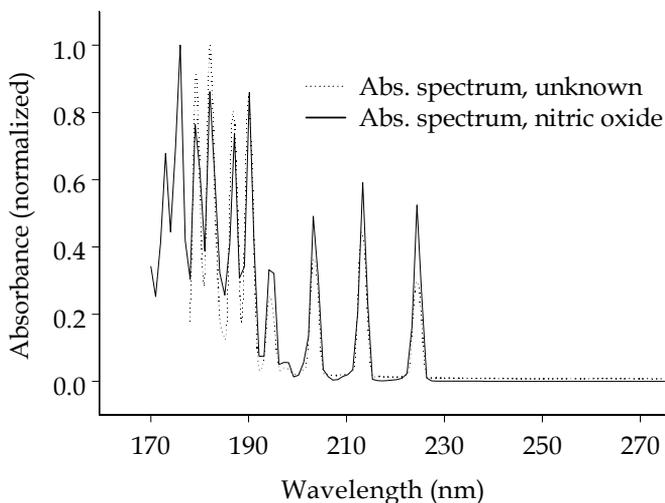
In paper V and VI the SPSS ver 11.0 and 11.5 program was applied (SPSS Inc, Chicago, IL, USA) for statistical determinations and for calculations of mean concentrations and standard deviations. In paper V the Kolmogorov-Smirnov test was used to determine if concentrations of compounds in indoor dust were normally distributed; a p-value  $> 0.05$  was taken to indicate normal distribution. In paper VI, the t-test was used together with calculations of odds ratios using stepwise logistic regression.

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## RESULTS AND DISCUSSION

### *Paper I*

In this paper, a novel technique was demonstrated for the analysis of low molecular weight compounds adsorbed to indoor dust. Indoor dust samples were taken from a wide variety of indoor locations (apartments, single-family houses, offices and schools) and analysed using GC-UV. Compounds were identified by comparing the spectrum of an unknown compound with reference spectra from a user library. An example is given in Figure 5, which shows the identification of nitric oxide in a dust sample from a residence.



*Figure 5. Identification of nitric oxide in a dust sample from a residence. The figure shows the spectrum of the unknown compound overlaid with a reference spectrum of nitric oxide.*

Water present in dust samples can impair chromatography in capillary GC columns and disrupt GC detectors. However, the miniaturized GC column and the PDA-detector in the present system were able to cope with the water present in indoor dust samples.

A number of inorganic and organic volatile compounds (such as nitric oxide, ammonia, 2-furaldehyde and isoprene) could be simultaneously determined in a single analysis, both on airborne and settled dust. Several compounds that were found have considerable biological or toxic potential. Among these are nitric oxide, different aldehydes and isoprene.

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Quantification of nitric oxide and ammonia were performed in all the samples and concentrations were found to be well over detection limits in most cases. There were large differences in the amounts of adsorbed nitric oxide and ammonia on dust obtained from different sampling sites. At present, there is no conclusive explanation for these differences. However, considering the potential biological effects of these compounds, it would seem important to be able to measure their concentration in indoor dust. It can be anticipated that such measurements will improve the overall survey of the indoor environment and help to clarify building-related illnesses including SBS.

### *Paper II*

In Scandinavia, linoleum flooring is very common indoors. To extend the life of the products, linoleum carpets are sometimes treated with acrylate polish to provide a more durable and easier-to-clean surface. However, a common complaint from residents is the phenomenon of powdering polish on linoleum carpets; this involves breakdown of the polish into a fine white dust that is visible on clothes and shoes. Until recently, the phenomenon of powdering floor polish was considered to be only a technical problem. However, if the powder contains acrylate monomers, this might also cause medical problems. Acrylic monomers are known to give allergic contact dermatitis in areas such as the printing industry (Björkner 1984) and dentistry (Kanerva et al., 1994). There are also several cases reported in the medical literature indicating that at least some acrylate monomers might have an irritating effect on mucous membranes and also cause asthma (Savonius et al., 1993; Piirilä et al., 1998). The effect of floor dust exposure on mucous membranes has been described by Skov et al (1990), who showed a clearly significant positive correlation between floor dust and mucosal irritation.

In paper II it was shown that the floor dust from a school with problems due to powdering floor polish contained acrylate monomers. This might explain why pupils in this school showed symptoms of respiratory system irritation. A possible mechanism of action could be that acrylic monomers are transported on respirable dust particles that reach the lower airways, thereby causing irritation of the mucous membranes. Such a mechanism is proposed as an explanation for the additive effect seen from formaldehyde in the presence of wood dust, where formaldehyde exerts a stronger irritating effect in combination with wood dust than it does alone in the same concentration range. This is possibly because formaldehyde is adsorbed on the particles of wood dust and transported deep into the airways (Ulfvarson and Alexandersson 1990).

