

Review

On the Water-Soluble Organic Matter in Inhalable Air Particles: Why Should Outdoor Experience Motivate Indoor Studies?

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Abstract: The current understanding of water-soluble organic aerosol (OA) composition, sources, transformations, and effects is still limited to outdoor scenarios. However, the OA is also an important component of particulate matter indoors, whose complexity impairs a full structural and molecular identification. The current limited knowledge on indoor OA, and particularly on its water-soluble organic matter (WSOM) fraction is the basis of this feature paper. Inspired by studies on outdoor OA, this paper discusses and prioritizes issues related to indoor water-soluble OA and their effects on human health, providing a basis for future research in the field. The following three main topics are addressed: (1) what is known about the origin, mass contribution, and health effects of WSOM in outdoor air particles; (2) the current state-of-the-art on the WSOM in indoor air particles, the main challenges and opportunities for its chemical characterization and cytotoxicity evaluation; and (3) why the aerosol WSOM should be considered in future indoor air quality studies. While challenging, studies on the WSOM fraction in air particles are highly necessary to fully understand its origin, fate, toxicity, and long-term risks indoors.



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1. Introduction

Particulate matter (PM) of different sizes has been one of the most studied outdoor air pollutants. This interest in atmospheric PM is fueled by the realization of its negative impacts on air quality and human health, and large, but uncertain, effects on radiative climate forcing and atmospheric chemistry [1,2]. Both size and chemical composition of atmospheric PM influences the climate and human health, with the PM_{2.5} (aerodynamic diameter ≤ 2.5 μm) and PM₁₀ (aerodynamic diameter ≤ 10 μm) being the aerosol metrics measured systematically in national and international air pollution monitoring networks [2,3]. The chemical composition and sources of atmospheric PM, either PM_{2.5}, PM₁₀, or size-segregated PM have also been the focus of extensive research over the past 20 years. While the analysis of the inorganic component of atmospheric PM is reasonably straightforward, the characterization of their organic counterpart is a much more challenging task [4]. This organic component constitutes an important and highly variable fraction (~20–50%) of PM_{2.5} mass at continental mid-latitudes [3,5–7], exhibiting a multitude of molecular forms, sources, and physical properties. While the task of determining the detailed molecular composition of the atmospheric organic component is daunting, it offers unparalleled rewards for a better understanding of its origin, physicochemical transformation in the atmosphere, and role on the climatic system [8] as well as its effects on air quality and health [2,9,10].

Over the past two decades, it has become also clear that an important fraction of airborne particulate organic matter (also known as organic aerosol, OA) is water-soluble. Observations made in Northern Hemisphere midlatitudes showed that water-soluble organic matter (WSOM) accounts for 10 to 80% of OA [11–14], whereas lower percentage

values (up to 13%) have been reported for Southern Hemisphere locations [15]. The WSOM is ubiquitous in rural, urban, and marine aerosols, playing a key role in cloud formation and properties [16,17], Earth's radiative balance [5,18], and atmospheric chemistry [5,19]. Dry and wet deposition of aerosol WSOM can also affect carbon and nitrogen biogeochemical cycles in aquatic ecosystems [20–22]. The WSOM in fine air particles may also exert adverse health effects by generating reactive oxygen and nitrogen species (e.g., [23,24]) or by promoting a moderate pro-inflammatory status [11]. Therefore, the structural and molecular identification of aerosol WSOM constituents in outdoor air and how they influence the climatic and health effects of fine OA has become an active area of research.

In contrast to outdoor environments, the contribution, and chemical features of the WSOM of fine particles in indoor air remain poorly characterized. However, considering that secondary organic aerosols (SOA) contribute significantly to aerosol WSOM burden in outdoor PM_{2.5} (e.g., [14]), and that indoor SOA can be a substantial fraction of indoor aerosols (e.g., [25]), one can hypothesize that the WSOM is an important component of indoor PM_{2.5}. Moreover, it has been suggested that indoor SOA composition is dominated by highly oxygenated organic molecules [26], whose characteristics may resemble those of WSOM. Furthermore, recent measurements showed that total polar water-soluble organic gases (WSOGs) concentrations are much higher indoors than directly outdoors (on average 15 times higher, on a carbon-mass basis) [27]. The aqueous processing of these WSOGs can alter the composition of residential indoor air in ways that are not yet understood [27]. This current lack of knowledge in indoor aerosol WSOM warrants further attention as well as ascertaining whether this indoor OA fraction could plausibly induce adverse health effects. The outdoor studies can provide guidance on issues such as the characterization and cytotoxicity of WSOM in indoor environments. Encouraged by this topic, this feature paper aims to reflect on (1) what is known about the origin, contribution, and health effects of the WSOM in outdoor PM_{2.5}; (2) the current state-of-the-art on the WSOM fraction in indoor air particles, the main challenges and opportunities for its chemical characterization and toxicity assessment; and (3) why the WSOM should be considered a key particle-phase component in indoor air quality studies.

