



LUND UNIVERSITY

Health effects of residential wood smoke particles: the importance of combustion conditions and physicochemical particle properties

Bolling, Anette Kocbach; Pagels, Joakim; Yttri, Karl Espen; Barregard, Lars; Sallsten, Gerd; Schwarze, Per E.; Boman, Christoffer

Published in:
Particle and Fibre Toxicology

DOI:
[10.1186/1743-8977-6-29](https://doi.org/10.1186/1743-8977-6-29)

2009

[Link to publication](#)

Citation for published version (APA):

Bolling, A. K., Pagels, J., Yttri, K. E., Barregard, L., Sallsten, G., Schwarze, P. E., & Boman, C. (2009). Health effects of residential wood smoke particles: the importance of combustion conditions and physicochemical particle properties. *Particle and Fibre Toxicology*, 6. <https://doi.org/10.1186/1743-8977-6-29>

Total number of authors:
7

General rights

Unless other specific re-use rights are stated the following general rights apply:

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Read more about Creative commons licenses: <https://creativecommons.org/licenses/>

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

LUND UNIVERSITY

PO Box 117
221 00 Lund
+46 46-222 00 00

Review

Open Access

Health effects of residential wood smoke particles: the importance of combustion conditions and physicochemical particle properties

Anette Kocbach Bølling*¹, Joakim Pagels², Karl Espen Yttri³, Lars Barregard⁴, Gerd Sallsten⁴, Per E Schwarze¹ and Christoffer Boman⁵

Address: ¹Division of Environmental Medicine, Norwegian Institute of Public Health, Oslo, Norway, ²Division of Ergonomics & Aerosol Technology (EAT), Lund University, Lund, Sweden, ³Department of Atmospheric and Climate Research, Norwegian Institute for Air Research, Kjeller, Norway, ⁴Department of Occupational and Environmental Medicine, Sahlgrenska University Hospital and Academy, University of Gothenburg, Gothenburg, Sweden and ⁵Energy Technology and Thermal Process Chemistry, Umeå University, Umeå, Sweden

Email: Anette Kocbach Bølling* - anette.kocbach@fhi.no; Joakim Pagels - joakim.pagels@design.lth.se; Karl Espen Yttri - karl.espen.yttri@nilu.no; Lars Barregard - lars.barregard@amm.gu.se; Gerd Sallsten - gerd.sallsten@amm.gu.se; Per E Schwarze - per.schwarze@fhi.no; Christoffer Boman - christoffer.boman@chem.umu.se

* Corresponding author

Published: 6 November 2009

Received: 3 June 2009

Particle and Fibre Toxicology 2009, 6:29 doi:10.1186/1743-8977-6-29

Accepted: 6 November 2009

This article is available from: <http://www.particleandfibretoxicology.com/content/6/1/29>

© 2009 Bølling et al; licensee BioMed Central Ltd.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract

Background: Residential wood combustion is now recognized as a major particle source in many developed countries, and the number of studies investigating the negative health effects associated with wood smoke exposure is currently increasing. The combustion appliances in use today provide highly variable combustion conditions resulting in large variations in the physicochemical characteristics of the emitted particles. These differences in physicochemical properties are likely to influence the biological effects induced by the wood smoke particles.

Outline: The focus of this review is to discuss the present knowledge on physicochemical properties of wood smoke particles from different combustion conditions in relation to wood smoke-induced health effects. In addition, the human wood smoke exposure in developed countries is explored in order to identify the particle characteristics that are relevant for experimental studies of wood smoke-induced health effects. Finally, recent experimental studies regarding wood smoke exposure are discussed with respect to the applied combustion conditions and particle properties.

Conclusion: Overall, the reviewed literature regarding the physicochemical properties of wood smoke particles provides a relatively clear picture of how these properties vary with the combustion conditions, whereas particle emissions from specific classes of combustion appliances are less well characterised. The major gaps in knowledge concern; (i) characterisation of the atmospheric transformations of wood smoke particles, (ii) characterisation of the physicochemical properties of wood smoke particles in ambient and indoor environments, and (iii) identification of the physicochemical properties that influence the biological effects of wood smoke particles.

Background

Exposure to ambient particulate matter (PM) has been associated with a range of negative health effects, including increased morbidity and mortality from pulmonary and cardiovascular diseases [1-3]. Although residential wood combustion is a major source of particulate air pollution in many countries, relatively few studies have been performed to investigate the health effects associated with wood smoke exposure. The two most recent reviews on the topic concluded that the adverse health effects associated with wood smoke exposure in developed countries do not seem to be weaker than for ambient particles from other sources [4,5]. However, the reviewed literature suggested that the respiratory effects of wood smoke may be somewhat larger than the cardiovascular effects [5]. The use of wood or charcoal for heating or cooking during female adolescence was recently associated with chronic obstructive pulmonary disease later in life [6], providing further support for an association between wood smoke exposure and negative respiratory effects. In addition, a human inhalation study reported that wood smoke exposure affected both systemic and lung biomarkers, suggesting a potential impact of wood smoke particles also for cardiovascular diseases [7,8]. Recently, the International Agency for Research on Cancer (IARC) classified indoor emissions from household combustion of biomass fuel (mainly wood) as probably carcinogenic to humans (group 2A) [9].

The term residential wood smoke comprises emissions from a variety of biomass combustion appliances, such as open fireplaces, wood and pellet stoves, masonry heaters, and boilers for wood, wood chips and pellets [10-12] (see Additional file 1 for a brief description of the different types of combustion appliances). The combustion technology and air supply varies considerably between these different appliances, but also between old and new models of each type of appliance. In addition, the fuel type (e.g. wood logs, wood chips and pellets) and the condition of the fuel (e.g. moisture content and log size) also influence the efficiency of the combustion [11,13,14]. The physicochemical properties of particles emitted from residential biomass combustion differ considerably with combustion conditions and between combustion appliances [13,15]. Since epidemiological and experimental studies provide increasing evidence for the importance of physicochemical characteristics in the particle-induced biological effects [16,17], the differences in the physicochemical properties of particles originating from varying combustion conditions may influence their potential to induce biological effects.

Exposure to ambient PM in general has been associated with a range of pulmonary effects, such as decreased lung development and function, exacerbation of asthma,

allergy, chronic obstructive pulmonary disease (COPD), pulmonary fibrosis and increased risk of lung cancer (reviewed in [3,18,19]). The cardiovascular diseases associated with particle exposure include atherosclerosis, myocardial infarction and stroke [20,21]. Several mechanisms, including particle-induced oxidative stress, inflammation, cytotoxicity and genotoxicity, have been proposed to explain the associations between particle exposure and adverse health effects observed in epidemiological studies. The inflammatory potential of particles has been linked to chronic pulmonary diseases, but has also been suggested to contribute to atherosclerosis and acute cardiac effects [20,22,23]. Particle-induced cytotoxicity may be involved in tissue damage in the lung and in other organs, whereas the carcinogenic risk primarily is linked to genotoxicity [17,24]. Markers of negative health effects (i.e. oxidative stress, inflammation, cytotoxicity and genotoxicity) are commonly monitored in cultured cells (*in vitro*), acute and chronic animal models (*in vivo*) or voluntary individuals in exposure chambers (*in vivo*) to study the effects of particles on human health.

The two previous wood smoke reviews focused on the health effects of residential wood smoke particles based on epidemiological studies [4,5] and experimental studies [5], whereas the present review focuses on the physicochemical properties of the particles, but from a health based perspective. Naeher et al. (2007) concluded that wood smoke may affect pulmonary immune defence mechanisms, with the lung macrophages as a likely target for wood smoke induced immunotoxicity, based on *in vivo* toxicological studies of wood smoke [5]. However, the combustion conditions used to generate wood smoke particles and their physicochemical properties were not discussed, neither was the relevance of these particles with respect to ambient exposure. In the end of their paper Naeher et al. (2007) recommended topics for further research, including; i) 'Better understanding of the similarities and differences of smokes generated by combustion of different categories of biomass in different conditions (...)' and ii) 'Source and exposure apportionment studies to determine the degree to which residential wood combustion contributes to both indoor and outdoor particle exposures (...)'. Although further research is necessary, a notable amount of information is available in the literature concerning both topics. In the present review, we summarise current knowledge on physicochemical properties of PM from residential wood combustion in developed countries with focus on how these properties change with varying combustion conditions and their relevance to human exposure. We also discuss the combustion conditions and the resulting particle properties applied in recent experimental studies of the biological effects of wood smoke, and the relative toxicity

of different types of wood smoke particles. The review is organized according to the following outline:

Particle characteristics relevant for health effects

Brief introduction to how the physicochemical properties of particles may influence their biological effects

Physical and chemical characteristics of wood smoke particles

Summary of the current knowledge on the physicochemical properties of wood smoke particles from different combustion conditions, organised into three different particle classes:

- spherical organic carbon particles
- soot particles/carbon aggregates
- inorganic ash particles

Wood smoke exposure

The exposure studies are reviewed to investigate to what extent they provide information about the physicochemical properties of the wood smoke particles

Emissions from different wood combustion appliances

As an alternative to the exposure studies, the emission factors, activity data and emission characteristics of different types of wood combustion appliances are combined to obtain information about the type of wood smoke particles we are exposed to

Transformation of wood smoke emissions in the atmosphere

Discussion of the influence of atmospheric transformations on the physicochemical properties of wood smoke particles and its potential influence on their biological effects

Experimental studies of wood smoke toxicity

Discussion of the combustion conditions and the resulting particle properties applied in recent experimental studies, divided into three parts:

- human inhalation studies
- *in vivo* animal studies
- *in vitro* studies

Summary and conclusions

Particle characteristics relevant for health effects

The adverse health effects of inhaled particles are highly dependent on the deposition and retention of particles in the lung. The deposition probability and deposition site of particles is governed by their aerodynamic properties, such as size, density and shape, but also by other physicochemical properties such as hygroscopicity (i.e. water uptake) [25,26]. Experimental studies have identified a range of physicochemical properties that influence the toxic and inflammatory potential of PM, and possibly particle-induced health effects (reviewed in [16,17,27,28]). Since these data are discussed in detail in several reviews, they are only described in brief in the following. The most relevant particle properties and a selection of references are summarized in Table 1.

Small particles, exhibiting a large surface area per mass, have been found to induce a more pronounced pro-inflammatory response than larger particles of the same material. This has been demonstrated in both *in vitro* and *in vivo* experiments where ultrafine particles are more potent in inducing inflammatory responses than fine particles [29-32]. Consequently, surface area has been suggested as a new dose metric for the inflammatory effects induced by low-solubility low-toxicity particles *in vitro* and *in vivo* [32-34]. However, particle structure, surface properties and chemistry may override the importance of particle size and surface area. For example, inflammation and cytotoxicity after exposure to ultrafine TiO₂ has been found to depend on crystal structure (anatase vs. rutile) rather than size and surface area [35,36]. Furthermore, the inflammatory, cytotoxic and genotoxic responses to quartz particles were reduced by surface coating, indicating that surface properties were important for the toxicity of quartz [37-39]. With respect to chemical composition, the content of metals such as vanadium, zinc, iron, copper and nickel, as well as the content of organic compounds such as polycyclic aromatic hydrocarbons (PAHs), seem to influence the particle-elicited health effects [17,40-42].

Table 1: Physicochemical properties reported to influence the biological effects of PM in experimental studies

Physicochemical properties	References
Particle size	[29-32]
Surface area per mass	[32-34]
Crystal structure	[35-39]
Chemical composition	
- metals	[41,42]
- organic compounds	[40,43-45]
Solubility	[50,51]

The table lists the most relevant physicochemical particle properties and the references used in the text. For a more comprehensive reference list please refer to one of the reviews [16,17,27,28].

Quinones, a special group of carbonyl containing PAH compounds, have recently been pointed out as particularly reactive organic components of PM with potential to produce reactive oxygen species (ROS) and to induce oxidative stress via their redox capacity [43]. Accordingly, various oxy-PAHs, including quinones, were found to be involved in inducing cellular oxidative stress in a murine monocyte-macrophage cell line during exposure to organic extracts of wood smoke and diesel exhaust particles [44,45]. However, the organic fraction of particles from various sources comprises a large number of compounds besides PAHs, such as aldehydes, ketones, organic acids and various chlorinated organics [5,46,47], and the biological effects of many of these compounds, and their contributions to particle-induced inflammation, are largely unknown.

Solubility is another property that may influence the toxicity of PM. For particles that dissolve upon contact with aqueous solutions, such as most salt particles, cellular uptake of dissolved ions may occur through ion channels. In contrast, insoluble particles are usually taken up by phagocytosis, which subsequently may initiate a cascade of intracellular signalling [48]. Organic compounds, on the other hand, can enter cells directly through the cell membrane by a partitioning process [49], which in turn may result in activation of other intracellular signalling pathways. Insoluble particles exert a prolonged exposure, while dissolved particulate material is likely to be cleared more rapidly. *In vitro* studies indicate that insoluble nickel compounds are more cytotoxic than soluble nickel salts [50]. On the other hand, the *in vitro* cytotoxicity of manufactured nanoparticles was greater for partly soluble than insoluble particles [51]. Thus, for different types of particles the solubility seems to influence the particle-induced cytotoxicity to different extents.