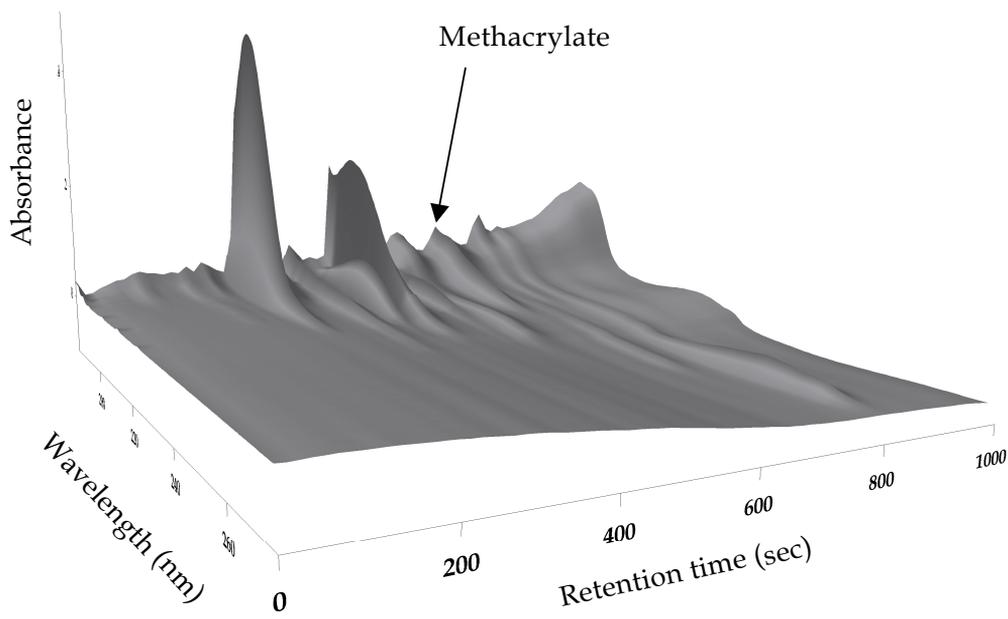


Figure 6. GC-UV analysis of a dust sample from a school with powdering floor polish.

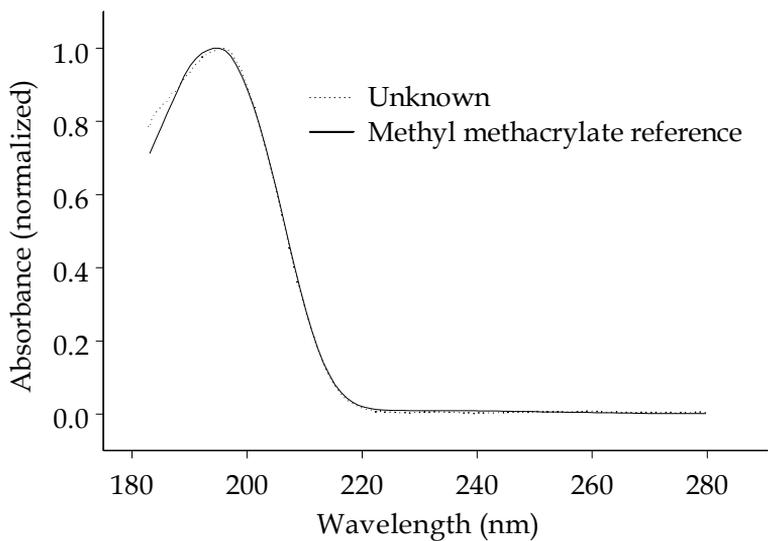


Figure 7. Classification of an unknown compound as a methacrylate in a dust sample from a school with powdering floor polish.

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The identification of acrylate monomers was accomplished using GC-UV. One advantage with GC-UV as compared to other techniques such as GC-MS is that compounds can readily be classified as to which functional group they contain. Since it was known that the floor polish used in the school was an acrylate-styren product, the dust sample could be analysed for breakdown components of this product. It appeared that the sample contained methacrylate (Figure 6).

This paper illustrates both advantages and limitations of GC-UV in the analysis of acrylate monomers. Classification of compounds as acrylate monomers was readily done, since the functional group of acrylate monomers gives a characteristic gas-phase spectrum (Figure 7). However, the different saturated chains attached to the functional group do not alter the spectrum enough to facilitate identification of a specific monomer. With a more complete UV-spectra library of various acrylate monomers, identifications could have been improved, but this was not possible at the time of the study.

### *Paper III*

To further improve the GC-UV analysis of VOC in indoor dust, a capillary gas chromatograph column was coupled to the gas flow cell, bypassing the built in miniaturized gas chromatograph. Fifteen dust samples were then analysed by this system and by GC-MS under similar conditions of thermal desorption and GC separation. This way, the GC-UV technique was compared to GC-MS for the analysis of volatile compounds in indoor dust.

A total of 192 different compounds were identified or classified to their functional group. It was shown that GC-MS is considerably more successful in the determination of compounds such as alkanes, non-aromatic carboxylic acids, non-aromatic alcohols and glycols and non-aromatic esters, all of which are known to have low absorptivities in the UV wavelength range covered. For non-aromatic aldehydes, GC-MS and GC-UV are about equally good. For groups of compounds containing isolated C-C double bonds like alkenes and terpenes, the possibilities for determination also seem to be about equally good for the two methods.