2. Characteristics and Sources of Aerosol WSOM in Outdoor Environments

As mentioned earlier, the water-soluble OA fraction, generally measured as water-soluble organic carbon (WSOC), can contribute substantially to the aerosol carbon mass. Table 1 shows examples of ambient concentrations of organic carbon (OC), elemental carbon (EC), and WSOC in locations with different levels of pollution around the globe. The lowest WSOC concentrations are typically found in pristine locations, far from anthropogenic sources. Nevertheless, the WSOC is the most abundant carbon fraction at these locations; for example, for the Canadian High Arctic, it has been reported that the WSOC can account to 40–89% of the OC [28], and in the Colorado Rocky Mountains, more than 90% of the OC was found to be water soluble [29]. The origin of WSOC at these pristine locations include primary biological aerosol particles [28], long-range transported aerosols, and SOA formation via the photooxidation of anthropogenic and biogenic volatile organic compounds (VOCs) originating from either short- or long-term transport [28–30]. The Antarctic Peninsula is another a pristine location, where the analysis of WSOC in aerosol samples revealed fingerprints of three different sources: primary marine organics (i.e., sea spray), primary biological particles emitted from land biota and land vegetation (grasses, mosses, lichens), and SOA originating from VOCs emitted from algal communities colonizing the sea ice [31]. On average, outdoor studies worldwide have shown a decreasing gradient for the WSOC/OC ratios in the order rural/agricultural—suburban—urban—industrial, which reflects a less aged aerosol OC at the urban and industrial sites, although the contribution of secondary organics to the WSOC fraction cannot be disregarded (e.g., [13,15,32]). In fact, it has been reported that the WSOC/OC is higher in summer than in other seasons at a variety of locations, both urban and rural, with this feature associated with the strong photochemical processes due to higher sun radiation (e.g., [33,34]). Nevertheless, SOA as-

sociated with anthropogenic precursors (e.g., nitro-monoaromatic hydrocarbons (NMAHs), nitrated and oxygenated derivatives of polycyclic aromatic hydrocarbons (PAHs), and phthalic acids) can also contribute to the water-soluble OA load in urban locations, even in colder seasons [13,15,32,35]. This contribution can also change between urban locations; for example, Kitanovski et al. [35] reported that NMAH contribution to the so-called humic-like substances (HULIS) mass was higher in Thessaloniki ($\approx 1.8\%$) than in Mainz ($\approx 0.4\%$). Less oxidized OA originating from fossil fuel combustion emissions can also dominate in urban and industrial areas, which explains the low WSOC/OC ratios (0.3 to 0.4) and demonstrates that these anthropogenic emissions are not the main source of WSOC at these locations [15,34,36]. On the other hand, the temporal variations reported for the WSOC concentrations at both urban and industrial sites, with the highest values occurring at colder periods, have been associated with fresh and aged biomass combustion emissions. These results confirm the dominant contribution of these sources for the aerosol WSOC load in low temperature conditions [13,32,37].

Table 1. A few examples of ambient concentrations (either range or average values) of OC, EC, and WSOC in areas with different levels of pollution.

Sampling Site	OC ($\mu\text{g C m}^{-3}$)	EC ($\mu\text{g C m}^{-3}$)	WSOC ($\mu\text{g C m}^{-3}$)	Reference
<i>Pristine</i>				
Jungfraujoch, CH	1.2 ± 0.4	0.19 ± 0.08	0.63 ± 0.23	[38]
Alert, Canadian High Arctic	0.07–0.39		0.04–0.30	[28]
Antarctic Peninsula			0.07–0.14	[31]
Colorado Rocky Mountains, US	0.43 ± 0.24	0.04 ± 0.07	0.41 ± 0.27	[29]
Chichijima Island, JP	0.60–1.13	0.04–0.28	0.20–0.59	[30]
<i>Rural/Agricultural</i>				
Rondonia, pasture site, BR			2.2–39.6	[39]
Moitinhos, agricultural, PT	2.56–11.6	0.45–1.30	1.11–4.62	[33]
Porto Velho, forest, MBB ¹ , BR			0.03–0.10	[15]
Porto Velho, forest, IBB ¹ , BR			0.01–0.43	[40]
Thompson Farm, US	4.49		3.23	[40]
Sainte-Anne-de-Bellevue, Montreal, CA			0.96	[41]
<i>Suburban</i>				
Coruña, Summer, ES			0.06–0.15	[14]
Coruña, Winter, ES			0.13–0.69	[14]
Saitama, JP	5.18–12.1	0.90–1.44	2.74–7.64	[42]
Drummond, Montreal, CA			1.19	[41]
<i>Urban</i>				
Aveiro, PT	4.99–8.22	0.13–1.10	1.81–3.12	[13]
Lisbon, Summer, PT			0.95–5.7	[15]
Mainz, DE			2.07	[35]
Thessaloniki, GR			4.20	[35]
Helsinki, FI	0.67–7.5		0.26–4.6	[37]
Rio de Janeiro, Summer, BR			0.83–1.3	
São Paulo, BR			0.07–0.45	
Medellín, Dry season, CO			0.05–0.34	[15]
Bogotá, Wet season, CO			0.04–0.13	[15]
Lima, Winter, PE			0.27–0.38	
Buenos Aires, Winter, AR			0.07–4.7	
Atlanta, Summer, US	4.30		3.12	[43]
Little Rock, US			0.7–5.9	[32]
Anjou, Montreal, CA			1.13	[41]
Gwangju, Winter, KR	2.5–17.7	0.7–8.5	1.2–6.7	[44]
Beijing, CN	3.4–36.7	1.6–10.6	1.3–14.7	[36]

Table 1. Cont.