Physical and chemical characteristics of wood smoke particles

The physical and chemical properties of wood smoke particles emitted during various combustion conditions differ considerably. Fine particles (equivalent aerodynamic diameter $< 2.5 \mu\text{m}$, $\text{PM}_{2.5}$) emitted from residential wood combustion appliances may be divided into three typical classes based on chemical composition and morphology; spherical organic carbon particles, aggregated soot particles and inorganic ash particles. The physicochemical properties of these three classes are described in the following sections, and summarised in Figure 1. It should be pointed out that in real combustion situations, especially during transient cycles, the particle classes may co-exist and interact. Since the combustion conditions in an appliance change during a burn cycle, especially during batch-wise combustion of wood logs, the emissions are likely to contain several of the defined particle classes.

Spherical organic carbon particles

Burning wood of poor quality (e.g. high moisture content), overloading the firebox or insufficient air supply, are examples of conditions that can lead to incomplete combustion, characterised by low temperature [11]. In a conventional wood stove without modern combustion technology, emissions from such poor combustion conditions (low temperature, air deficiency and/or poor mixing) are dominated by spherical organic carbon particles with diameters that have been measured to be between 50 and 600 nm by electron microscopy [52,53]. Spherical organic carbon particles have also been observed during smouldering combustion [54-56], and are therefore likely to be emitted from open fireplaces. The origin of this organic material is the thermal degradation products of the wood constituents (i.e. cellulose, hemi-cellulose and lignin) that are released at low temperatures (300-500°C) without being further combusted due to poor mixing conditions.

Freshly generated particles from smouldering combustion contain large amounts of highly oxygenated water-soluble organic species, including monosaccharide anhydrides and methoxyphenols [57-60]. During ageing in the atmosphere (> 10 min) insoluble 'tar-balls' may be formed through polymerisation of primary emitted organic matter [61]. These tar-balls contain low levels of elemental carbon and lack the internal turbostratic microstructure exhibited by the primary particles of carbon aggregates generated at higher temperatures [61]. Particles from incomplete combustion are also characterised by a low content of inorganic constituents such as potassium, sulphur and chlorine [12,62,63]. Wood smoke emissions contain a large number of organic compounds, and detailed chemical speciation of several hundred individual compounds has been reported [57,58,64]. Using online aerosol mass spectrometry (AMS), Weimer et al. (2007) showed that organic emissions, particularly those with signatures similar to levoglucosan, were strongly enhanced during the start up phase. The mass spectra recorded during the smouldering phase were, in contrast, dominated by highly oxygenated species [65]. However, the changes in organic chemistry for different combustion conditions and temperatures and for the various phases of the combustion cycle are not well described in the literature.

The carbon present in combustion particles can be classified as either organic or elemental carbon, and may be determined in thermal/optical carbon analysers. Organic carbon (OC) comprises hundreds to thousands of organic compounds, whereas elemental carbon (EC) is defined as the carbon that is not organic, but EC can also be characterised as refractory carbon [66]. The sum of the organic and elemental carbon in a sample is defined as the total

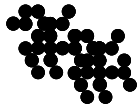
	Spherical organic carbon particles	Soot (elemental carbon aggregates)	Inorganic ash particles
Schematic drawing			
Diameter measured by electron microscopy*	50-600 nm ^{52, 53}	20-50 nm ^{52, 73}	50-125 nm ⁹⁷
Mobility diameter	100-300 nm ⁶⁸⁻⁷⁰	50-300 nm ^{68, 76}	50-125 nm ^{69, 98, 99}
Internal turbostratic microstructure	No ⁶¹	Yes / No ⁸¹⁻⁸³	No
Solubility (H ₂ O)	Depends on ageing ⁶¹	Insoluble	Soluble
Main chemical characteristic	Organic carbon ^{62, 64, 67} (Most abundant organic compounds: methoxyphenols and monosaccharide anhydrides) ⁵⁷⁻⁶⁰	Elemental carbon with variable amounts of organics condensed on the surface ^{12, 62, 81} (Most abundant organic compounds: hydrocarbons and polycyclic aromatic hydrocarbons) ^{84, 85}	Alkali salts (mainly KCl and K ₂ SO ₄ with small amounts of trace elements (e.g. Zn)) ^{78, 92}
Combustion conditions	Low-temperature, incomplete combustion ^{11, 52-56}	High-temperature, incomplete combustion ⁵²	High-temperature, complete combustion ¹²⁰
Possible sources	Air starved combustion or start-up phase of batch wise combustion in conventional stoves, open fireplaces ^{58, 62, 64, 67}	Combustion in conventional stoves, open fireplaces, boilers for wood, wood chips and pellets ^{14, 52, 75-79}	Combustion in pellets stoves, boilers for wood, wood chips and pellets ^{69, 120}

Figure 1

The physicochemical characteristics of the three classes of wood combustion particles. The numbers refer to the references used in the text. * For the aggregated soot particles the listed diameter refers to the primary particle diameter.

carbon (TC). For low-temperature combustion in conventional stoves, the reported ratios of elemental to total carbon (EC/TC) range from 0.01 to 0.11 [62,64,67], confirming that PM from these combustion conditions are dominated by organic carbon. It should be kept in mind though that different measurement techniques give rise to large differences in the EC/TC ratio [66], hence great caution should be taken when comparing such data.

The mobility equivalent diameter, which determines the deposition by diffusion in the human lung (typically

important for mobility diameters below about 500 nm), equals the physical diameter for spherical particles. The count mean diameter (CMD) of particles from low temperature biomass combustion has been found to range from 100-175 nm [68,69]. Similarly, Hueglin et al. (1997) measured mobility sizes with CMD between 200 and 300 nm during the start up phase of a residential wood stove, when organic emissions are expected to dominate [70]. Thus, the CMD seems to range from 100 to 300 nm for spherical organic carbon particles. The aerodynamic equivalent diameter determines particle deposition

by sedimentation in the lung (typically important for aerodynamic diameters larger than about 200 nm). Since these spherical organic carbon particles have densities of around 1-1.5 g/cm³ [71], the CMD based on aerodynamic equivalent diameter is slightly larger than the CMD based on mobility diameter.

The organic compounds from wood combustion are not only emitted in the particulate phase, but also in the gas phase. In the hot flue gas leaving the combustion chamber of boilers and stoves, most of the organic material is present in the gas phase, but can condense on existing particles (e.g. soot and/or inorganics) during cooling in the heat exchanger and chimney [13,57,64]. Atmospheric processes, for example reactions with OH and O₃, can result in reaction products with lower vapour pressure that may condense onto existing particles through formation of secondary organic aerosols [72]. There is still insufficient knowledge about the relative contributions of primary emissions and secondary particle formation to the total particulate organic carbon from biomass combustion. It should be pointed out that the gas to particle partitioning of organic compounds depends relatively strongly on concentration. To accurately represent the particle phase of primary organic aerosols from biomass combustion, measurements should preferentially be made at conditions relevant for ambient air.

Soot (Elemental carbon aggregates)

During incomplete combustion with air-starved conditions at higher temperatures (~800-1000°C), PM emissions are more dominated by solid carbon aggregates (soot). These consist of a large number of primary spherical carbon particles with diameters that have been measured to be between 20 and 50 nm by electron microscopy [52,73]. The formation of soot is very complex and Bockhorn has given a well adapted soot formation pathway, via polycyclic aromatic clusters, particle inception, surface growth and coagulation [74]. Carbon aggregates of soot may be emitted during incomplete combustion in conventional wood stoves and masonry heaters [52,75,76], from open fireplaces [14] or during incomplete combustion in boilers for wood, wood chips or pellets [77-79].

In general, soot can contain some percent of hydrogen, originating from the primary aromatic compounds, and is subsequently more or less graphitized in the combustion process. Primary particles of soot have been reported to exhibit an internal turbostratic microstructure, consisting of a concentric arrangement of layer planes with a two dimensional graphitic structure, lacking the ordered stacking of graphite, and thus its three dimensional structure [80]. Kocbach et al. (2006) observed a turbostratic microstructure consisting of concentric carbon layers surrounding a single nucleus in primary particles from incomplete

high-temperature wood combustion by high resolution transmission electron microscopy (HR-TEM) [81]. In the same study, the graphitic character, defined as the degree of similarity to the structure of graphitic carbon, was investigated by selected area electron diffraction (SAED) and electron energy loss spectroscopy (EELS). Wood smoke particles from high-temperature combustion were found to have graphitic character similar to that of traffic-derived particles, confirming the observations by HR-TEM. In contrast, Braun and colleagues recently reported that particles from a range of residential wood stoves did not have a graphitic character or a less graphitic character than diesel exhaust particles by application of near-edge X-ray absorption fine structure spectroscopy (NEXAFS) [82,83]. Whereas the wood smoke particles in Kocbach et al. (2006) were collected by aerosol sampling, Braun and co-authors analysed samples collected either from the interior walls of various wood stoves or from chimneys. The differences in applied collection methods could lead to a selection of different populations of particles. This might explain the conflicting results concerning the graphitic structure of wood smoke soot particles. The present data is insufficient to conclude on a possible difference in the graphitic character of soot particles from different combustion conditions.

Aggregated soot particles contain higher levels of elemental carbon and lower levels of organic carbon compared to carbonaceous particles emitted at lower temperatures, and the EC/TC ratios for incomplete high-temperature combustion in conventional stoves and masonry heaters have been reported to range from approximately 0.5 to 0.75 [12,62,81]. Both the concentration and the relative contribution of various particle associated organic compounds change with combustion temperature. Overall, the total concentration of non-combusted organic matter in the emissions decreases with increasing combustion temperatures, and the primary organic pyrolysis products formed at lower temperatures are "transformed" to purer aromatic hydrocarbons at higher temperatures. Accordingly, the content of methoxyphenols decreases with increasing combustion temperature, whereas the levels of PAHs increase [84,85]. Thus, soot emitted from different combustion conditions may differ in organic chemistry. The most abundant PAHs in wood smoke emissions are naphthalene, acenaphthene, fluorene, phenanthrene, anthracene, fluoranthene and pyrene [15,47,64], but with regard to carcinogenicity, benzo(a)pyrene (B(a)P) and fluoranthene seem to be the most important compounds in wood smoke emissions [47,86,87]. Although a rather extensive amount of work has been performed to characterise the organic fraction of wood smoke [47,57,58,64,88], little information is so far available concerning compounds that influence the biological effects of wood smoke particles and on how the organic composi-

tion varies with the combustion temperature. However, fractionation of organic extracts, chemical analyses and measurements of oxidative stress were recently combined in order to identify the organic compounds involved in the biological effects of wood smoke particles [44]. In that study, oxy-PAHs and quinones were found to contribute to oxidative stress. Interestingly, emissions of oxy-PAHs have been reported to increase with increasing wood combustion temperature [85].

A particle diameter is hard to define for aggregated particles such as soot, and the mobility equivalent aggregate diameter for soot from wood combustion has been found to vary considerably between different studies; from 50 to 300 nm [68,76]. The aerodynamic equivalent diameter of soot from wood smoke has not been reported in the literature, but may be considerably smaller than the mobility equivalent diameter [89]. Condensation of organic compounds onto soot agglomerates may lead to a transition from highly agglomerated to compact particles. This has been demonstrated for soot from other sources during interaction with water or H_2SO_4 [90,91]. The present knowledge of the morphology and the mobility and aerodynamic diameters of aggregated particles from wood combustion is, however, limited.

Inorganic ash particles

Combustion of pellets, wood chips and wood logs in boilers or stoves with modern technology provides favourable combustion conditions with high temperatures ($> 900^\circ\text{C}$), good oxygen supply and sufficient mixing between combustible gases and air in the combustion chamber. This results in almost complete combustion and the emissions are dominated by inorganic ash particles, such as the alkali salts of potassium/sodium-sulphates, chlorides and carbonates [78,92]. The content of organic and elemental carbon can be below 1% of the particle mass emitted during these favourable combustion conditions [69]. Fine particles emitted during combustion of some types of wood and bark pellets may also contain phosphorous, which is probably related to elevated combustion temperatures [93]. It is also believed that potassium phosphates may be present in fine particles during combustion of more phosphorous rich (non-woody) biomass, as demonstrated during combustion of agricultural fuels in some recent studies [94-96].