When conjugation was present or an aromatic structure was involved, the GC-UV method gave more favourable results. With regard to the further applications of the present work, this is a potentially important finding, because 2-alkenales (found in all dust samples) are known to be potentially harmful to the skin and eyes and irritating to the nose and throat. 2-alkenales are a good example of the possibilities for classification of compounds regarding functional group. The functional group of 2-alkenales has a characteristic UV-spectrum, which enables rapid and accurate classification.

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For aromatic compounds, the GC-UV method gave even more favourable results. In the 15 dust samples, the GC-UV method detected 22 unique aromatic compounds and a total of 150 determinations of these compounds, whereas only 4 unique aromatic compounds were detected and a total of 7 determinations were made by the GC-MS method. One of the aromatic compounds found was benzaldehyde, which was determined in all samples by GC-UV, while GC-MS detected this compound in only two of the samples. These two samples contained the highest concentrations according to the GC-UV measurements.

Knowing that benzaldehyde was present in all samples according to the GC-UV analysis, its presence was then confirmed by the GC-MS method at the predicted retention time by forming chromatograms for the 105  $m/z$  (a predominant fragment of benzaldehyde) fragment alone.

Concerning isomers, GC-MS identified a compound as 3-furfuraldehyde using the NIST 97 search algorithm, while Perkin-Elmer's own Turbo Mass search system identified it as 2-furfuraldehyde. By contrast, the GC-UV identification clearly indicated 2-furfuraldehyde. It should be emphasized that in the vast majority of cases gas-phase UV spectra are able to distinguish between structural isomers. This is not the case for GC-MS. On the other hand, GC-UV cannot easily differentiate between compounds of homologous series, where the only difference between compounds is the length of a saturated chain. Use of the two methods in combination is therefore very advantageous. In addition, due to its ability to classify substances, the GC-UV method can confirm or disprove evidence suggested by GC-MS for identification purposes.

#### **Paper IV**

To further examine the use of GC-UV for indoor environment analysis, airborne dust samples were taken from nine damp and nine control residences and analysed for VOC (using GC-UV and GC-MS). In addition, the dust samples were analysed for their content of bacteria and mould, as well as 3-hydroxy fatty acids and muramic acid (marker substances for LPS and peptidoglycan, respectively).

The results show that the number of mould species was greater in the damp residences than in the controls (23 vs. 18), and nine species were found only in damp residences. The levels of 3-hydroxy fatty acids and muramic acid correlated better in damp residences than in controls, indicating that damp conditions selectively favour growth of certain bacterial species. Identifications made by culture and microscopy of the major moulds found, i.e. *Aspergillus*, *Cladosporium* and *Penicillium*, coincided with the identification of VOC known to be produced by these species. By contrast, this was not the case for *Alternaria*, *Botrytis*, *Eurotium*, *Fusarium*, *Paecilomyces*, *Phialophora* and *Trichoderma*. It is known that MVOC

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production is dependent on the growth conditions, so that MVOC produced under laboratory conditions are not necessarily produced under field conditions.

Of the 19 MVOC identified in the dust samples, eight MVOC (1,3-octadiene, 1-octene, 2-pentylfuran, cyclopentanone, hexanal, nonanal, octanal and pinene) were identified equally well by GC-MS and GC-UV. Seven MVOC (1-hexanol, 1-octanol, 2,3,5-trimethylfuran, 2-ethyl-1-hexanol, acetic acid, heptane and methyl acetate) were better identified by GC-MS, while four MVOC (1-octen-3-ol, 2-hexenal, acetone and benzaldehyde) were better identified by GC-UV. Thus, the combination of GC-MS and GC-UV could identify a larger number of MVOC than either technique alone.

Aside from MVOC, a number of additional VOC were found. Some of these may be irritating to the skin, eyes or respiratory tract if present at higher concentrations.

Altogether, 27 compounds classified as skin, eye or respiratory irritants were identified. Some of these were found in damp residences only, e.g. acetic acid methyl ester, 3-buten-2-one, propanoic acid, 1,2-propanediol, butanoic acid, 6-methyl-5-hepten-2-one, 2-undecenal and 1-nonanol. Others were found only in control residences (formic acid and 2-furanmethanol). 2-Ethyl-1-hexanol, hexanal, pentanal and acetic acid were found in all residences. It can be noted that 2-ethyl-1-hexanol, a compound originating from the common plasticiser diethylhexyl phthalate, is also produced by *Streptomyces* as well as by *Aspergillus* and *Penicillium* (Sunesson 1995).

The results demonstrate the diversity of microorganisms and VOC present in airborne dust in damp as well as in non-damp residences, and suggest that analysis of airborne dust may give important clues to human exposure to microorganisms and chemical compounds in the indoor environment. The results demonstrate the use of GC-MS and GC-UV in combination for the analysis of MVOC on airborne dust.

### ***Paper V***

In this paper, GC-UV was used for the quantitative analysis of VOC in indoor dust from a large number of residences. Settled indoor dust from 389 residences was collected and 28 different compounds were quantified in each sample. The compounds analysed were previously found at the highest relative concentrations in the majority of dust samples from both apartments and single-family houses (papers III and IV). Some of the compounds, e.g. 2-alkenals and furfurals, are potential irritants (to the skin, eyes or respiratory system) if present at high concentrations, while others, e.g. diethyl phthalate and 2,6-di-*tert*-butyl-4-methylphenol (BHT), are due to human actions and activities and therefore of

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particular interest. To illustrate the versatility of the technique for quantitative determinations, all 28 compounds were quantified in all the 389 dust samples.