Sampling Site	OC ($\mu\text{g C m}^{-3}$)	EC ($\mu\text{g C m}^{-3}$)	WSOC ($\mu\text{g C m}^{-3}$)	Reference
	<i>Industrial</i>			
Lanzhou, Summer, CN	3.1–59.5	1.5–24.5	1.2–13.2	[34]
Saint-Jean-Baptiste, Montreal, CA			1.26	[41]

¹ MBB—moderate biomass burning; IBB—Intense biomass burning.

As for the chemical features of aerosol WSOM in outdoor environments, this fraction covers a huge variety of molecular structures with different physicochemical properties, which reflects its different sources. To further enhance the diversity and structural complexity of this aerosol component, the chemical aging of primary OA during its transport can also be an important pathway for the formation of WSOM [45,46]. Therefore, it has become important to assess the structural and molecular characteristics of the WSOC to discriminate between primary OA and SOA because their quantitative contributions are a key aspect in evaluating air pollution control strategies. With the purpose of unravelling the complex structural composition of this aerosol component, several different offline and online analytical methodologies have been developed and applied by the outdoor research community [12–15,33,43,47–54]. Figure 1 summarizes the different state-of-the-art multidimensional analytical strategies currently available to quantify and characterize the atmospheric WSOM constituents and their various levels of identification.

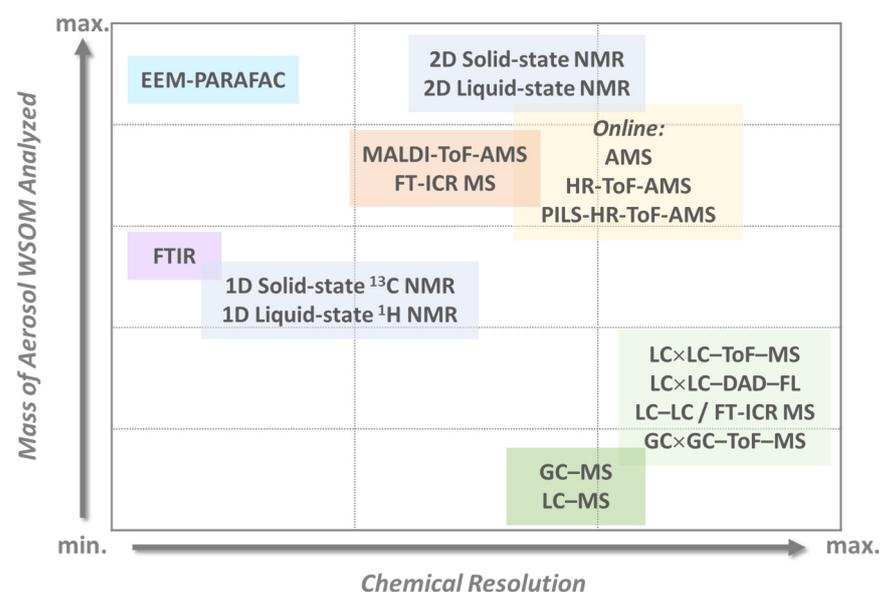


Figure 1. Schematic representation of the range of multidimensional analytical strategies currently employed in the characterization of aerosol WSOM as a function of the level of speciation and quantification achieved. Reprinted from the work of Duarte et al. [50], under the Creative Commons Attribution (CC BY) license. Acronyms: 1D: one-dimensional; 2D: two-dimensional; DAD: diode array detector; FL: fluorescence; EEM: excitation-emission matrix fluorescence spectroscopy; PARAFAC: parallel factor analysis; FTIR: Fourier transform infrared spectroscopy; NMR: nuclear magnetic resonance spectroscopy; MS: mass spectrometry; AMS: aerosol mass spectrometry; HR-ToF-AMS: high-resolution time-of-flight AMS; PILS: particle-into-liquid sampler; MALDI: matrix-assisted laser desorption/ionization; FT-ICR MS: Fourier transform-ion cyclotron resonance MS; GC-MS: gas chromatography-MS; LC-MS: liquid chromatography-MS; LC × LC: comprehensive 2D LC; LC-LC: heart-cutting 2D LC; GC × GC: comprehensive 2D GC.

The studies published thus far have demonstrated that the aerosol WSOM fraction consists of a highly diverse suite of oxygenated compounds including dicarboxylic acids, keto-carboxylic acids, aliphatic aldehydes and alcohols, saccharides, saccharide anhydrides,

aromatic acids, phenols, but also amines, amino acids, organic nitrates, and organic sulfates [15,33,47,52,55–62]. While this information on the major organic compound classes provides a good overview of the different types of potential functionalities within the complex organic mixtures, it is important to use these molecular-scale data to reconstruct the structural properties of the whole aerosol WSOC mass, for example, to infer on the physical properties of organic air particles. The recent work of Duarte et al. [48] is an example of how the compositional data of two urban aerosol WSOM samples collected in two short periods of time (one week each) under different wintry weather conditions was used to construct a structural model (presented in Figure 2) of the complex organic samples. The authors concluded that the studied urban aerosol WSOM exhibited three independent classes of compounds that varied both in content and molecular diversity: heteroatom-rich aliphatics (either chain or branched), carbohydrate-like moieties, and highly substituted aromatic units [48]. Despite the advances in understanding the atmospheric importance of the aerosol WSOM component, there are still knowledge gaps related to the complexity of its chemical composition, mechanisms of formation, atmospheric fate, and reactivity [4,18]. Furthermore, due to its dynamic nature, building a common model for the structure of the water-soluble fraction of OA is a challenging task [48], and further studies are needed by addressing additional aerosol WSOM sample sets from other locations (e.g., pristine, rural, agricultural) across different time scales [48]. Such a structural model would be of utmost importance because different chemical states are key factors determining the physical properties of OA.