Studies using electron microscopy have revealed that the fine inorganic ash particles emitted from complete combustion conditions have a sphere-like shape with diameters between 50 and 125 nm [97]. The corresponding mobility diameters have been measured to be in the same size range [69,98,99]. Since mobility diameters are close to the physical diameter for compact particles, the inorganic ash particles from biomass combustion are also likely to have physical diameters in the same range. Aero-

dynamic diameters may be calculated assuming an effective density of about 2.0 g/cm^3 [68,70]. For example a particle with an equivalent mobility diameter of 100 nm and effective density of 2.0 g/cm^3 would have an equivalent aerodynamic diameter of 168 nm. Overall, the particle morphology and size distribution has been relatively well described for inorganic ash particles.

Inorganic ash particles such as potassium sulphates and chlorides have rather high hygroscopic growth factors and are mainly water soluble. This solubility may affect the biological effects induced by these particles in two manners; (i) hygroscopic particles may grow at the high humidity in the respiratory tract, which can reduce the deposition probability and may alter the deposition site [25,100] and (ii) the solubility may increase the clearance rate from the lung. In addition, the solubility of PM may affect the biological effects on a cellular level, for instance with respect to uptake mechanisms and activation of intracellular pathways.

In addition to the three classes of particles described above, coarse inorganic fly-ash particles with diameters larger than $1 \mu\text{m}$, containing refractory species such as calcium, magnesium, silicon, phosphorus and aluminium, have been detected in emissions from large scale grate fired biomass boilers [78,101] and wood chip burners [70]. In grate fired appliances, the air is supplied to the combustion chamber through a grate beneath the chamber. The coarse fly-ash particles are entrained from the fuel bed and their emissions may therefore be strongly dependent on the primary air flow through the grate [98].

Wood smoke exposure

In order to evaluate the negative health effects that may be associated with exposure to wood smoke particles, it is necessary to determine the human exposure to these particles. The number of studies regarding ambient wood smoke exposure in developed countries increases rapidly. Source apportionment studies have estimated that wood/biomass combustion contribute with 10-40% to the fine particle concentrations ($\text{PM}_{2.5}$) in large cities such as Seattle, Phoenix, Beijing, Prague and Helsinki [102-105]. Residential wood combustion has also been reported to contribute substantially to increased levels of air pollution locally, both with respect to increased levels of $\text{PM}_{2.5}$, the organic particle fraction, particle bound PAH and volatile organic compounds [106-111]. The contribution of wood smoke to ambient air pollution is, however, highly dependent on season, time point and week day [105,112].

In general, people in developed countries spend the majority of their time indoors. For instance, the participants in a recent Swedish study reported that they spent more than 90% of their time indoors and around 60% at home [113]. Thus, the indoor particle levels have a large

impact on human exposure. The penetration of wood smoke from ambient sources to indoor environments has not been investigated in any detail. However, both the personal exposure and the indoor concentrations of particle associated K, Ca, Zn, and possibly Cl, Mn, Cu, Rb, Pb and black smoke (~soot), were found to be increased in homes heated with a wood stove or boiler [114]. Personal exposure and indoor levels showed high correlations for all elements, and the personal exposure levels were usually higher than or equal to the indoor levels, but the associations between personal exposure and outdoor levels were generally weak [114]. Residential wood combustion also increased personal exposure to 1,3-butadiene as well as indoor levels of 1,3-butadiene and benzene and possibly acetaldehyde [115]. The cancer risk from these compounds due to wood smoke exposure in developed countries was estimated to be low [115]. In the same study, the levels of B(a)P and several other PAHs were found to be significantly higher (3- to 5-fold) in homes with wood combustion appliances compared to homes without [87]. While phenanthrene made the largest contribution to the total PAH concentration in indoor and outdoor air, most of the cancer potency was due to B(a)P (about 60%) and fluoranthene (about 20%). Moreover, the median indoor B(a)P concentration in the homes with wood combustion appliances (0.52 ng/m³) was 5 times higher than the Swedish health-based guideline of 0.1 ng/m³.

The physicochemical characteristics of ambient wood smoke particles are highly dependent on factors that vary between locations, such as the relative numbers of different types of residential combustion appliances, and on factors that vary with both time and location, such as the combustion activity (e.g. use frequency and burn rate), the wood species and wood quality. The contribution from residential wood combustion to ambient, indoor and personal wood smoke exposure is commonly estimated by application of various markers for wood smoke, such as the content of organic and elemental carbon, specific organic compounds (levoglucosan, 1,3-butadiene, benzene, or PAHs) or metals (K, Ca, Zn) [87,105,114-117]. However, these markers provide limited information regarding the exposure to the different classes of wood smoke particles, as they are usually only representative for one of the three classes of residential wood combustion particles. Thus, a broader range of wood smoke markers with specificity for each of the three classes of wood smoke particles should be applied in future exposure studies. This would provide a better characterisation of wood smoke exposure in epidemiological studies, and also a better basis for choosing relevant particles in experimental/toxicological studies. Further characterisation of the personal and indoor wood smoke exposure is also necessary, since we generally spend more than 60% of our time indoors at home.

Emissions from different wood combustion appliances

The physicochemical properties of ambient wood smoke particles depend on the wood smoke emissions to ambient air. Data collected for individual classes of combustion appliances may be applied to obtain information about the physicochemical characteristics of residential wood smoke emissions in a specific area, as illustrated in the flowchart in Figure 2. For each class of wood smoke appliances it is possible to determine emission factors, activity data and emission characteristics. By combining the activity data with the emission factors the classes of combustion appliances that account for the majority of the emissions are determined, and in combination with the emission characteristics the classes of PM that dominate the residential wood smoke emissions can be suggested. This approach provides a rough estimate for the main characteristics i.e. the particle class(es) dominating the emissions, but application of exposure studies provide more relevant chemical characterisation and also includes the atmospheric modifications that have occurred in the time span between emission and exposure.

Emission characteristics

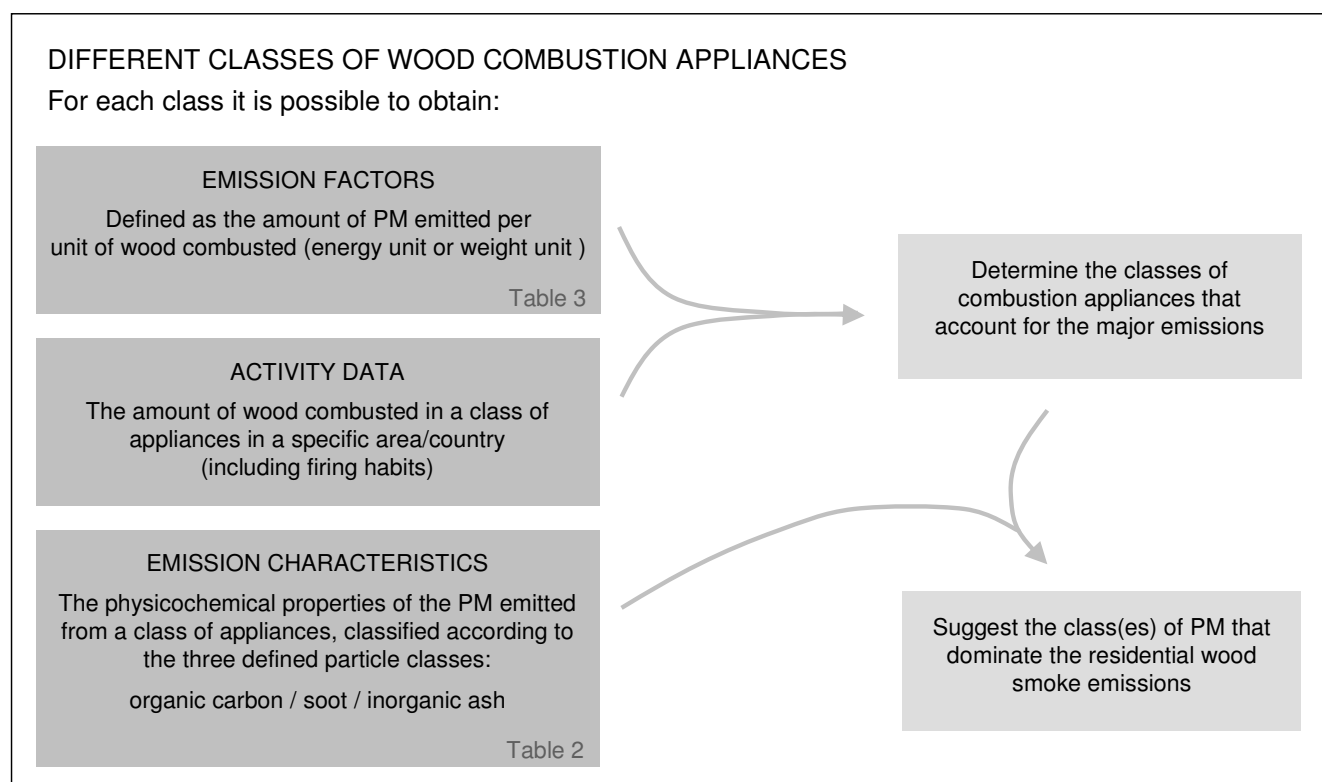
In this section, the class of PM (i.e. organic carbon/soot/inorganic ash) that dominates the emissions from the different types of combustion appliances is suggested based on the available data for EC/TC ratios and morphology of the emitted PM (Table 2). If the data is limited a suggestion is made based on knowledge about the combustion conditions in that type of appliances.

Open fireplaces

Wood combustion in open fireplaces is a mixture of flaming and smouldering combustion. These emissions are therefore likely to be dominated by spherical organic carbon particles and soot. Scanning electron microscopy of samples from a range of fireplace emissions suggested that carbon aggregates (soot) was the dominating particle class [14]. However, the reported EC/TC ratios, ranging from 0.04 - 0.46 [14,58,62,64,67], indicate that organic carbon is the major component of PM emissions from open fireplaces. A possible explanation for the discrepancy between the EC/TC ratios and the morphology observed by electron microscopy may be condensation of organic carbon onto soot particles. Overall, the reported data on emission characteristics from open fireplaces suggest that the contribution to ambient air from this class of wood combustion appliances is a mixture of soot and organic carbon.

Conventional wood stoves

As discussed previously, particle emissions from incomplete low-temperature combustion conditions are dominated by spherical organic carbon particles and low levels of elemental carbon (EC/TC ratios 0.01-0.11), while soot

**Figure 2**

Flowchart illustrating how information about the physicochemical properties of ambient wood smoke particles may be obtained from data collected for individual classes of combustion appliances. See text for explanation.

and high EC/TC ratios (0.50-0.75) characterise emissions from incomplete combustion at higher temperatures [12,62,64,67,81]. Kocbach et al. (2005) observed soot, but not spherical organic carbon particles, in ambient samples collected in two areas dominated by smoke from conventional stoves. The samples comprised emissions from different combustion conditions and several wood species, suggesting that the contribution from conventional stoves to ambient air was mainly soot [52]. In contrast, another study indicated that spherical carbon particles observed in ambient air samples originated from

household wood combustion [61]. Although soot seems to constitute a large part of the emissions from conventional wood stoves, organic carbon, either condensed onto soot or as individual spherical carbon particles, also appears to be an important contributor to the particle emissions from this class of combustion appliances. Gaseous organics emitted during poor combustion conditions are also likely to contribute to the particulate OC levels due to formation of secondary organic aerosols [118].

Table 2: Emission characteristics for the different classes of wood combustion appliances

Type of combustion appliance	Particle class(es) dominating the emissions	References
Open fireplaces	organic carbon/soot	[14,58,62,64,67]
Conventional wood stoves	organic carbon/soot	[12,62,64,67,81]
Masonry heaters	organic carbon/soot	[11,76,119]
Conventional boilers for wood logs	organic carbon/soot *	
Modern wood stoves	inorganic ash/organic carbon/soot *	
Modern boilers for wood logs	inorganic ash/organic carbon/soot *	
Pellet stoves and boilers	inorganic ash	[69,120]

Based on the available data on the physicochemical properties of particles emitted from different types of combustion appliances we have suggested the class(es) of particles that are likely to dominate the emissions. The references used to support the text are included in the table.

* Limited data available, see text for details

Conventional wood log boilers and masonry heaters

Conventional wood log boilers and masonry heaters can be defined as appliances without new technology, such as down-draft combustion, sucking fan and electric combustion control. Conventional wood log boilers may be installed with a water heat accumulation tank, which improves the user comfort and combustion efficiency considerably. In Sweden, less than 30% of the households with wood log boilers have a water heat accumulation tank. Analyses of carbon content or morphology of the particulate emissions from wood log boilers have not been reported in the literature. However, since the combustion conditions (e.g. temperature, residence time and mixing) in such systems can vary significantly, the emissions can be expected to vary with respect to the fractions of organic carbon, elemental carbon (soot) and inorganic ash constituents. In general, the PM is dominated by carbonaceous material and for conventional masonry heaters, the EC/TC ratios have been reported to range from approximately 0.10 to 0.35 in both field and laboratory studies [11,76,119]. Thus, the emissions from conventional wood log boilers and masonry heaters are likely to be dominated by soot and organic carbon.