Of the 28 VOC analysed, benzaldehyde was the most frequently found compound (found in 373 out of 389 residences). Other frequently found compounds were 2-butenal, decanal, furfurales, and other aldehydes (both saturated and unsaturated). Diethyl phthalate, heptenal, and 2-methyl-propenal (methacrolein) were found in a minority of samples.

The compounds found in highest concentrations were saturated aldehydes (C<sub>5</sub>-C<sub>10</sub>), furfuryl alcohol, BHT, 2-furaldehyde, and benzaldehyde. Alkenals were also found, notably 2-butenal (crotonaldehyde), 2-methyl-propenal (methacrolein), hexenal, heptenal, octenal, and nonenal. The concentrations of each of the 28 compounds ranged between two to three orders of magnitude, or even more. The 28 compounds were frequently found in relatively high concentrations, thus forming a pattern that reflects the VOC content of indoor dust in Swedish residences.

Several previous studies have identified VOC in indoor dust using GC-MS. However, the study described in paper V is the first to quantify a larger number of VOC in indoor dust from a large number of residences. Wolkoff and Wilkins used GC-MS and identified 188 VOC in indoor floor dust pooled from residences (Wolkoff and Wilkins 1994); however, compounds such as 2-methyl-propenal, octenal, furfurals and furfuryl alcohol were not identified in their study. By contrast, all these compounds were shown to be abundant in indoor dust from residences in Sweden (paper V). The reason for this may be that GC-UV is better suited for the analysis of these compounds than is GC-MS.

Although previous studies have identified a large number of VOC in indoor dust, there are few publications in which the identified compounds have been quantified. Øie and co-workers quantified diethyl phthalate in settled dust from 38 residences in Norway and found concentrations around 10 µg/g (Øie et al., 1997), which is in agreement with our findings. Mølhave and co-workers quantified saturated aldehydes (hexanal, heptanal, octanal, nonanal and decanal), benzaldehyde, 2-furaldehyde and pentylfuran in pooled settled indoor dust from seven offices (Mølhave et al., 2000b) and found concentrations similar to those in paper V. The differences can be attributed at least in part to differences in techniques for desorption of samples and injection of compounds to the analytical column.

The sources of chemical compounds in indoor dust are complex (Wolkoff 1995), and it is therefore difficult to determine the precise origin of the different compounds. For example, saturated aldehydes may originate from a wide range of pressed wood products as well as furniture, linoleum and parquet floors, lacquer, thermal insulation, wallpaper, tobacco smoke and mould growth (Wolkoff 1995;

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Salthammer et al., 1999; Jensen et al., 2001). Benzaldehyde can arise from growing moulds and linoleum floors, but also through the oxidation of styrene emitted from carpets, rubber and adhesives (Zhang et al., 1994; Wolkoff 1995). BHT is an antioxidant used in food as well as in rubbers and plastics (Williams et al., 1999). As to the origin of alkenals in indoor air and dust, it has been hypothesized (Morrison and Nazaroff 2002) that ozone may be the driving force for a cascade reaction in which alkenals are formed from olefins like linoleic acid in linseed oil. Other possible alkenal precursors are isoprene, a plant and microbial metabolite and also a human effluent (Wilkins et al., 2001), and oleic and linolenic acid from building products such as linoleum and furniture coatings (Salthammer et al., 1999). Diethylphthalate (DEP) is widely used as a vehicle for cosmetic products and fragrances (Api 2001), but it has also been found in the emission from shredded paper insulation (Kelman et al., 1999). Acetone is found in human exhaled breath, but can also be emitted from mould growth (Wolkoff 1995). Phenol and phenones (e.g. acetophenone) have been found in emissions from wood products (Jensen et al., 2001) and floor materials (Wolkoff 1995), respectively. Furfurals are emitted from particle board (Jensen et al., 2001) and composite cork products, e.g. floor coverings, during the degradation of hemicelluloses (Horn et al., 1998; Salthammer and Fuhrman 2000). In addition, hemicellulose (a non-cellulose polymer of various monosaccharides) is a major component of paper (Molin and Teder 2002), which could imply that furfural in indoor dust may also originate from paper. Indeed, paper dust analysed by thermal desorption and GC-UV was found to contain furfural (unpublished data). Furfuryl alcohol is used as a component in adhesives and resins, e.g. polyfurfuryl alcohol/urea-formaldehyde adhesive in particle board (Dao and Zavarin 1996; Schneider et al., 1996). Taken together, it appears that many of the compounds found at the highest concentrations in indoor dust are probably emitted or produced from pressed wood products such as particle board. This would be consistent with the finding that particle board can emit over 2 mg of aldehydes (excluding formaldehyde) per hour per square meter of particle board (Baumann et al., 2000).