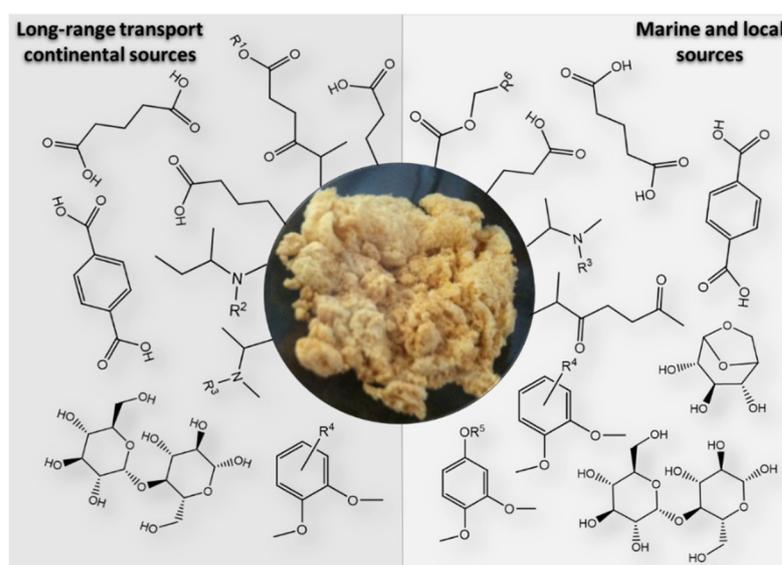


Figure 2. Structural model of two urban aerosol WSOM samples collected under different atmospheric conditions: long-range transport from continental sources and marine and local sources, exhibiting a ratio of aliphatic $-\text{CH}_3$, $\text{C}-\text{CH}_2-\text{C}$, $-\text{COO}$, aromatic $\text{C}-\text{O}$, and anomeric $\text{O}-\text{C}-\text{O}$ of 5:11:7:2:2 and 4:8:6:4:3, respectively (R^1 to R^6 = H or alkyl group; photo: aerosol WSOM, after freeze-drying). Reprinted/adapted from *Atmospheric Environment*, 230, R.M.B.O. Duarte, P. Duan, J. Mao, W. Chu, A.C. Duarte, K. Schmidt-Rohr, Exploring water-soluble organic aerosols structures in the urban atmosphere using advanced solid-state ^{13}C NMR spectroscopy, 117503, Copyright (2020), with permission from Elsevier.

3. Implications of WSOM to the Toxicity of Outdoor Air Particles

The atmospheric concentration of fine particulate matter ($\text{PM}_{2.5}$) has been recognized for decades as one of the most important risk factors associated with the adverse health effects of air pollution including cardiovascular impairments, respiratory diseases, and neurodevelopment deceleration, particularly in children [63–65]. Aside from the $\text{PM}_{2.5}$ mass, epidemiological studies have suggested the use of additional air quality metrics

that are valuable in evaluating the health risks of inhalable air particles (e.g., [2,10,66]). In this regard, Riediker et al. [67] has published a very important review work highlighting the importance of the physicochemical properties of particles in producing toxicity, particularly those related to the particles' surface reactivity, solubility, surface–tissue interactions, and biodurability. Parallel to this viewpoint on particle toxicology and health, it has been also demonstrated that the oxidative properties of some PM_{2.5} constituents (e.g., transition metals, PAHs, bioaerosols (primary biological particles), levoglucosan (tracer of biomass burning), black carbon, and SOA) are at the base of the damage in cellular bio-macromolecules (e.g., plasmatic lipids, proteins, and DNA) [2,9,10,24,63,68–73]. The presence of free radicals in PM_{2.5} (e.g., in combustion-derived particles), the transformation of aerosol organic constituents into reactive electrophilic metabolites (REMs) or the presence of transition metals, both inducing the production of intracellular reactive oxygen species (ROS) and the decrease of the cell's antioxidant capacity (by the modification of the expression of antioxidant enzymes) due to PM_{2.5} exposure, have been highlighted as important mechanisms of PM_{2.5}-mediated toxicities [63,73]. As reviewed by Feng et al. [63] and Molina et al. [73], other potential mechanisms include: (a) metabolic activation, by the release of organics (e.g., PAHs) from PM_{2.5}, which will be metabolically activated into REMs, thus causing toxic effects on cells; (b) mutagenicity/genotoxicity, caused by the presence of PAHs and/or nitro-compounds (i.e., nitro-PAHs and hydroxylamines) and transition metals in PM_{2.5}; and (c) inflammation, as a result of an increase in the gene expression and protein secretion of pro-inflammatory mediators due to PM_{2.5} exposure.