Modern stoves, masonry heaters and boilers for wood logs

In "modern" residential combustion appliances for wood logs, the applied combustion technology leads to improved combustion conditions with good burn out and low emissions of PM [120]. The emissions from modern appliances for combustion of wood logs are dominated by inorganic ash during ideal operation, and organic carbon and soot may constitute less than 10% of the emitted particle mass [120]. However, during the start-up phase and during low burn-rates, the combustion performance can be deteriorated causing increased emissions of both organics and soot. Moreover, the emissions from modern appliances for wood logs may increase ten-fold if they are not operated appropriately [118] and then the emissions are most likely dominated by soot and organic carbon rather than inorganic ash. The data reported concerning detailed chemical composition of the PM for modern wood boilers and stoves are still very scarce.

Pellets stoves and boilers

Wood pellet boilers and stoves can in general be considered as "modern" technology with high combustion efficiency, and situations with poor combustion conditions are assumed to be very rare in these systems due to for instance the homogeneous character of the fuel, continuous fuel feeding and fan driven air supply [118]. Based on laboratory studies, the emitted PM from these appliances is therefore assumed to be dominated by inorganic ash and to contain very low levels of elemental and organic carbon (TC ~5 - 12% and EC/TC ~0.65 - 0.80) [120]. The total carbon level may be as low as < 1% [69]. However,

the efficiency of these appliances may be deteriorated if they are installed or operated in an inappropriate manner, this could possibly cause emission of soot or organic carbon.

Overall, the emissions of gases and PM from the various types of combustion appliances have been rather well described, although the data available for modern wood stoves and boilers for wood logs have some limitations. A more detailed characterization of the variations in particle properties between the different types of appliances is however still missing. Efforts should be made to resolve this issue, since a more complete characterisation of the variation in particle properties would provide a better basis for an evaluation of the impact of wood smoke exposure on human health.

Emission factors and estimates

The emission factors of PM for different classes of residential biomass combustion appliances have recently been discussed in several reports [118,120-122], and are summarised in Table 3. Conventional stoves and boilers for wood logs account for the highest emission factors, followed by open fireplaces and modern stoves and boilers and finally pellet stoves and boilers. Generally, the ranges of emission factors reported for the various classes of appliances are very large. This variation is partly due to application of different measuring techniques; both sampling of particles in the chimney at gas temperatures of 120-160°C and sampling of particles in a dilution tunnel at lower temperatures (< 35°C) are commonly applied. Application of a dilution tunnel allows for condensation of organic compounds onto the particles, and the resulting emission factors can be up to 10 times higher than the factors based on collection of particles in the undiluted chimney gas [118,120]. However, if even higher dilution ratios are applied (above 20:1) the emission estimates for organic carbon may decrease with increasing dilution ratios [123]. The fraction of primary formed organics (i.e. products of incomplete combustion) which partitions to the particle phase is strongly dependent on both concentration and temperature [118,123-125]. Thus, to accurately quantify the primary organic particle phase fraction in atmospheric wood smoke pollution, dilution conditions close to ambient should be applied. It should also be kept in mind that wood combustion appliances are often pre-heated when their emission factors are determined. This is in contrast to real-life wood combustion, where the burning of wood starts in a cold stove. Since organic compounds are likely to dominate the emissions from a cold stove, this procedure may contribute to an underestimation of the real-life emissions of organic carbon.

The operation conditions, e.g. ideal, typical or poor operation, also have great impact on the measured emission

Table 3: Emission factors for different types of residential combustion appliances

Type of combustion appliance	Reported emission factors	
	Approximate range (mg/MJ)	Reported data (mg/MJ)
Open fireplaces	160 - 910	800 ^a 160 - 447 ^{b,1} 860 - 910 ^{b,2}
Conventional wood stoves	50 - 2100	700 ^a 94 - 650 ^{b,1} 50 - 1932 ^{b,2} 100 ^c 150 - 2100 ^d
Other conventional stoves, including masonry heaters and sauna stoves	30 - 140	140 ^a 30 - 100 ^c
Conventional boilers for wood logs <i>without accumulator tank</i>	50 - 2000	700 ^a 300 - 2000 ^{b,1 and 2} 1300 ^c 300-900 ^d
<i>with accumulator tank</i>	50 - 250	80 ^a 50 - 300 ^{b,1 and 2} 95 ^d
Modern wood stoves	34 - 330	34 ^c 330 ^d
Modern boilers for wood chips or logs	5 - 450	5-450 ^{b,1} 20 - 25 ^c 30-100 ^d
Pellet stoves and boilers	10 - 50	30 ^a 10 - 50 ^{b,1 and 2} 20 ^c 30 ^d

Emission factors are reported as mg particles emitted per MJ of fuel burnt (MJ = Mega Joule)

^a mean emission factors based on available literature, as reported in [121].

^b range of emission factors based on data from members of the International Energy Agency, as reported in [118]. 1 = measurement of particles at temperatures > 100°C, 2 = measurement of particles in dilution tunnel at temperatures < 100°C.

^c range of emission factors [120].

^d data from [122].

factors for appliances fired with wood logs, and the emission factors for wood stoves and boilers have been estimated to increase with a factor of 10 during typical operation as compared to ideal operation [118]. In addition, the large variations in combustion technology within each class of combustion appliances also contribute to increased variation in the reported emission factors. The data in Table 3 suggest that the emission factors for residential wood combustion appliances are highly uncertain, and their uncertainty was recently estimated to be $\pm 54 - 88\%$ for Finland (95% confidence interval) [121]. As illustrated in Figure 2, emission estimates for the different class of combustion appliances may be obtained by com-

binning the activity data with the corresponding emission factors. In comparison to the large uncertainty determined for the emission factors, the uncertainty related to the activity in the domestic wood combustion sector was found to be considerably lower ($\pm 10\%$), while the uncertainty regarding the activity in different types of combustion appliances were between $\pm 15\%$ and $\pm 25\%$ [121].

Recently, the number of biomass combustion appliances, the activity, and the calculated estimated emissions based on emission factors were summarized for several European countries (Denmark, Finland, Norway, Sweden, Germany and Switzerland) [120-122]. To our knowledge,

emission estimates for the different classes of wood combustion appliances have not been calculated for other European countries, the US, Canada, Australia or New Zealand. As mentioned above, considerable uncertainty is associated with these numbers, they do however provide an estimate of the residential wood combustion emissions. All studies reported that wood logs is the most commonly applied fuel in biomass-based residential heating, and that the majority of the wood was combusted in conventional stoves and manually fed boilers [120-122]. Since these combustion appliances have high emission factors (Table 3), they also account for the majority of the emissions of PM from residential biomass combustion, generally more than 80% [120-122]. Due to low activity or low emission factors, fireplaces and modern wood log appliances account for less than 15% of the residential biomass emissions in the Nordic countries [121,122]. This is in contrast to the US, where open fireplaces are considered to be one of the major contributors to residential wood smoke emissions [12].

Over the last 10-20 years, the development of new combustion technologies for densified wood fuels, such as pellets, has been considerable in several countries, like Sweden, Austria and Germany [10]. Although log wood is still the dominating fuel type in most European countries, wood pellets have gained increasing relevance and this trend is expected to continue [120]. Due to their low emission factors and the relatively low number of appliances, the relative contribution from pellets burning to the total biomass combustion emissions is generally below 10% [120-122]. The share of modern biomass combustion appliances, for both wood log and pellets, is likely to grow steadily, particularly due to replacement of older stoves/boilers and due to conversion from oil and electricity. The relative contribution from these appliances to the total residential wood smoke emissions is, however, likely to remain low due to their low emission factors.

Emissions of the different classes of wood smoke particles

As discussed in the previous section, conventional wood stoves and boilers for wood logs account for the majority of the domestic biomass emissions to ambient air in Europe. Since these emissions consist of variable fractions of soot and organic carbon depending on combustion appliances, operation and fuel quality, these two classes of particles are likely to dominate the emissions in European countries. The organic compounds may be condensed onto soot and/or inorganic particles or be present as individual spherical organic particles in emissions from very poor combustion conditions.

With respect to relevance for experimental studies, particles generated solely during smouldering combustion, not containing soot, seem to be more representative for bush

and structural fires, and hence for fire fighter exposure, than for residential wood smoke exposure. In addition, smouldering combustion and spherical organic carbon particles are also relevant for the domestic exposure in developing countries, since open fires that provide poor combustion conditions are commonly burned indoors in these countries. Inorganic ash particles are primarily emitted from pellets stoves and boilers and from modern wood log boilers under optimal firing. Due to the low emission factors of these appliances, inorganic ash particles make a small contribution to ambient wood smoke concentrations presently, but their contribution may increase in the future.

Combining the activity data with the emission factors and emission characteristics for the different types of combustion appliances provides some information about the classes of PM that dominate the residential wood smoke emissions in specific areas/countries. A major limitation of this approach is the high uncertainty associated with the acquired information. In addition, activity data are unavailable for many regions and the emission characteristics are insufficient for some types of appliances. This approach does, however, have promising aspects as it has the potential to provide information about the general type of emissions to a specific area/country without performing time consuming and expensive field measurements.

Transformation of wood smoke emissions in the atmosphere

The physiochemical properties of ambient particles may change through interaction with atmospheric photo-oxidants (e.g. OH, O₃, NO₃, NO₂), acids (e.g. HNO₃, H₂SO₄), water and UV radiation [126]. Possible atmospheric transformations include altered size, morphology and chemical composition [90,91,127-129]. Few studies have investigated the atmospheric transformations of wood smoke particles, but the methoxyphenols present in wood smoke particles have been suggested to enhance the photochemical degradation of PAHs [128]. In addition, more volatile compounds have been reported to condense onto particles, and heavy compounds to be photo-degraded into lighter ones [129,130]. Photo-oxidation of wood stove emissions at atmospherically relevant or slightly elevated concentrations in a Teflon chamber has been found to increase the organic aerosol mass by a factor of 1.5-2.8 [130]. The condensed material was highly oxidised, distinctly different from the primary organic particle mass. Less than 20% of the formed secondary aerosol mass could be explained by known pre-cursors, indicating involvement of large classes of organic compounds [130]. These effects are qualitatively similar to those previously reported for diesel exhaust [125]. It is obvious that more research is needed on this topic, for example on how

the combustion conditions influence the formation of secondary organic aerosols [131].

Atmospheric alterations could affect the biological activity of PM, and cause either increased or decreased potency with respect to mutagenicity, inflammatory potential or toxicity [132-136]. The performed studies also suggest that the effect of ageing on the biological activity could be related to the particle source.

The present data on atmospheric alterations of particulate matter suggest that it is necessary to take into account the atmospheric alterations of the emitted particles in order to elucidate the potential health effects of wood smoke. Further studies are necessary both with respect to changes in physicochemical particle properties but also with respect to the influence of these changes on the biological effects.

Experimental studies of wood smoke toxicity

The physicochemical properties of wood smoke particles applied in experimental studies, have not been discussed in recent reviews of health effects of wood smoke [4,5,137]. As discussed previously, particles generated under varying combustion conditions differ with respect to physicochemical properties, and this may influence their potential to induce biological effects. Therefore, the applied combustion conditions and, if possible, the physicochemical properties of the wood smoke used in recent experimental studies are discussed in this section, and summarised in Table 4.

Human inhalation studies

A limited number of human inhalation studies have investigated the negative effects of wood smoke exposure. Barregard and colleagues used a conventional stove to generate wood smoke [7,8,138,139]. The mass concentration (PM_{10}) was approximately $250 \mu g/m^3$ with levels of B(a)P around $20 ng/m^3$ and total PAH levels around $800-1000 ng/m^3$ (sum of 14 measured PAHs). The major inorganic elements, K, Zn and Cl, accounted for less than 6% of the total mass concentration [138], thus soot and organic carbon seemed to dominate the PM inhaled in this study rather than inorganic ash. The geometric mean diameters were 42 and 112 nm in the two different rounds of wood smoke exposure. Blood and urine measurements suggested that wood smoke may be associated with systemic inflammation (the acute phase protein serum Amyloid A and to some extent serum C-reactive protein), blood coagulation (Factor VIII) and lipid peroxidation (urinary excretion of the isoprostane 8-isoPGF 2α) [7]. In addition, wood smoke exposure increased markers of inflammatory effects on distal airways (alveolar nitric oxide and Clara cell protein in serum) [8]. Several of these biomarkers are cardiovascular risk factors. The oxidative DNA damage and related repair capacity in peripheral

blood mononuclear cells was investigated in the same study. Although wood smoke exposure was followed by significant up-regulation of the repair gene hOGG1, no direct genotoxic effects were observed [139].

Recently, another human inhalation study was performed by a Swedish interdisciplinary group at Umeå University, Umeå University Hospital and Lund University, investigating the effects of wood smoke from an adjusted residential wood pellet burner under low temperature incomplete combustion conditions in a human chamber study [120,140]. The exposures were performed at $224 \pm 22 \mu g PM_{10}/m^3$ where the PM was dominated ($\sim 90\%$) by carbonaceous matter [68]. The preliminary human exposure effect data indicate a moderate response, including increased levels of glutathione which indicates that the antioxidant defense was activated, possibly due to oxidative stress [120,140].