Hexanal (which was found to be one of the most prevalent compounds in indoor dust) is emitted in large quantities from particle board (Baumann et al., 2000). The proposed mechanism in the literature for the formation of hexanal from wood products is the autooxidation of linoleic acid (Noordermeer et al., 2000), which is schematically described in Figure 8. Linoleic acid is found in large quantities in pine wood, which is commonly used in the manufacture of particle board in Sweden.

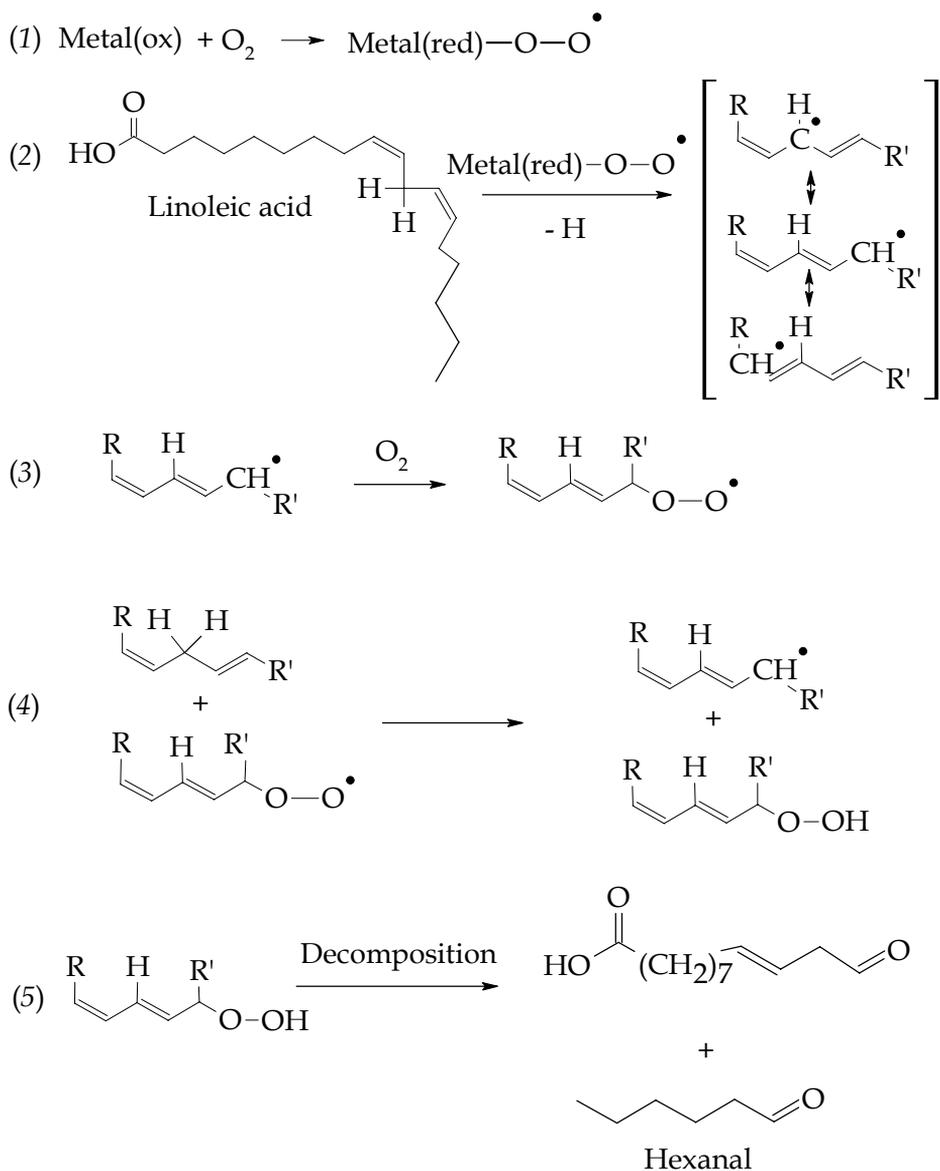


Figure 8. A possible mechanism for the autoxidation of linoleic acid into hexanal. (1) and (2): Initiation reaction, oxygen reacts with a metal ion resulting in a metallic peroxyradical. Initiation can also be caused by photolysis and thermolysis (Pine 1987). The radical then abstracts one of the allylic methylene hydrogen atoms resulting in a allylic radical (Porter et al., 1995). (3) and (4): Propagation, the allylic radical reacts with oxygen resulting in a peroxy radical which then abstracts an allylic methylene hydrogen from a new fatty acid producing a new allylic radical and a peroxide (Porter et al., 1995). (5) The peroxide decomposes spontaneously into hexanal as the dominating volatile product (Schieberle and Grosch 1981).

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When oxidation of furnishings other than wood products is studied, hexanal is no longer the most prevalent oxidation product found. When ozone interaction with nylon and olefin wall-to-wall carpet was studied, it was found that nonanal was the most prevalent oxidation product (Morrison and Nazaroff 2002). The precursor to nonanal in an oxidation process has to be unsaturated in the "9" position, counting from a straight-chain hydrocarbon end. Oleic acid is such a compound (Morrison and Nazaroff 2002) and can be autooxidated in a similar process as that for linoleic acid. Oleic acid is one of the important fatty acids comprising linseed oil, and nonanal is the major oxidation product of linseed oil.