As for the aerosol WSOM, which is usually taken as a measure of SOA formation, most of the studies have been focused on the contribution of this OA component to the ROS-generating potential of PM_{2.5} [9,23,24,68,74–79]. The oxidative capacity of the aerosol WSOM has been commonly assessed by means of the cell-free assay dithiothreitol (DTT), which is highly sensitive to organic species present in atmospheric PM (e.g., [24,68,78,80]). It has been shown that ROS-activity is strongly influenced by the presence of WSOC in air particles, thus suggesting that SOA formation during transport/aging of OA in the atmosphere is a potential driver of ROS generation. Although this association between aerosol WSOC (and therefore, SOA) and ROS activity has been reported for both urban and non-urban locations, specific local sources and/or seasons might also contribute to the oxidative activity of water-soluble OA. For example, in an urban-traffic location, in the city of Thessaloniki, a significant correlation between WSOC and DTT activity was obtained for wintertime samples, suggesting the presence of a wintertime WSOC source, other than SOA formation, which contributes to the ROS activity in winter [24]. Biomass burning emissions (a known source of water-soluble OA, particularly in cold seasons) has been highlighted as a significant contributor to the oxidative potential of aerosol WSOC in the studied location [24,79]. In their recent review work, Rao et al. [68] also highlighted that the presence of a large amount of quinones in fresh wood smoke OA could be associated with an oxidative potential response. In the metropolitan Atlanta area, Fang et al. [78] also reported the important role of biomass burning to winter ROS activity of ambient water-soluble OA, whereas photochemical activity and SOA processing is likely to have a higher contribution to the summer ROS activity. Verma et al. [23] also concluded that SOA was the dominant source of ROS in summer as opposed to biomass burning in winter, leading to a significant seasonal variability in the oxidative activity of aerosol WSOM. Overall, the studies published thus far on this topic have showed that the ROS activity of the water-soluble organic fraction of outdoor air particles is likely to be driven by the relative dominance of aerosol WSOC sources at different locations and/or seasons (either primary water-soluble OA, chemical aging of OA, or SOA formation).

In the process of assessing which aerosol WSOM constituents contribute to the oxidative activity of this OA fraction, it has been shown that the most hydrophobic fraction of the WSOM—the so-called HULIS—is an active component generating ROS [74,75]. According to Lin and Yu [74], it is assumed that HULIS contains reversible redox sites (either quinone-like or nonquinone) that serve as electron carriers to catalyze the generation of

ROS. If combined with redox-active water-soluble transition metals (e.g., Cu and Fe) [81], the most hydrophobic fraction of the water-soluble OA can further enhance the production of ROS [68,79,82], thus suggesting the need to further clarify the interaction mechanisms between the most hydrophobic WSOM and redox-active metals and their impacts on ROS activity.

Studies on the cytotoxicity and pro-inflammatory effects induced by aerosol WSOM are exceptionally limited [11,69,79]. Using human lung cell lines, Akhtar et al. [69] showed that urban quasi-ultrafine PM (aerodynamic diameter $\leq 0.2 \mu\text{m}$), which was found to be enriched in WSOC, were capable of inducing a higher activation of antioxidant (heme oxygenase (HMOX-1) mRNA expression) and inflammatory (interleukin-8 (IL-8) mRNA expression) responses. The authors further suggested that differences in composition within different PM size-fractions (coarse (2.5–10 μm), fine (0.15–2.5 μm), and quasi-ultrafine) played an important role in the observed biological responses [69]. Velali et al. [79] also explored the *in vitro* cytotoxicity of the WSOC of size-segregated PM from two urban sites (traffic and urban background) in cold and warm periods. The authors reported that the cytotoxicity of PM peaked in the 0.49–0.97 μm size range, and correlated significantly with WSOC at both sites in the cold period [79]. Recently, Almeida et al. [11] investigated the relationship between the oxidative and pro-inflammatory potential of aerosol WSOM and their atmospheric concentrations and structural characteristics under different seasonal (autumn versus spring) and daily (day versus night) scenarios. The authors pinpointed a linkage between the compositional features of aerosol WSOM (namely at night, in autumn) and their ability to induce a moderate inflammatory status in macrophages. Furthermore, they also suggested that long-term exposure to very small amounts of WSOM may compromise the capacity of macrophages to respond to a subsequent inflammatory stimulus, which could result in increased susceptibility to respiratory infections [11]. It is obvious that the mechanisms by which outdoor aerosol WSOM may impair respiratory functions need to be further investigated as this would be beneficial for a better understanding of outdoor PM toxicity.