Future human inhalation studies should be designed to compare the effects induced by wood smoke from different combustion conditions, as comparative studies would be a useful tool in the process of targeting strategies for reducing human wood smoke exposure to the appropriate particle fractions.

In vivo animal studies

In vivo wood smoke studies in animal models may be divided into exposure conditions relevant for a) fire-fighters or fire victims (studies using high doses and short exposure time) and b) ambient residential wood smoke exposure in developed countries (studies using lower concentrations and acute, intermediate or long-term exposure). The majority of the *in vivo* animal studies using low exposure conditions were performed at the Lovelace Respiratory Research Institute (LRRI, New Mexico, US) [75,141-145]. A conventional wood stove was applied to generate the smoke, using a three-phase burn cycle (kindling, high and low burn rate). Since $> 70\%$ of the combustion was performed with a low burn rate, the particles used in these inhalation studies were most likely dominated by spherical organic carbon particles, as supported by the high OC content reported in these studies (90-94% of total carbon content) [143]. However, one early study used particles that were dominated by carbon aggregates (soot) [75]. In light of the discussion in the sections concerning wood smoke exposure, these studies applying particles with very low content of soot (EC/TC ratio < 0.06) may not be fully representative for wood smoke exposure in general in developed countries. Wood smoke-induced effects in mice and rats reported in the studies performed at LRRI include exacerbation of allergic airway inflammation, decreased lung function, mild lung inflammation and toxicity, systemic immunotoxicity and increases in platelet levels [75,141-145]. In contrast to these studies,

Table 4: Experimental studies of wood smoke toxicity

Stove/combustion conditions	Dominating particle class	Model system	Biological response	Comparison of combustion conditions	References
Human inhalation studies					
Conventional wood stove	organic carbon/soot	inhalation, <i>human</i>	- inflammation in distal airways - systemic inflammation - blood coagulation - lipid peroxidation - increased oxidative stress ?	-	[7,8,138,139]
Pellets burner/ <i>incomplete combustion</i>	organic carbon/soot	inhalation, <i>human</i>	- increased oxidative stress ?	-	[120,140]
In vivo animal studies					
Conventional wood stove/ <i>mixed burn-cycle</i>	organic carbon/soot	inhalation, <i>rat</i>	- mild chronic inflammation	-	[75]
Conventional wood stove/ <i>incomplete combustion</i>	organic carbon	inhalation, <i>mouse/rat</i>	- allergic airway inflammation - decreased lung function - mild lung inflammation - systemic immunotoxicity - increases in platelet levels	-	[141-145]
Conventional wood stove/ <i>high-temperature incomplete combustion</i>	soot	footpad immunisation model, <i>mouse</i>	- enhanced allergic sensitisation	-	[146]
In vitro studies					
Old boiler, modern boiler, pellets boiler	organic carbon	epithelial cell line, <i>human</i>	- genotoxicity - inflammation	no large differences	[147]
Thermolysis of bark/ <i>incomplete combustion</i>		macrophage-like cell line, <i>mouse</i>	- DNA damage - oxidative stress - inflammation	-	[148]
Conventional wood stove/ <i>high-temperature incomplete combustion</i>	soot	epithelial and monocytic cell lines, <i>human</i>	- DNA damage	-	[149]
Modern boiler, conventional wood stove/ <i>normal and poor combustion conditions</i>	inorganic ash soot, organic carbon	fibroblast cell line, <i>hamster</i>	- chromosome breakage - cytotoxicity	organic carbon > soot > ash	[53]
Conventional masonry heater/ <i>normal and poor combustion conditions</i>	soot	macrophage-like cell line, <i>mouse</i>	- cytotoxicity - inflammation: TNF- α MIP-2	poor > normal poor < normal poor > normal	Salonen et al. in [120]
Conventional wood stove/ <i>high-temperature incomplete combustion</i>		epithelial and monocytic cell lines, <i>human</i>	- inflammation	-	[150,151]
Large biomass combustion plant		epithelial cell line, <i>human</i>	- inflammation	-	Bellman et al. in [120]

The table summarizes the studies discussed in the text. Only the endpoints or biological effects that were influenced during exposure to wood smoke particles are listed in the table, not all the endpoints investigated in each study.

Samuelson et al. (2008) used particles from incomplete high-temperature combustion in a conventional wood stove (soot dominated) to investigate the allergy adjuvant effect in mice, and observed enhanced allergic sensitisation after wood smoke exposure [146]. The applied model system, a footpad immunisation model, differed considerably from the model systems used in the studies performed at LLRI, with respect to both exposure route and analysed biological endpoints. This precludes a comparison of the results from these studies.

In vitro studies

The mutagenic potential of wood smoke particles has been relatively well documented in bacterial systems and seems to depend on the PAH content, which is influenced by the combustion conditions [5]. Wood smoke particles have also been reported to induce DNA damage in human monocytic and epithelial cell lines and in a murine macrophage cell line [147-149]. Surprisingly, particles from three different combustion appliances (old boiler, modern boiler and pellets boiler) with varying content of organic carbon showed a similar genotoxic potency [147]. On the contrary, the combustion conditions were found to have great influence on the ability of wood smoke particles to induce chromosome breakage, when investigated by the micronucleus test in a lung fibroblast cell line from Chinese hamsters; particles generated during incomplete combustion conditions induced much higher levels of chromosome breakage than particles generated during more complete combustion conditions [53].

Particles emitted from a variety of stoves and combustion conditions have been reported to increase the release of pro-inflammatory cytokines in different *in vitro* model systems [120,147,148,150,151]. However, only one study compared the influence of the combustion conditions on the inflammatory response. Particles from normal combustion conditions in a conventional masonry heater were found to induce a slightly higher release of the pro-inflammatory cytokine tumour necrosis factor (TNF)- α from a murine macrophage cell line than particles from poor combustion conditions (Salonen et al. in [120]). The latter were, however, more potent inducers of macrophage-inflammatory protein (MIP)-2, the murine analogue of IL-8. One study compared particles emitted from three different combustion appliances, a modern wood pellet boiler, a pellets burner and an old boiler, but the reported differences in inflammatory potential were small [147]. This study only used one concentration and time point in their experiments, which limits the reliability of the presented data, as the relative responses induced by the different wood smoke samples could change with particle concentration and exposure time.

Particles from large biomass combustion plants from combustion of waste wood or bark, consisting mainly of

inorganic salts, were found to induce an inflammatory response in a human epithelial cell line, but the same particles did not induce an influx of inflammatory cells to the lungs of rats (Bellmann et al. in [120]). The authors suggested that this may be due to rapid clearance of soluble constituents in the *in vivo* model systems, whereas clearance was not possible *in vitro*.

Particles from incomplete high-temperature combustion were found to induce low cytotoxicity in human monocytic and epithelial cell lines [150,151]. In another study, soot from a poorly operated stove exhibited much higher cytotoxicity than particles from normal combustion conditions in a fibroblast cell line, whereas inorganic particles from complete combustion conditions were even less toxic [53]. Similarly, particles from incomplete combustion conditions induced greater increases in cytotoxicity and programmed cell death (apoptosis) in a murine macrophage cell line than particles from normal combustion conditions (Salonen et al. in [120]).

The organic fraction of wood smoke particles has been suggested to be involved in the release of inflammatory mediators and DNA damage [149-151]. Klippel and Nussbaumer compared the toxicity of the condensable organic matter collected during poor, normal and complete combustion conditions [53]. Interestingly, the condensable organic matter from the three different combustion conditions had a similar toxicity when compared on equal mass concentration, but the amount of condensable organic matter emitted increased with decreasing combustion efficiency. Kubatova et al. (2006) applied a novel method for fractionation of organic extracts in combination with chemical analysis to determine the groups of organic compounds that contribute to cellular oxidative stress. Mid-polarity and non-polar compounds, including oxy-PAHs, were identified as inducers of oxidative stress in a macrophage cell line [44]. Further similar studies are necessary to determine how these groups of compounds or other organic compounds influence a wider range of biological endpoints, but also to determine the influence of varying combustion conditions.

The available literature concerning wood smoke exposure in human volunteers and animal model systems is not sufficient for comparison of the effects induced by particles from different combustion conditions or to discuss the influence of the physicochemical properties on the biological response. However, the number of *in vitro* studies that compare wood smoke particles generated under varying combustion conditions is currently increasing. As discussed above, particles from different combustion conditions seem to induce differential pro-inflammatory response patterns, whereas particles from poor combustion seem to have greater effects on both cytotoxicity and DNA damage than particles from more complete combus-

tion conditions. However, *in vitro* model systems have several limitations. For instance, the particle exposure does not mimic the conditions during *in vivo* exposures and these models also lack the cellular interactions and neurological signals that are of importance in animals. The physicochemical properties of collected particles may also be altered compared to the properties of particles deposited directly from the gas-phase, which occurs during human exposure. In *in vitro* experiments, different particle samples are usually compared on an equal mass basis. However, the pulmonary deposition and retention of particles partly depends on the physicochemical particle properties [25,26]. Thus, during inhalation of equal concentrations of wood smoke particles with different physicochemical properties, pulmonary cells may be exposed to different particle concentrations due to differences in deposition efficiency. This was recently demonstrated for biomass combustion aerosols generated under different combustion conditions [69]. Particles generated during complete combustion conditions (inorganic ash) and particles generated during incomplete combustion conditions (soot/organic carbon) showed relatively low respiratory tract deposition compared to traffic-derived particles due to their size and hygroscopicity [69]. This demonstrates the importance of considering the deposited dose when estimating the toxicological potential of air pollution particles.

In order to target the strategies applied to reduce wood smoke emissions, it is crucial that future toxicological studies provide information about how physicochemical properties, combustion conditions and the type of fuel and combustion appliance influence the toxicity of the emitted particles. We suggest that future toxicological studies perform a minimum of physicochemical characterisation, i.e. determine the fractions of organic carbon, soot and inorganic ash, and perform further characterisation of the organic fraction. We also emphasize the need for further studies comparing wood smoke particles from different combustion conditions generated from the same stove, particularly in *in vivo* model systems.

Summary and conclusion

Summary

Wood smoke particles were divided into three classes based on their physicochemical properties; spherical organic carbon particles, soot particles and inorganic ash particles. These particle classes differ with respect to properties that are likely to influence their toxicity, such as size, morphology, internal microstructure, solubility, hygroscopicity, organic chemistry and content of inorganic compounds (Figure 1). Emissions from various appliances often contain several of the defined particle classes.

The reviewed studies of ambient, indoor and personal exposure applied various markers to estimate the wood smoke exposure. These markers are usually only representative for one class of residential wood combustion particles, and therefore provide limited information regarding the physicochemical properties of the particles we are exposed to. However, by considering the physicochemical properties of emissions from different types of combustion appliances (Table 2), and their emission factors (Table 3) and estimates, soot and organic carbon were suggested to be the dominating classes in wood smoke exposure in European countries. Inorganic ash particles, primarily emitted from pellets burners and modern wood log boilers, were found to make a small contribution to ambient concentrations at present, although their contribution is likely to increase in the future.

Only a few experimental studies have compared the biological effects induced by particles from different combustion conditions (Table 4). The conducted *in vitro* studies suggested that the biological potential varied with the combustion conditions; particles from poor combustion induced more severe effects on both cytotoxicity and DNA damage than particles from more complete combustion conditions. However, the current *in vivo* data concerning biological effects of particles from varying combustion conditions is scarce, and further investigations are necessary.

Conclusion

Epidemiological and experimental studies provide increasing evidence for an association between wood smoke exposure and various health outcomes such as decreased lung function, reduced resistance to infections and increased severity/incidences of acute asthma. Moreover, inhalation studies have demonstrated that wood smoke exposure may induce systemic effects, providing a possible link to cardiovascular effects. The influence of the physicochemical properties of wood smoke particles, and of the combustion conditions, on various biological endpoints is presently largely unknown, although *in vitro* studies suggest that particles from incomplete combustion conditions are more toxic than particles generated under more complete combustion conditions. In order to establish targeted strategies to reduce wood smoke emissions in developed countries, more research is needed concerning the physicochemical properties of the wood smoke particles we are exposed to and the influence of these properties on the induced biological effects. To achieve this, there is need for a stronger collaboration between the different fields of research including combustion science, aerosol science, epidemiology and toxicology.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

AKB planned and coordinated the study. All authors provided essential contributions to the manuscript and were involved in drafting the manuscript or revising it critically. All authors read and approved the final manuscript.

Additional material

Additional file 1

Different types of wood combustion appliances. The table provides a description of the four main types of wood combustion appliances mentioned in the text.