In summary, two of the most prevalent compounds in indoor dust, hexanal and nonanal, may be due to the autooxidation of unsaturated fatty acids in wood products. Several of the other aldehydes found in indoor dust can be formed in similar oxidation processes or alternate reaction pathways.

### *Paper VI*

In this paper, GC-UV is used (together with GC-MS) for the quantitative analysis of VOC in indoor dust from residences of 198 children with symptoms of allergy and/or asthma (cases) and 202 children without symptoms (controls). Altogether 43 VOC were identified and quantified in each dust sample using gas chromatography with mass spectrometric or ultraviolet detection. The mean concentration of nicotine was found to be significantly higher in dust from case residences, while the mean concentrations of hexane, nonanal, octane, 2-pentylfuran and tridecanol were significantly higher in dust from control residences. In a stepwise logistic regression model, not only nicotine but also a number of other VOC showed increased relative risks, expressed as odds ratios comparing cases with controls (hexanal 2.55, furfuryl alcohol 1.85, nonane 1.50, butanol 1.30 and octenal 1.27). By contrast, still other VOC showed decreased relative risks (benzaldehyde 0.25, nonanal 0.56, butenal 0.64, hexane 0.72, tridecanol 0.73, and pentylfuran 0.82).

Of the compounds with an increased relative risk, only nicotine was present in higher mean concentrations in dust from case residences. By contrast, of the compounds with a decreased relative risk, all except benzaldehyde and butenal were found in lower mean concentrations in dust from case residences.

Altogether 12 compounds were retained in the stepwise logistic regression model. The concentrations of these compounds were categorized into three categories: (I) under the detection limit, (II) above the detection limit but below the median value, and (III) above the median value), and a further logistic regression analysis was performed on the 12 compounds. The relative risks for hexanal and nicotine were further increased, while the relative risk for nonanal was further decreased. This

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suggests a dose-response relationship and indicates that the ORs derived from the continuous (linear) analysis are reliable.

The results thus showed that the mean concentration of nicotine was significantly higher in dust from case residences, and nicotine also had a significantly increased relative risk. These findings further support the notion that environmental tobacco smoke is a risk factor for asthma in children (Gold 2000). Nicotine in indoor air has previously been used as a marker for passive smoking (Rothberg et al., 1998). It was then concluded that nicotine is a major and unique component of ETS (Rothberg et al., 1998). Nicotine in indoor dust has also been used as a marker for smoking behaviour (Hein et al., 1991). The amount of nicotine in indoor dust was found to correlate very well with the total amount of tobacco smoked in the residence. The exposure to nicotine from inhaling indoor dust was estimated to be low compared to that from inhaling room smoke, so indoor dust was not considered to be a significant source of ETS exposure. Nevertheless, it can be advantageous to measure nicotine in indoor dust to estimate smoking over a longer period of time (Hein et al., 1991). Matt and co-workers examined the connection between smoking behaviour and amounts of nicotine in indoor dust (Matt et al., 2004). Residences in which at least one parent smoked indoors had 3-8 times higher concentrations of nicotine in air, on surfaces and in indoor dust, compared to residences in which smokers tried to protect infants from ETS by smoking outdoors (Matt et al., 2004). Thus the amount of nicotine found in indoor dust from the child's bedroom in paper VI is likely to reflect the exposure to ETS.

The findings thus give further support to the notion that ETS is a risk factor for asthma and/or allergy in children. As to the significance of the other compounds that also show an increased relative risk (hexanal, furfuryl alcohol, 1-butanol, nonane and octenal), the implications of these findings are not yet clear, especially since the sources of these chemicals in the indoor environment are complex and it is difficult to tell the precise origin of each individual compound. Hexanal has been shown to be emitted in large quantities from wood products (Colombo et al., 1990; Baumann et al., 2000). It is suggested, therefore, that the major sources of hexanal in indoor dust are uncoated and coated pressed wood products such as particle board and plywood. A major component of pine wood (commonly used in particle board) is linoleic acid, which can be autooxidised and yield hexanal as a major product (Figure 8); this way, particle board may emit hexanal for a long time. Notably, plywood coated with polyurethane lacquer emits a large proportion of hexanal compared to other compounds (Salthammer et al., 1999; Morrison and Nazaroff 2002). Furfuryl alcohol is emitted from polyfurfuryl alcohol/urea-formaldehyde adhesive in particle board (Dao and Zavarin 1996; Schneider et al., 1996), but it can also be formed from furaldehyde (which is emitted from various wood products) through the action of bacteria (Gutierrez et al., 2002). Butanol, on the other hand, is

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emitted from vinyl and PVC floorings as well as from plastic panelling (Yu and Crump 1998) and veneered wood products (Jensen et al., 2001).