4. Water-Soluble Indoor Organic Aerosols: Challenges and Opportunities

4.1. What Is Known about the WSOM of Indoor Air Particles?

The study of the WSOM fraction in indoor air particles is at a very early stage of development compared to its outdoor counterpart. The body of knowledge produced thus far concerns only the amount of WSOC (or WSOM) present in indoor PM, and these data have mostly been used as an indicator of indoor SOA formation. This implies that nothing is known about the structural and molecular composition of the indoor aerosol WSOM. Table 2 summarizes the available data on the concentrations of WSOC in $\text{PM}_{2.5}$ collected under different indoor scenarios. To the best of the authors' knowledge, the first study reporting the quantification of the WSOC in indoor air particles was performed in the Refectory of Santa Maria Delle Grazie Church, which holds Leonardo Da Vinci's "Last Supper" [83]. The WSOM, estimated using a WSOM-to-WSOC conversion factor of 1.7, was identified as the second most abundant component of $\text{PM}_{2.5}$, after the water-insoluble organic matter, although it only contributed to a minor fraction, ca. 17.8 to 19.9%, of the fine aerosol organic matter (OM) [83]. Nevertheless, these WSOM/OC values should be viewed with caution due to the uncertainties associated with the use of a WSOM-to-WSOC conversion factor of 1.7. This conversion factor was selected based on the recommendations of Turpin and Lim [84], Russel [85], and Sheesley et al. [86] for outdoor air particles, and it was considered a reasonable compromise between the values of 1.6 for urban aerosols and 2.1 for aged (nonurban) aerosols [84]. The empirical WSOM-to-WSOC factor of 2, proposed by Turpin and Lim [84], has also been used by Secrest et al. [87] and Lai et al. [88] for estimating the contribution of WSOM to $\text{PM}_{2.5}$ from personal exposure in Chinese rural locations. In both studies, the WSOM was reported as the highest component out of all bulk $\text{PM}_{2.5}$ chemical constituents, with higher levels in winter than in the summer season. These findings were associated with the use of biomass residues for cooking activities and space

heating, with the latter source being more important during the colder periods [87,88]. Additional measurements of WSOC in indoor PM_{2.5} was performed by Hasheminassab et al. [89], who reported that WSOC can account for a highly variable fraction (1% to 13%) of PM_{2.5} collected in three retirement communities of the Los Angeles Basin.

The variability in the WSOM-to-WSOC conversion factor values recommended for outdoor OA studies should be noted, which highlights the importance of measuring the WSOM-to-WSOC ratios to reduce the uncertainties associated with the chemical mass closure assessment of atmospheric OA [13,33,38]. The use of such empirical conversion factor values is even more challenging in chemical mass balance studies of indoor air particles, and the reason is twofold: (1) not only do the WSOM-to-WSOC ratios depend on the class of organic compounds present in the WSOC component [85], and there is a clear lack of knowledge on the chemical composition of indoor particulate WSOC; (2) but also, the OC in indoor PM seems to be particularly unaffected by outdoor sources (e.g., [90,91]). Measurements and chemical characterization of the indoor WSOC fraction are, therefore, highly recommended to better ascertain the bulk chemical composition of indoor PM.

Table 2. Average indoor concentrations (either range or average values) of WSOC in PM_{2.5} collected under different indoor scenarios.

Indoor Scenario	WSOC ($\mu\text{g C m}^{-3}$)	Reference
Refectory of Santa Maria delle Grazie Church	0.31 ± 0.02	[83]
Retirement homes		
<i>Warm season</i>	0.8–1.4	[89]
<i>Cold season</i>	0.7–1.0	
Personal exposure during cooking or space heating, rural sites		
<i>Meizi, Summer</i>	15.8 ± 9.9	[92]
<i>Meizi, Winter</i>	39.3 ± 22.7	
<i>Anshang, Summer</i>	16.8 ± 11.9	
<i>Anshang, Winter</i>	23.0 ± 11.9	
<i>Inner Mongolia, Fall/Winter</i>	5.11–263 ¹	[87]
<i>Sichuan, Fall/Winter</i>	11.5–17.7 ¹	
Personal exposure, rural Sichuan ²		
<i>Summer</i>	24.8 ± 19.0 ¹	[88]
<i>Winter</i>	126 ± 131 ¹	
Household (kitchen), rural Sichuan ²		
<i>Summer</i>	44.4 ± 56.7 ¹	
<i>Winter</i>	143 ± 150 ¹	

¹ Available data: concentration of WSOM ($\mu\text{g m}^{-3}$), calculated as [WSOM] = [WSOC] × 2. ² PM_{2.5} samples collected concurrently during a 3-year period.

Nowadays, the importance of water-soluble OA in climate and human health is widely recognized by the outdoor research community. Nonetheless, understanding the dynamic processes and climate and health impacts involving aerosol WSOM depends on how well one can identify its organic constituents. In a similar vein, one can anticipate that the composition of water-soluble OA can influence the health effects and fate of OA in indoor environments. However, unravelling the structural features of WSOM in indoor air particles is a true analytical challenge, mostly due to the low levels of PM found inside closed spaces. In the quest to find the best analytical approach for particulate WSOC analysis, the outdoor atmospheric chemistry community has developed multiple targeted and non-targeted analytical strategies for both offline and real-time water-soluble OA composition measurements [4,50]. As recently reviewed by Duarte et al. [50], offline methodologies are commonly applied to attain high chemical resolution, while online methodologies mainly ensure high-time resolution for insights into the effects of short-term events on the WSOC features. Considering that a complete characterization of atmospheric WSOC is hardly possible on a routine basis in outdoor environments, a similar approach

seems to be even more logistically complicated for investigations of particulate WSOC in indoor environments. However, once the structural composition and fate of indoor WSOC are understood, recommendations can be provided regarding source control of indoor OA.