Click here for file

[<http://www.biomedcentral.com/content/supplementary/1743-8977-6-29-S1.doc>]

References

- Ostro B, Broadwin R, Green S, Feng WY, Lipsett M: **Fine particulate air pollution and mortality in nine California counties: results from CALFINE.** *Environ Health Perspect* 2006, **114**:29-33.
- Pope CA III, Burnett RT, Thun MJ, Calle EE, Krewski D, Ito K, Thurston GD: **Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution.** *J Am Med Assoc* 2002, **287**:1132-1141.
- Pope CA III, Dockery DW: **Health effects of fine particulate air pollution: lines that connect.** *J Air Waste Manag Assoc* 2006, **56**:709-742.
- Boman BC, Forsberg AB, Järholm BG: **Adverse health effects from ambient air pollution in relation to residential wood combustion in modern society.** *Scand J Work Environ Health* 2003, **29**:251-260.
- Naeher LP, Brauer M, Lipsett M, Zelikoff JT, Simpson CD, Koenig JQ, Smith KR: **Woodsmoke health effects: a review.** *Inhal Toxicol* 2007, **19**:67-106.
- Orozco-Levi M, Garcia-Aymerich J, Villar J, Ramirez-Sarmiento A, Anto JM, Gea J: **Wood smoke exposure and risk of chronic obstructive pulmonary disease.** *Eur Respir J* 2006, **27**:542-546.
- Barregard L, Sällsten G, Gustafson P, Andersson L, Johansson L, Basu S, Stigendal L: **Experimental exposure to wood-smoke particles in healthy humans: effects on markers of inflammation, coagulation, and lipid peroxidation.** *Inhal Toxicol* 2006, **18**:845-853.
- Barregard L, Sällsten G, Andersson L, Almstrand AC, Gustafson P, Andersson M, Olin AC: **Experimental exposure to wood smoke: effects on airway inflammation and oxidative stress.** *Occup Environ Med* 2008, **65**:319-324.
- Straif K, Baan R, Grosse Y, Secretan B, El Ghissassi F, Coglian V: **Carcinogenicity of household solid fuel combustion and of high-temperature frying.** *Lancet Oncol* 2006, **7**:977-978.
- Fiedler F: **The state of the art of small-scale pellet-based heating systems and relevant regulations in Sweden, Austria and Germany.** *Renew Sustain Energy Rev* 2004, **8**:201-221.
- Tissari J, Hytönen K, Lyyrinen J, Jokiniemi J: **A novel field measurement method for determining fine particle and gas emissions from residential wood combustion.** *Atm Environ* 2007, **41**:8330-8344.
- Frey A, Tissari J, Saarnio KM, Timonen H, Tolonen-Kivimäki O, Aurela M, Saarikoski SK, Makkonen U, Hytönen K, Jokiniemi J, Salonen RO, Hillamo REJ: **Chemical composition and mass size distribution of fine particulate matter emitted by a small masonry heater.** *Bolean Environ Res* 2009, **14**:255-271.
- Johansson LS, Leckner B, Gustavsson L, Cooper D, Tullin C, Potter A: **Emission characteristics of modern and old-type residential boilers fired with wood logs and wood pellets.** *Atm Environ* 2004, **38**:4183-4195.
- Dasch MJ: **Particulate and gaseous emissions from wood-burning fireplaces.** *Environ Sci Technol* 1982, **16**:639-645.
- Boman BC: **Particulate and gaseous emissions from residential biomass combustion.** PhD thesis Umeå University, Sweden; 2005.
- Dreher KL: **Particulate matter physicochemistry and toxicology: In search of causality - A critical perspective.** *Inhal Toxicol* 2000, **12**:45-57.
- Schwarze PE, Øvreivik J, Låg M, Refsnes M, Nafstad P, Hetland RB, Dybing E: **Particulate matter properties and health effects: consistency of epidemiological and toxicological studies.** *Hum Exp Toxicol* 2006, **25**:559-579.
- Kappos AD, Bruckmann P, Eikmann T, Englert N, Heinrich U, Hoppe P, Koch E, Krause GH, Kreyling WG, Rauchfuss K, Rombout P, Schulz-Klemp V, Thiel WR, Wichmann HE: **Health effects of particles in ambient air.** *Int J Hyg Environ Health* 2004, **207**:399-407.
- Borm P, Donaldson K: **An introduction to particle toxicology: from coal mining to nanotechnology.** In *Particle toxicology* Edited by: Donaldson K, Borm P. CRC Press, Taylor & Francis group; 2007:1-12.
- Bai N, Khazaei M, van Eeden SF, Laher I: **The pharmacology of particulate matter air pollution-induced cardiovascular dysfunction.** *Pharmacol Ther* 2007, **113**:16-29.
- Schulz H, Harder V, Ibal-Mulli A, Khandoga A, Koenig W, Krombach F, Radykewicz R, Stampfl A, Thorand B, Peters A: **Cardiovascular effects of fine and ultrafine particles.** *J Aerosol Med* 2005, **18**:1-22.
- Kofler S, Nickel T, Weis M: **Role of cytokines in cardiovascular diseases: a focus on endothelial responses to inflammation.** *Clin Sci (Lond)* 2005, **108**:205-213.
- Tousoulis D, Antoniadis C, Koumallos N, Stefanadis C: **Pro-inflammatory cytokines in acute coronary syndromes: from bench to bedside.** *Cytokine Growth Factor Rev* 2006, **17**:225-233.
- Schins RP, Knaapen AM: **Genotoxicity of poorly soluble particles.** *Inhal Toxicol* 2007, **19**(Suppl 1):189-198.
- Löndahl J, Massling A, Pagels J, Swietlicki E, Vaclavik E, Loft S: **Size-resolved respiratory-tract deposition of fine and ultrafine hydrophobic and hygroscopic aerosol particles during rest and exercise.** *Inhal Toxicol* 2007, **19**:109-116.
- Kreyling W, Möller W, Semmler-Behnke M, Oberdörster G: **Particle dosimetry: deposition and clearance from the respiratory tract and translocation towards extrapulmonary sites.** In *Particle toxicology* Edited by: Donaldson K, Borm P. CRC Press, Taylor & Francis group; 2007:47-74.
- Schlesinger RB, Kunzli N, Hidy GM, Gotschi T, Jerrett M: **The health relevance of ambient particulate matter characteristics: coherence of toxicological and epidemiological inferences.** *Inhal Toxicol* 2006, **18**:95-125.
- de Kok TCM, Driessens HAL, Hogervorst JGF, Briede JJ: **Toxicological assessment of ambient and traffic-related particulate matter: A review of recent studies.** *Mut Res/Rev Mut Res* 2006, **613**:103-122.
- Brown DM, Stone V, Findlay P, MacNee W, Donaldson K: **Increased inflammation and intracellular calcium caused by ultrafine carbon black is independent of transition metals or other soluble components.** *Occup Environ Med* 2000, **57**:685-691.
- Murphy SAM, Berube KA, Richards RJ: **Bioreactivity of carbon black and diesel exhaust particles to primary Clara and type II epithelial cell cultures.** *Occup Environ Med* 1999, **56**:813-819.
- Höhr D, Steinfartz Y, Schins RPF, Knaapen AM, Martra G, Fubini B, Borm PJA: **The surface area rather than the surface coating determines the acute inflammatory response after instillation of fine and ultrafine TiO₂ in the rat.** *Int J Hyg Environ Health* 2002, **205**:239-244.
- Monteiller C, Tran L, MacNee W, Faux S, Jones A, Miller B, Donaldson K: **The pro-inflammatory effects of low-toxicity low-solubility particles, nanoparticles and fine particles, on epithelial cells in vitro: the role of surface area.** *Occup Environ Med* 2007, **64**:609-615.
- Stoeger T, Reinhard C, Takenaka S, Schroepel A, Karg E, Ritter B, Heyder J, Schulz H: **Instillation of six different ultrafine carbon particles indicates a surface area threshold dose for acute lung inflammation in mice.** *Environ Health Perspect* 2006, **114**:328-333.