Benzaldehyde, butenal, hexane, nonanal, pentylfuran and tridecanol showed decreased relative risks. The implications of these findings, too, are unclear. Benzaldehyde is emitted from wood products but to a much lesser degree than is hexanal (Colombo et al., 1990; Baumann et al., 2000). It is likely, therefore, that benzaldehyde in indoor dust originates instead from linoleum carpets (Yu and Crump 1998), furniture coatings (Salthammer et al., 1999) or from cements and adhesives that have polystyren as a major component (Wolkoff et al., 1990; Zhang et al., 1994; Wolkoff 1995). Analogously, nonanal can be emitted not only from wood products, but also from linoleum carpets (Yu and Crump 1998) or from building materials such as mineral wool and gypsum board (Sunesson et al., 1996). Nonanal may be formed through the oxidation of oleic acid, a component of linseed oil, as described in paper V (Morrison and Nazaroff 2002). Linseed oil is the most commonly used vegetable oil in paints and varnishes and serves as the liquid base for the production of linoleum (Morrison and Nazaroff 2002). It thus seems possible that the VOC associated with decreased relative risks reflect the use of traditional building and furnishing materials.

In summary, the results give further support to the notion that tobacco smoke is a risk factor for asthma and/or allergy in children and point to the possibility that new building materials such as particle board and polyvinyl chloride floorings may be linked to the increased prevalence of allergy and hypersensitivity. Traditional building materials, on the other hand, might be linked to a decreased risk. It should be emphasized that much additional investigation is needed to identify the sources of compounds associated with increased or reduced risks and to clarify the nature of the associations.

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## METHODOLOGICAL ASPECTS

### *Thermal desorption of indoor dust*

In this thesis, thermal desorption has been used throughout the different studies. One advantage with this procedure compared to solvent extraction is that less sample material is required. Furthermore, solvent extraction of very volatile compounds may sometimes be difficult (if the compound is more volatile than the solvent the compound may evaporate before it can be analysed or it may be concealed in the solvent peak in the analysis). The advantage of thermal desorption in combination with GC-UV is that the solvent peak containing air and water does not disrupt the detection and thus unhindered detection of compounds can take place from the start of the analysis. In addition, thermal desorption does not extract compounds with very low volatility as solvent extraction does, thus the analytical column can be chosen to separate the volatile components of interest rather than to make sure that the components with very low volatility are able to pass. In conclusion, thermal desorption holds the advantage of simplicity, less sample is required, less time is required for sample preparation and less time and resources are required compared with solvent extraction.

In papers I and II a one-stage desorption method is presented. This is especially advantageous for the analysis of very volatile compounds that are difficult or even impossible to analyse in a two-stage desorption method using cryo-focusing before GC-analysis. An example of such a compound is nitric oxide, which has also been analysed on mineral fibers using this method (Leanderson et al., 1997).

Concerning the possible formation of degradation products during thermal desorption of dust, based on the appearance of the chromatographic peaks we have no reason to believe that the compounds identified were due to pyrolysis. This claim is supported by a previous study (Hirvonen et al., 1994), where it was found that heating dust in an inert atmosphere did not cause degradation of adsorbed chemicals at the temperatures used in the present investigation. A recent doctoral thesis lends further support to this conclusion (Pedersen 2001). With respect to ammonia, the question of thermal degradation is not completely settled. It can be argued that ammonia found in indoor dust may come from the degradation of urea, which would explain the observed connection between human load and amounts of ammonia found in indoor dust.

### *Advantages of GC-UV*

The use of gas-phase UV spectra has several advantages. There is no cut-off wavelength as is the case with liquid phase UV spectrometry. It is therefore possible to use the wavelength range between 168 and 190 nm, where the highest absorptivities and the most important spectral details of many compounds are

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found. UV spectra are very precisely defined (not instrument-dependent), exhibit a high degree of details, and can be denoted as “fingerprints” of the compounds. Libraries of UV-spectra of reference compounds can be created and unknown compounds can be identified in computer searches where UV-spectra of the unknown compound are compared against UV-spectra of references (Lagesson-Andrasko et al., 1998). Structural isomers that are difficult to discriminate by MS are often clearly distinguished from one another by way of their gas-phase UV spectra, since the positioning of substituents near a functional group affects the UV-spectrum. GC-UV has been used to investigate 95 different groups of isomers so far, in all cases the GC-UV method was able to distinguish between different structural isomers (Lagesson and Lagesson-Andrasko 2000).

Other advantages of GC-UV are that the limits of detection, quantification, and identification are low. The limits are of the same magnitude as for full scan quadropole GC-MS, and several magnitudes lower than for GC-FTIR (Kaye 1962; Lagesson 1992). The UV-detector response is linear over a range of  $\sim 10^4$  and there are no deviations from the Lambert-Beer’s law in the range of mass loading limits imposed by capillary columns (Lagesson and Lagesson-Andrasko 2000).

The UV-spectra of compounds are determined by the functional groups. Absorptivities of unknown compounds can therefore be determined by analysing a compound with the same functional group. Thus the need for standard curves for individual compounds is partly eliminated. Furthermore, selective analysis is possible by recording UV-absorbance in a range specific for a certain functional group. GC-UV can classify at least 50 functional groups (Lagesson et al., 2000).