The indoor air chemistry community has a good understanding of the sophisticated instrumentation as well as extensive quality control, quality assurance, and data treatment based on chemometric tools that are needed to understand the chemical features and dynamics of organic PM [93]. Most of these powerful tools, combining multidimensional hyphenated technologies and data mining methods, stem from the extensive and intensive field and laboratory studies produced by the outdoor air chemistry community [50], being as relevant to interpreting indoor OA as they are to outdoor OA. For example, online monitoring instruments such as the aerosol mass spectrometer (AMS) coupled with multivariate factor analysis tools (e.g., positive matrix factorization, PMF) and high-resolution time-of-flight AMS (HR-ToF-AMS) analyzers have been used to study the sources and composition of water-soluble OA and their evolution in the atmosphere (for additional details, see the recent review work of Duarte et al. [50] and references therein). Another example of an analytical multidimensional approach applied to the online chemical characterization of water-soluble OA has been described in the work of Xu et al. [94]. In this work, a particle-into-liquid sampler (PILS) was coupled upstream of an HR-ToF-AMS for the online characterization of the water-solubility of OA in contrasting urban and rural environments. Other semi-online configurations of interest to address the water-soluble OA include PILS coupled to a total organic carbon (TOC) analyzer for online measurements of WSOC concentrations (e.g., [60,95]), PILS combined with ion chromatography for the real-time detection of water-soluble low-molecular weight organic acids in aerosols (e.g., [96]), and a mist-chamber TOC system for measuring the gas-phase WSOC content (e.g., [95]). All these configurations are promising approaches for the real-time analysis of either particle- or gas-phase WSOC in indoor air. However, no structural characterization of water-soluble OA constituents has been reported from these applications thus far. Indeed, the HR-ToF-AMS only provides bulk elemental composition and O/C and H/C ratios on the analyzed OA samples. In fact, the use of these online MS strategies is still far from replacing the offline techniques for an in-depth structural characterization of aerosol WSOC. Therefore, these online measurements should be complemented with offline monitoring approaches, entailing PM sampling using filters, extraction of the WSOC with ultrapure water, and non-target analysis using advanced multidimensional analytical techniques (e.g., high-resolution mass spectrometry (HR-MS) and NMR spectroscopy and their hyphenation with chromatographic systems) [50]. The non-target chemical characterization of aerosol WSOC can provide a detailed description and structural identification of the main substructures and/or molecules present in the water-soluble OA. Coupling these structural data to multivariate factor analysis has proven to be particularly important for OA source apportionment [4,50]. Although such offline multidimensional analytical strategies have yet to be applied to indoor air chemistry studies, adapting these approaches to indoor WSOC analysis could be promising for the speciated investigation and identification of the organic structures present in this OA component. Still, one of the main challenges that need to be addressed before delving into the structural elucidation of indoor WSOC, is the collection of an adequate amount of PM sample, which allows surpassing the issues of low sensitivity of some offline analytical techniques (e.g., NMR spectroscopy) [4]. In this regard, the rapidly-evolving field of analytical instrumentation has produced sophisticated tools capable of providing molecular level information on aerosol WSOC collected in short periods of time [48,50,97]. Hence, the focus should be to ensure that the aerosol WSOC sample is representative of the indoor conditions being studied, while simultaneously guaranteeing a sufficient amount of sample for structural and/or molecular characterization.

4.2. Why Should Aerosol WSOC Be Considered in Indoor Air Chemistry Studies?

Almost two decades of WSOC measurements and characterization in outdoor air particles worldwide have highlighted the compositionally specific signatures associated with

either chemical processing of OA or seasonal and emission source differences [50]. These compositional data have contributed greatly to our understanding of outdoor water-soluble OA and their effects on climate and human health. The indoor air chemistry community also has a long history with respect to the specific chemical species to be measured (mostly in the gas-phase) and their rationale, the analytical techniques to be employed in such measurements, and the most interesting indoor spaces to be studied (e.g., [98,99]). As recently reviewed by Abbat and Wang [99], indoor chemistry differs greatly from the outdoor chemistry, with the former being mostly driven by non-reactive partitioning and reactive processes that occur between gases, aerosol particles, and surfaces. The current understanding of indoor air chemistry and the nature of organic compounds in the indoor environment seems to be inevitably driven by the characterization according to volatility. Nonetheless, aerosol particles are also a dynamic player in indoor air chemistry [99,100], which means that the characterization of indoor aerosol composition, evolution, sources, and potential to affect human health is likewise highly needed.