34. Donaldson K, Borm PJ, Oberdorster G, Pinkerton KE, Stone V, Tran CL: **Concordance between in vitro and in vivo dosimetry in the proinflammatory effects of low-toxicity, low-solubility particles: the key role of the proximal alveolar region.** *Inhal Toxicol* 2008, **20**:53-62.
35. Sayes CM, Wahi R, Kurian PA, Liu Y, West JL, Ausman KD, Warheit DB, Colvin VL: **Correlating nanoscale titania structure with toxicity: a cytotoxicity and inflammatory response study with human dermal fibroblasts and human lung epithelial cells.** *Toxicol Sci* 2006, **92**:174-185.
36. Warheit DB, Webb TR, Reed KL, Frerichs S, Sayes CM: **Pulmonary toxicity study in rats with three forms of ultrafine-TiO₂ particles: differential responses related to surface properties.** *Toxicol* 2007, **230**:90-104.
37. Schins RP, Duffin R, Höhr D, Knaapen AM, Shi T, Weishaupt C, Stone V, Donaldson K, Borm PJ: **Surface modification of quartz inhibits toxicity, particle uptake, and oxidative DNA damage in human lung epithelial cells.** *Chem Res Toxicol* 2002, **15**:1166-1173.
38. Albrecht C, Höhr D, Haberzettl P, Becker A, Borm PJ, Schins RP: **Surface-dependent quartz uptake by macrophages: potential role in pulmonary inflammation and lung clearance.** *Inhal Toxicol* 2007, **19**(Suppl 1):39-48.
39. Duffin R, Tran L, Brown D, Stone V, Donaldson K: **Proinflammatory effects of low-toxicity and metal nanoparticles in vivo and in vitro: highlighting the role of particle surface area and surface reactivity.** *Inhal Toxicol* 2007, **19**:849-856.
40. Li N, Sioutas C, Cho A, Schmitz D, Misra C, Sempf J, Wang M, Oberley T, Froines J, Nel A: **Ultrafine particulate pollutants induce oxidative stress and mitochondrial damage.** *Environ Health Perspect* 2003, **111**:455-460.
41. Ghio AJ, Stonehuerner J, Dailey LA, Carter JD: **Metals associated with both the water-soluble and insoluble fractions of an ambient air pollution particle catalyze an oxidative stress.** *Inhal Toxicol* 1999, **11**:37-49.
42. Pagan I, Costa DL, McGee JK, Richards JH, Dye JA: **Metals mimic airway epithelial injury induced by in vitro exposure to Utah Valley ambient particulate matter extracts.** *J Toxicol Environ Health A* 2003, **66**:1087-1112.
43. Squadrito GL, Cueto R, Dellinger B, Pryor WA: **Quinoid redox cycling as a mechanism for sustained free radical generation by inhaled airborne particulate matter.** *Free Radic Biol Med* 2001, **31**:1132-1138.
44. Kubatova A, Dronen LC, Picklo MJ Sr, Hawthorne SB: **Midpolarity and nonpolar wood smoke particulate matter fractions deplete glutathione in RAW 264.7 macrophages.** *Chem Res Toxicol* 2006, **19**:255-261.
45. Xia T, Korge P, Weiss JN, Li N, Venkatesen MI, Sioutas C, Nel A: **Quinones and aromatic chemical compounds in particulate matter induce mitochondrial dysfunction: implications for ultrafine particle toxicity.** *Environ Health Perspect* 2004, **112**:1347-1358.
46. Zielinska B, Sagebiel J, McDonald JD, Whitney K, Lawson DR: **Emission rates and comparative chemical composition from selected in-use diesel and gasoline-fueled vehicles.** *J Air Waste Manag Assoc* 2004, **54**:1138-1150.
47. Hedberg E, Kristensson A, Ohlsson M, Johansson C, Johansson PA, Swietlicki E, Vesely V, Wideqvist U, Westerholm R: **Chemical and physical characterization of emissions from birch wood combustion in a wood stove.** *Atm Environ* 2002, **36**:4823-4837.
48. Salvi S, Holgate ST: **Mechanisms of particulate matter toxicity.** *Clin Exp Allergy* 1999, **29**:1187-1194.
49. Penn A, Murphy G, Barker S, Henk W, Penn L: **Combustion-derived ultrafine particles transport organic toxicants to target respiratory cells.** *Environ Health Perspect* 2005, **113**:956-963.
50. Fletcher GG, Rossetto FE, Turnbull JD, Nieboer E: **Toxicity, uptake, and mutagenicity of particulate and soluble nickel compounds.** *Environ Health Perspect* 1994, **102**(Suppl 3):69-79.
51. Brunner TJ, Wick P, Manser P, Spohn P, Grass RN, Limbach LK, Brunink A, Stark WJ: **In vitro cytotoxicity of oxide nanoparticles: comparison to asbestos, silica, and the effect of particle solubility.** *Environ Sci Technol* 2006, **40**:4374-4381.
52. Kocbach A, Johansen BV, Schwarze PE, Namork E: **Analytical electron microscopy of combustion particles: a comparison of vehicle exhaust and residential wood smoke.** *Sci Total Environ* 2005, **346**:231-243.
53. Klippel N, Nussbaumer T: **Wirkung von verbrennungspartikeln. Vergleich der Gesundheitsrelevanz von Holzfeuerungen und Dieselmotoren 2007** [<http://www.verenum.ch/Publikationen/SBPartikelw.pdf>]. Final report to Eidgenössisches Department für Umwelt, Verkehr, Energie und Kommunikation (UVEK), Switzerland.
54. Colbeck I, Atkinson B, Johar Y: **The morphology and optical properties of soot produced by different fuels.** *J Aerosol Sci* 1997, **28**:715-723.
55. Hallett J, Hudson JG, Rogers CF: **Characterization of combustion aerosols for haze and cloud formation.** *Aerosol Sci Technol* 1989, **10**:70-83.
56. Pósfai M, Simonics R, Li J, Hobbs PV, Buseck PR: **Individual aerosol particles from biomass burning in southern Africa: I. Composition and size distributions of carbonaceous particles.** *J Geophys Res* 2002, **108**:1-13.
57. Schauer JJ, Kleeman MJ, Cass GR, Simoneit BRT: **Measurement of emissions from air pollution sources. 3. C₁ - C₂₉ Organic compounds from fireplace combustion of wood.** *Environ Sci Technol* 2001, **35**:1716-1728.
58. Fine PM, Cass GR, Simoneit BRT: **Chemical characterization of fine particle emissions from fireplace combustion of woods grown in the Northeastern United States.** *Environ Sci Technol* 2001, **35**:2665-2675.
59. Kjällstrand J: **Phenolic antioxidants in wood smoke.** Chalmers University of Technology, Göteborg, Sweden; 2002.
60. Simoneit BRT, Schauer JJ, Nolte CG, Oros DR, Elias VO, Fraser MP, Rogge WF, Cass GR: **Levoglucosan, a tracer for cellulose in biomass burning and atmospheric particles.** *Atm Environ* 1999, **33**:173-182.
61. Pósfai M, Gelencsér A, Simonics R, Arató K, Li J, Hobbs PV, Buseck PR: **Atmospheric tar balls: particles from biomass and biofuel burning.** *J Geophys Res* 2004, **109**:1-9.
62. Rau JA: **Composition and size distribution of residential wood smoke particles.** *Aerosol Sci Technol* 1989, **10**:181-192.
63. Khalil MAK, Rasmussen RA: **Tracers of wood smoke.** *Atm Environ* 2003, **37**:1211-1222.
64. McDonald JD, Zielinska B, Fujita EM, Sagebiel J, Chow GM, Watson JG: **Fine Particle and Gaseous Emission Rates from Residential Wood Combustion.** *Environ Sci Technol* 2000, **34**:2080-2091.
65. Weimer S, Alfara MR, Schreiber D, Mohr M, Prévôt ASH, Baltensperger U: **Organic aerosol mass spectral signatures from wood-burning emissions: influence of burning conditions and wood type.** *J Geophys Res* 2007, **113**: doi:10.1029/2007JD009309.
66. Schauer JJ: **Evaluation of elemental carbon as a marker for diesel particulate matter.** *J Expo Anal Environ Epidemiol* 2003, **13**:443-453.
67. Hays MD, Smith ND, Kinsey J, Dong Y, Kariher P: **Polycyclic aromatic hydrocarbon size distributions in aerosols from appliances of residential wood combustion as determined by direct thermal desorption-GC/MS.** *J Aerosol Sci* 2003, **34**:1061-1084.
68. Pagels J, Boman C, Rissler J, Massling A, Löndahl J, Wierzbicka A, Swietlicki E: **Residential biomass combustion aerosols - influence of combustion conditions on physical and chemical particle characteristics. [abstract].** 7th International Aerosol Conference (IAC) 2006.St.Paul, Minnesota, September 10-15, 2006 :240-241.
69. Löndahl J, Pagels J, Boman C, Swietlicki E, Massling A, Rissler J, Blomborg A, Bohgard M, Sandström T: **Deposition of biomass combustion aerosol particles in the human respiratory tract.** *Inhal Toxicol* 2008, **20**:923-933.
70. Hueglin CH, Gaegauf CH, Kunzel S, Burtscher H: **Characterization of wood combustion particles: Morphology, mobility and photoelectric activity.** *Environ Sci Technol* 1997, **31**:3439-3447.
71. Reid JS, Koppmann R, Eck TF, Eluterio DP: **A review of biomass burning emissions part II: intensive physical properties of biomass burning particles.** *Atmos Chem Phys* 2005, **5**:799-825.
72. Hallquist M, Wenger JC, Baltensperger U, Rudich Y, Simpson D, Claeys M, Dommen J, Donahue NM, George C, Goldstein AH, Hamilton JF, Herrmann H, Hoffmann T, Iinuma Y, Jang M, Jenkin ME, Jimenez JL, Kiendler-Scharr A, Maenhaut W, McFiggans G, Mentel THF, Monod A, Prévôt ASH, Seinfeld JH, Surrat JD, Szmigielski R, Wildt J: **The formation, properties and impact of secondary organic aerosol: current and emerging issues.** *Atmos Chem Phys* 2009, **9**:5155-5236.

73. Gwaze P, Schmid O, Annegarn HJ, Andreae MO, Huth J, Helas G: **Comparison of three methods of fractal analysis applied to soot aggregates from wood combustion.** *J Aerosol Sci* 2006, **37**:820-838.
74. Bockhorn H: *Soot formation in combustion, mechanisms and models* Berlin: Springer Verlag; 1994.
75. Tesfaigzi Y, Singh SP, Foster JE, Kubatko J, Barr EB, Fine PM, McDonald JD, Hahn FF, Mauderly JL: **Health effects of subchronic exposure to low levels of wood smoke in rats.** *Toxicol Sci* 2002, **65**:115-125.
76. Tissari J, Lyyrinen J, Hytönen K, Sippula O, Tapper U, Frey A, Saarnio K, Pennanen AS, Hillamo R, Salonen RO, Hirvonen MR, Jokiniemi J: **Fine particle and gaseous emissions from normal and smouldering wood combustion in a conventional masonry heater.** *Atm Environ* 2008, **42**:7862-7873.
77. Hindsgeul C, Schramm J, Gratz L, Henriksen U, Dall Bentzen J: **Physical and chemical characterization of particles in producer gas from wood chips.** *Bioresource Technol* 2000, **73**:147-155.
78. Johansson LS, Tullin C, Leckner B, Sjövall P: **Particle emissions from biomass combustion in small combustors.** *Biomass Bioenergy* 2003, **25**:435-446.
79. Wierzbicka A, Lillieblad L, Pagels J, Strand M, Gudmundsson A, Gharibi A, Swietlicki E, Sanati M, Bohgard M: **Particle emissions from district heating units operating on three commonly used bio-fuels.** *Atm Environ* 2005, **39**:139-150.
80. Heckman FA: **Microstructure of carbon black.** *Rubber Chem Technol* 1964, **37**:1245-1298.
81. Kocbach A, Li Y, Yttri KE, Cassee FR, Schwarze PE, Namork E: **Physicochemical characterisation of combustion particles from vehicle exhaust and residential wood smoke.** *Part Fibre Toxicol* 2006, **3**:1.
82. Braun A: **Carbon speciation in airborne particulate matter with C(1s) NEXAFS spectroscopy.** *J Environ Monit* 2005, **7**:1059-1065.
83. Braun A, Huggins FE, Kubatova A, Wirick S, Maricq MM, Mun BS, McDonald JD, Kelly KE, Shah N, Huffman GP: **Toward distinguishing woodsmoke and diesel exhaust in ambient particulate matter.** *Environ Sci Technol* 2008, **42**:374-380.
84. Kjällstrand J, Olsson M: **Chimney emissions from small-scale burning of pellets and fuelwood - examples referring to different combustion appliances.** *Biomass Bioenergy* 2004, **27**:557-561.
85. Fitzpatrick EM, Ross AB, Bates J, Andrews G, Jones JM, Phylaktou H, Pourkashanian M, Williams A: **Emission of oxygenated species from the combustion of pine wood and its relation to soot formation.** *Process Safety Environ Protect* 2007, **85**:430-440.
86. Boström CE, Gerde P, Hanberg A, Jernström B, Johansson C, Kyrklund T, Rannug A, Törnqvist M, Victorin K, Westerholm R: **Cancer risk assessment, indicators, and guidelines for polycyclic aromatic hydrocarbons in the ambient air.** *Environ Health Perspect* 2002, **110**(Suppl 3):451-488.
87. Gustafson P, Ostman C, Sällsten G: **Indoor levels of polycyclic aromatic hydrocarbons in homes with or without wood burning for heating.** *Environ Sci Technol* 2008, **42**:5074-5080.
88. Smith JS, Laskin A, Laskin J: **Molecular characterization of biomass burning aerosols using high-resolution mass spectrometry.** *Anal Chem* 2009, **81**:1512-1521.
89. Park K, Cao F, Kittelson DB, McMurry PH: **Relationship between particle mass and mobility for diesel exhaust particles.** *Environ Sci Technol* 2003, **37**:577-583.
90. Zhang R, Khalizov AF, Pagels J, Zhang D, Xue H, McMurry PH: **Variability in morphology, hygroscopicity, and optical properties of soot aerosols during atmospheric processing.** *Proc Natl Acad Sci USA* 2008, **105**:10291-10296.
91. Mikhailov EF, Vlasenko SS, Kramer L, Niessner R: **Interaction of soot aerosol particles with water droplets: influence of surface hydrophilicity.** *J Aerosol Sci* 2001, **32**:697-711.
92. Boman BC, Nordin A, Boström D, Öhman M: **Characterisation of inorganic particulate matter from residential combustion of pelletized biomass fuels.** *Energy & Fuels* 2004, **18**:338-348.
93. Wiinikka H, Gebart R, Boman C, Boström D, Öhman M: **Influence of fuel ash composition on high temperature aerosol formation in fixed bed combustion of woody biomass pellets.** *Fuel* 2007, **86**:181-193.
94. Tissari J, Sippula O, Kouki J, Vuorio K, Jokiniemi J: **Fine particle and gas emissions from the combustion of agricultural fuels fired in a 20 kW burner.** *Energy Fuels* 2008, **22**:2033-2042.
95. Båfver LS, Rönnbäck M, Leckner B, Claesson F, Tullin C: **Particle emission from combustion of oat grain and its reduction by addition of limestone or kaolin.** *Fuel Process Technol* 2009, **90**:353-359.
96. Boström D, Grimm A, Boman C, Björnbom E, Öhman M: **Influence of kaolin and calcite additives on ash transformations in small scale combustion of oat.** *Energy Fuels* 2009, **23**:5184-5190.
97. Mavrocordatos D, Kaegi R, Schmatloch V: **Fractal analysis of wood combustion aggregates by contact mode atomic force microscopy.** *Atm Environ* 2002, **36**:5653-5660.
98. Pagels J, Strand M, Rissler J, Szpila A, Gudmundsson A, Bohgard M, Lillieblad L, Sanati M, Swietlicki E: **Characteristics of aerosol particles formed during grate combustion of moist forest residue.** *J Aerosol Sci* 2003, **34**:1043-1059.
99. Lillieblad L, Szpila A, Strand M, Pagels J, Rupar-Gadd K, Gudmundsson A, Swietlicki E, Bohgard M, Sanati M: **Boiler operation influence on the emissions of submicrometer-sized particles and polycyclic aromatic hydrocarbons from biomass-fired grate boilers.** *Energy Fuels* 2004, **18**:410-417.
100. Rissler J, Pagels J, Swietlicki E, Wierzbicka A, Strand M, Lillieblad L, Sanati M, Bohgard M: **Hygroscopic behavior of aerosol particles emitted from biomass fired grate boilers.** *Aerosol Sci Technol* 2005, **39**:919-930.
101. Lind T, Valmari T, Kauppinen E, Nilsson K, Sfiris G, Maenhaut W: **Ash formation mechanisms during combustion of wood in circulating fluidized beds.** *Proceed Comb Inst* 2000, **28**:2287-2295.
102. Wu CF, Larson TV, Wu SY, Williamson J, Westberg HH, Liu LJ: **Source apportionment of PM(2.5) and selected hazardous air pollutants in Seattle.** *Sci Total Environ* 2007, **386**:42-52.
103. Song Y, Tang X, Xie S, Zhang Y, Wei Y, Zhang M, Zeng L, Lu S: **Source apportionment of PM2.5 in Beijing in 2004.** *J Hazard Mat* 2007, **146**:124-130.
104. Lewis CW, Norris GA, Conner TL, Henry RC: **Source apportionment of Phoenix PM_{2.5} aerosol with the Unmix receptor model.** *J Air Waste Manag Assoc* 2003, **53**:325-338.
105. Saarikoski SK, Sillanpää M, Saarnio KM, Hillamo RE, Pennanen AS, Salonen RO: **Impact of biomass combustion on urban fine particulate matter in central and northern Europe.** *Water Air Soil Pollut* 2008, **191**:265-277.
106. Glasius M, Ketzel M, Wählin P, Jensen B, Monster J, Berkowicz R, Palmgren F: **Impact of wood combustion on particle levels in a residential area in Denmark.** *Atm Environ* 2006, **40**:7115-7124.
107. Mandalakis M, Gustafsson O, Alsberg T, Egeback AL, Reddy CM, Xu L, Klanova J, Holoubek I, Stephanou EG: **Contribution of biomass burning to atmospheric polycyclic aromatic hydrocarbons at three European background sites.** *Environ Sci Technol* 2005, **39**:2976-2982.
108. Glasius M, Ketzel M, Wählin P, Bossi R, Stubkjær J, Hertel O, Palmgren F: **Characterization of particles from residential wood combustion and modelling of spatial variation in a low-strength emission area.** *Atm Environ* 2008, **42**:8686-8697.
109. Marchand N, Besombes JL, Chevreton N, Masclat P, Aymoz G, Jaffrezo JL: **Polycyclic aromatic hydrocarbons (PAHs) in the atmospheres of two french alpine valleys: sources and temporal patterns.** *Atm Chem Phys* 2004, **4**:1167-1181.
110. Gaeggeler K, Prevot ASH, Dommen J, Legreid G, Reimann S, Baltensperger U: **Residential wood burning in an Alpine valley as a source for oxygenated volatile organic compounds, hydrocarbons and organic acids.** *Atm Environ* 2008, **42**:8278-8287.
111. Hellén H, Hakola H, Haaparanta S, Pietarila H, Kauhaniemi M: **Influence of residential wood combustion on local air quality.** *Sci Total Environ* 2008, **393**:283-290.
112. Kreef P, Hedberg Larsson E, Ström J, Johansson C: **Contribution of residential wood combustion and other sources to hourly winter aerosol in Northern Sweden determined by positive matrix factorization.** *Atmos Chem Phys* 2008, **8**:3639-3653.
113. Johannesson S, Gustafson P, Molnar P, Barregard L, Sällsten G: **Exposure to fine particles (PM(2.5) and PM(1)) and black smoke in the general population: personal, indoor, and outdoor levels.** *J Expo Sci Environ Epidemiol* 2007, **17**:613-624.
114. Molnar P, Gustafson S, Boman J, Barregard L, Sällsten G: **Domestic wood burning and PM2.5 trace elements: Per-**