If no reference spectrum is available, knowledge of which functional groups are present can lend significant support in the identification. This is illustrated in Figure 9, in which an unknown spectrum is superimposed on the reference spectrum of 2-furaldehyde; the unknown compound is very similar to that of 2-furaldehyde but is red-shifted about 9.5 nm. This similarity enables the classification of the unknown compound as a furaldehyde. This bathochromic (red) shift is typical for compounds with an additional methyl substituent adjacent to a double bond. Thus, a plausible identity for the unknown compound in Figure 9 is 5-methyl-2-furaldehyde.

In the future, it might be feasible to predict the UV-spectrum of a molecule from its chemical structure. This possibility shows some promise, but is yet to be evaluated fully. If it is shown to be practically possible, the economic costs involved in building spectra databases may be dramatically lowered.

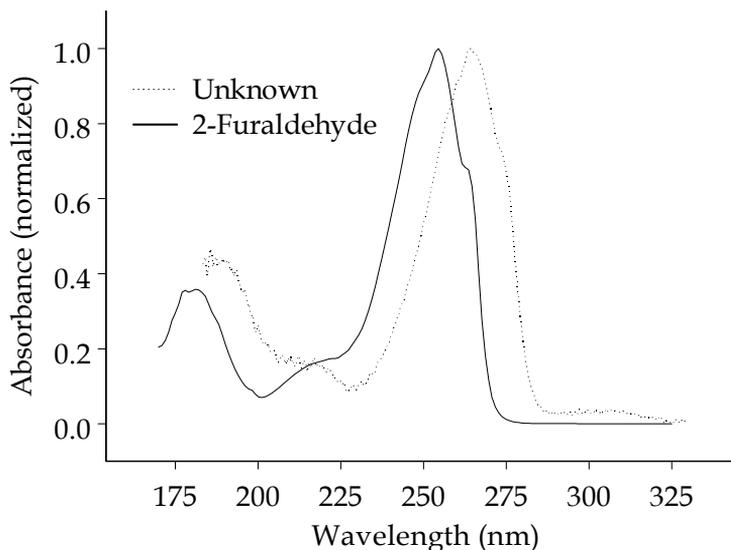


Figure 9. Classification of a compound as a furaldehyde by comparing its spectrum with a reference spectrum of 2-furaldehyde.

### **Limitations of GC-UV**

As to the limitations of the GC-UV-technique, it should be emphasized that certain compounds, e.g. alkanes, aliphatic alcohols, aliphatic esters and aliphatic chlorinated compounds, have low UV-absorptivity and are therefore not suitable for analysis. Compounds of homologous series differentiated by the length of a saturated hydrocarbon chain can also be difficult to tell apart in some cases, even though a small wavelength shift can be present.

### **GC-MS + GC-UV**

Environmental samples are often complex in composition, and compounds at trace levels are usually mixed with compounds at high concentrations. To analyse such complex samples a number of analytical techniques are employed, and the concept of “hyphenation” has been formulated to meet the increasing analytical demands. Hyphenation is the combination of separate analytical techniques via appropriate interfaces. The most common hyphenation for analyses of VOC is GC-MS. Although this is a powerful method, it may fail to distinguish isomers. In addition, functional group information is difficult to extract from mass spectra, and quantification is dependent on access to reference compounds. FTIR can supplement MS in these respects but lacks the sensitivity needed for trace analysis (the sensitivity of FTIR is about two to three orders of magnitude lower than that of full scan GC-MS).

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GC-UV shares the same complementary features as GC-FTIR, but its sensitivity is on par with full scan GC-MS. UV-spectra give comprehensive and reliable information and can help distinguish isomers and provide knowledge of functional groups present in an unknown compound. In combination with mass spectra, UV spectra provide unique possibilities to identify unknown compounds. Accordingly, if a complex sample like indoor dust is analysed for VOC by both GC-MS and GC-UV, substantially more compounds can be accurately identified than if only one method is used. It thus appears that GC-UV is a valuable complement to GC-MS and that the combination GC-MS + GC-UV may be a powerful tool in analytical chemistry.

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## CONCLUSIONS

GC-UV can be used to analyse airborne and settled indoor dust for both organic and inorganic volatile compounds.

GC-UV can be used to identify acrylate monomers in floor dust due to powdering floor polish.

GC-UV may be used as an alternative or complement to other methods such as GC-MS for measuring volatile compounds in indoor dust.

Volatile organic compounds known to be produced by microorganisms can be accurately determined by using GC-UV and GC-MS in combination.

Quantifications of volatile organic compounds in settled dust from 389 residences in Sweden show that saturated aldehydes (C<sub>5</sub>-C<sub>10</sub>), furfuryl alcohol, 2,6-di-*tert*-butyl-4-methylphenol, 2-furaldehyde, and benzaldehyde are frequently present in higher relative concentrations.

Nicotine is present in higher concentrations in indoor dust from residences of children with symptoms of asthma and/or allergy, while hexane, nonanal, octane, 2-pentylfuran and tridecanol are present in higher concentrations in indoor dust from residences of healthy control children.

Not only environmental tobacco smoke but also other emissions in the indoor environment may be linked to the prevalence of asthma and/or allergy in children

The combined use of GC-MS and GC-UV is appropriate for the analysis of volatile chemical compounds in indoor dust, thus improving the survey and control of human exposure to particle-bound irritants and other chemicals.

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