- sonal exposures, indoor and outdoor levels. *Atm Environ* 2005, **39**:2643-2653.
115. Gustafson P, Barregard L, Strandberg B, Sällsten G: **The impact of domestic wood burning on personal, indoor and outdoor levels of 1,3-butadiene, benzene, formaldehyde and acetaldehyde.** *J Environ Monit* 2007, **9**:23-32.
 116. Yttri KE, Dye C, Slørdal LH, Braathen OA: **Quantification of monosaccharide anhydrides by liquid chromatography combined with mass spectrometry: application to aerosol samples from an urban and a suburban site influenced by small-scale wood burning.** *J Air Waste Manag Assoc* 2005, **55**:1169-1177.
 117. Jordan TB, Seen AJ, Jacobsen GE: **Levogluconan as an atmospheric tracer for woodsmoke.** *Atm Environ* 2006, **40**:5316-5321.
 118. Nussbaumer T, Klippel N, Johansson L: **Survey on measurements and emission factors on particulate matter from biomass combustion in IEA countries [abstract].** 16th European Biomass Conference and Exhibition, 2-6 June Valencia, Spain 2008 [<http://www.verenum.ch/Publikationen/Biomass-Conf9.2.pdf>].
 119. Schmidl C, Marr JL, Caseiro A, Kotianová P, Berner A, Bauer H, Kasper-Giebl A, Puxbaum H: **Chemical characterisation of fine particle emissions from wood stove combustion of common woods growing in mid-European Alpine regions.** *Atm Environ* 2008, **42**:126-141.
 120. Jokiniemi J, Hytönen K, Tissari J, Obernberger I, Brunner T, Bärnthaler G, Friesenbichler J, Salonen RO, Hirvonen MR, Jalava P, Pennanen A, Happonen M, Vallius M, Markkanen P, Hartmann H, Turwoski P, Rossmann P, Ellner-Schubert T, Boman C, Pettersson E, Wiinikka H, Hillamo R, Saarinen K, Frey A, Saarikoski S, Timonen H, Teinilä K, Aurela M, Sillanpää M, Bellmann B, Sandström T, Sehlstedt M, Forsberg B: **Biomass combustion in residential heating: particulate measurements, sampling, and physicochemical and toxicological characterisation.** ISSN 0786-4728 Final report of the project 'Biomass-PM' funded by ERA-NET Bioenergy Programme 2007-2008; University of Kuopio, Report 1/2008; 2008.
 121. Karvosenoja N, Tainio M, Kupiainen K, Tuomisto JT, Kukkonen J, Johansson M: **Evaluation of the emissions and uncertainties of PM_{2.5} originated from vehicular traffic and domestic wood combustion in Finland.** *Boreal Environ Res* 2008, **13**:465-474.
 122. Sternhufvud C, Karvosenoja N, Illerup J, Kindbom K, Lükewille A, Johansson M, Jensen D: **Particulate matter emissions and abatement options in residential wood burning in the Nordic countries.** ANP 2004:735 2004 [http://www.norden.org/is/utgafa/utgefif-efni/2004-735/at_download/publicationfile]. Nordic Council of Ministers
 123. Lipsky EM, Robinson AL: **Effects of dilution on fine particle mass and partitioning of semivolatile organics in diesel exhaust and wood smoke.** *Environ Sci Technol* 2006, **40**:155-162.
 124. Donahue NM, Robinson AL, Pandis SN: **Atmospheric organic particulate matter: From smoke to secondary organic aerosol.** *Atmos Environ* 2009, **43**:94-106.
 125. Robinson AL, Donahue NM, Shrivastava MK, Weitkamp EA, Sage AM, Grieshop AP, Lane TE, Pierce JR, Pandis SN: **Rethinking organic aerosols: semivolatile emissions and photochemical aging.** *Science* 2007, **315**:1259-1262.
 126. Pöschl U: **Atmospheric aerosols: composition, transformation, climate and health effects.** *Angew Chem Int Ed Engl* 2005, **44**:7520-7540.
 127. Zielinska B: **Atmospheric transformation of diesel emissions.** *Exp Toxicol Pathol* 2005, **57**:31-42.
 128. Vione D, Maurino V, Minero C, Pelizzetti E, Harrison MA, Olariu RI, Arsene C: **Photochemical reactions in the tropospheric aqueous phase and on particulate matter.** *Chem Soc Rev* 2006, **35**:441-453.
 129. Leskinen AP, Jokiniemi JK, Lehtinen KEJ: **Characterization of aging wood chip combustion aerosol in an environmental chamber.** *Atm Environ* 2007, **41**:3713-3721.
 130. Grieshop AP, Donahue NM, Robinson AL: **Laboratory investigation of photochemical oxidation of organic aerosol from wood fires - Part 2: Analysis of aerosol mass spectrometer data.** *Atm Chem Phys Discuss* 2008, **8**:17095-17230.
 131. Grieshop AP, Logue JM, Donahue NM, Robinson AL: **Laboratory investigation of photochemical oxidation of organic aerosol from wood fires - Part 1: Measurement and simulation of organic aerosol evolution.** *Atm Chem Phys Discuss* 2008, **8**:15699-15737.
 132. Feilberg A, Nielsen T, Binderup ML, Skov H, Poulsen MWB: **Observations of the effect of atmospheric processes on the genotoxic potency of airborne particulate matter.** *Atm Environ* 2002, **36**:4617-4625.
 133. Jalava PI, Salonen RO, Halinen AI, Penttinen P, Pennanen AS, Sillanpää M, Sandell E, Hillamo R, Hirvonen MR: **In vitro inflammatory and cytotoxic effects of size-segregated particulate samples collected during long-range transport of wildfire smoke to Helsinki.** *Toxicol Appl Pharmacol* 2006, **215**:341-353.
 134. Zielinska B, McDonald JD, Samy S, Seagrave J: **Atmospheric transformations of diesel emissions [abstract].** *Health Effects Institute, 2008 Annual conference* [<http://www.healtheffects.org/Pubs/AnnualConferenceProgram2008.pdf>].
 135. de Bruijne K, Sexton DW, Ebersviller S, Doyle M, Jeffries H, Jaspers I: **Comparing the toxicity of fresh and aged diesel exhaust using a newly developed in vitro exposure system [abstract].** *Toxicol Sci* **96**(Suppl):106.
 136. Potts EN, de Bruijne K, Ebersviller S, Sexton DW, Jaspers I, Foster WM: **Realistic atmospheric aging enhances respiratory toxicity of diesel emissions [abstract].** *Toxicol Sci* **96**(Suppl):106.
 137. Zelikoff JT, Chen LC, Cohen MD, Schlesinger RB: **The toxicology of inhaled wood smoke.** *J Toxicol Environ Health* 2002, **5**:269-282.
 138. Sällsten G, Gustafson P, Johansson L, Johannesson S, Molnar P, Strandberg B, Tullin C, Barregard L: **Experimental wood smoke exposure in humans.** *Inhal Toxicol* 2006, **18**:855-864.
 139. Danielsen PH, Brauner EV, Barregard L, Sällsten G, Wallin M, Olinski R, Rozalski R, Möller P, Loft S: **Oxidatively damaged DNA and its repair after experimental exposure to wood smoke in healthy humans.** *Mutat Res* 2008, **642**:37-42.
 140. Boman C, Pagels J, Massling A, Löndahl J, Rissler J, Nordin A, Bohgard M, Swietlicki E, Blomberg A, Sandström T: **Controlled human chamber exposure studies of biomass combustion aerosols. [abstract].** 7th International Aerosol Conference (IAC) 2006.St.Paul, Minnesota.September 10-15, 2006 :982-983.
 141. Barrett EG, Henson RD, Seilkop SK, McDonald JD, Reed MD: **Effects of hardwood smoke exposure on allergic airway inflammation in mice.** *Inhal Toxicol* 2006, **18**:33-43.
 142. Burchiel SW, Lauer FT, Dunaway SL, Zawadzki J, McDonald JD, Reed MD: **Hardwood smoke alters murine splenic T cell responses to mitogens following a 6-month whole body inhalation exposure.** *Toxicol Appl Pharmacol* 2005, **202**:229-236.
 143. Reed MD, Campen MJ, Gigliotti AP, Harrod KS, McDonald JD, Seagrave JC, Mauderly JL, Seilkop SK: **Health effects of subchronic exposure to environmental levels of hardwood smoke.** *Inhal Toxicol* 2006, **18**:523-539.
 144. Seagrave J, McDonald JD, Reed MD, Seilkop SK, Mauderly JL: **Responses to subchronic inhalation of low concentrations of diesel exhaust and hardwood smoke measured in rat bronchoalveolar lavage fluid.** *Inhal Toxicol* 2005, **17**:657-670.
 145. Tesfaigzi Y, McDonald JD, Reed MD, Singh SP, De Sanctis GT, Eynott PR, Hahn FF, Campen MJ, Mauderly JL: **Low-level subchronic exposure to wood smoke exacerbates inflammatory responses in allergic rats.** *Toxicol Sci* 2005, **88**:505-513.
 146. Samuelsen M, Nygaard UC, Løvik M: **Allergy adjuvant effect of particles from wood smoke and road traffic.** *Toxicol* 2008, **246**:124-131.
 147. Karlsson HL, Ljungman AG, Lindbom J, Möller L: **Comparison of genotoxic and inflammatory effects of particles generated by wood combustion, a road simulator and collected from street and subway.** *Toxicol Lett* 2006, **165**:203-211.
 148. Leonard SS, Wang S, Shi X, Jordan BS, Castranova V, Dubick MA: **Wood smoke particles generate free radicals and cause lipid peroxidation, DNA damage, NFκB activation and TNF-α release in macrophages.** *Toxicol* 2000, **150**:147-157.
 149. Danielsen PH, Loft S, Kocbach A, Schwarze PE, Möller P: **Oxidative damage to DNA and repair induced by Norwegian wood smoke particles in human A549 and THP-1 cell lines.** *Mutat Res Gen Toxicol Environ Mut* 2009, **674**:116-122.
 150. Kocbach A, Namork E, Schwarze PE: **Pro-inflammatory potential of wood smoke and traffic-derived particles in a monocytic cell line.** *Toxicol* 2008, **247**:123-132.
 151. Kocbach A, Herseth JI, Låg M, Refsnes M, Schwarze PE: **Particles from wood smoke and traffic induce differential pro-inflammatory response patterns in co-cultures.** *Toxicol Appl Pharmacol* 2008, **232**:317-326.