The question brought about in this viewpoint (i.e., “why should aerosol WSOC be considered in indoor air chemistry studies?”) suggests an alternative untargeted, and yet complementary, screening approach toward an in-depth knowledge on indoor air particle composition. Residential indoor PM simulations have recently explored the assumption that hygroscopic constituents in indoor air particles may promote uptake of aerosol water, depending on relative humidity, which can constrain the phase state of OA [101]. Simulations suggest that residential OA is likely to be liquid in hot and humid climates, or when the indoor OA loading is high so that OA is less viscous [101]. A recent study in an occupied office further demonstrated that indoor “dampness” (i.e., high indoor humidity conditions) promotes the occurrence of high indoor SOA concentrations, thus increasing indoor organics exposure [102]. Using an Aerodyne Time-of-Flight Aerosol Chemical Speciation Monitor under these “dampness” conditions, the SOA was shown to be the most significant contributor (up to 99%) to total OA, with the more-oxidized oxygenated OA component becoming dominant (54%) indoors [102]. The presence of more-oxidized OA with high polarity tend to absorb water more rapidly, which might have implications on the aqueous-phase chemistry [103] and the uptake of semi-volatile or WSOGs indoors [27]. Considering that in outdoor OA studies a significant fraction (up to 88%) of the more-oxidized OA is water-soluble [60,94,104], one might expect a similar water-solubility behavior for the more-oxidized OA indoors. Furthermore, it has been also shown that the WSOC alters the hygroscopicity of outdoor air particles [105–107], with the chemical composition of WSOC being one of the main drivers of the particles’ hygroscopic growth behavior. These outdoor evidences suggest that the WSOC may also be a prime contributor to indoor OA and its hygroscopicity, and it might be helpful to use water-solubility to gain further insights into the chemical composition of OA indoors. This new challenge can be accomplished by bringing the WSOC measurement and characterization methods to the indoor environment by using the knowledge gained from outdoor studies. The use of an untargeted approach for studying the WSOC in indoor air particles is the most appropriate pathway to maximize the level of chemical information withdrawn from the complex WSOC pool and, therefore, provide the opportunity to detect unexpected compositional changes. Additional reasons to include the analysis of WSOC in indoor air chemistry studies are outlined in the following paragraphs.

As aforementioned, the WSOC fraction present in indoor PM is still poorly characterized, although there have been a few studies that have employed the WSOC as an indicator of SOA formation in indoor source apportionment studies [88,89,92,108]. Nonetheless, there is a certain level of uncertainty that one should be aware of when using the content of aerosol WSOC to perform indoor SOA estimates in a straightforward manner. First, the multiplication factor used to convert WSOC to SOA (a OM-to-OC ratio of 2.5) and the assumption that 20% of the SOA is water-insoluble OC [92]. Second, the aerosol WSOC can also have contributions from primary indoor emissions of water-soluble organics such as those from cleaning and other consumer products, cooking, and biomass burning [88,89,92].

Addressing these two issues alone should prompt a comprehensive investigation on the quantity and chemical features of the WSOC fraction present in indoor PM, considering different indoor spaces, occupancy purposes, and conditions as well as locations (e.g., urban, and rural). Furthermore, considering that indoor SOA formation can be a substantial fraction of indoor aerosols [25,102], and that indoor SOA composition is dominated by multifunctional and low-volatile highly oxygenated organic molecules [26,102], whose characteristics may resemble those of WSOC, more measurements of both WSOC and SOA composition indoors are warranted in order to improve the current knowledge on indoor air composition.

Another matter of debate is the oxidative aging of indoor OA, leading to changes in oxygen content and volatility, which may ultimately enhance the condensed-phase OA concentration [109]. Indoor chemical processes and chemical transformations have been highlighted as a research priority by the INDoor AIR POLLution NETwork (INDAIR-POLLNET), recently supported by the European Cooperation in Science and Technology (COST) [100]. Considering that for ambient air, the aging process in the atmosphere leads to the formation of increasingly oxidized, less volatile, more hygroscopic, and more water-soluble OA [7], it would be beneficial to consider the secondary formation and evolution of WSOC when predicting indoor OA concentrations. Recently, indoor WSOGs, comprising carbonyl compounds, carboxylic acids, epoxides, organic peroxides, organic nitrates, amines, and phenols, have been described as an ubiquitous and abundant component in residential indoor air, with potential implications on indoor air chemistry, air quality, and human health [27,110,111]. Nevertheless, little is still known about the concentration, composition, dynamics, fate, and health effects of WSOGs indoors. As it is quite possible that the indoor air composition of WSOGs is altered by aqueous chemistry reactions (in indoor surface films, skin or in wet particles) [27], one could argue that WSOGs will partition into the aqueous-phase and react further, thereby becoming less volatile and leading to the formation of condensed-phase secondary WSOC. This hypothesis is also critically needed to be assessed to predict its possible impact on indoor air composition and OA content.

As highlighted in Section 3, exposure to ambient fine aerosol WSOC is a potential driver of both ROS generation and pro-inflammatory effects, being therefore considered an important and prevalent form of air pollution. In indoor environments, however, very limited information is available on the cytotoxic effects upon exposure to the water-soluble OA component. Nonetheless, if one considers that indoor and outdoor PM_{2.5} share a similar bioactivity behavior including inflammatory reaction, oxidative stress, genetic toxicity, mutagenicity, and carcinogenicity [112], one could likely expect that exposure to healthy relevant indoor PM_{2.5} constituents might also trigger toxicity effects. In this regard, Xiang et al. [113] demonstrated that water-extracts of office dust were capable of inducing oxidative stress and inflammation, which the authors associated with the presence of high levels of Zn, Cu, Ni, and Mn. However, no other water-soluble dust constituent was assessed or quantified in the study of Xiang et al. [113], and therefore, nothing is known about the presence and potential redox activity of water-soluble organic dust constituents. Recently, Kogianni et al. [114] also reported significant positive correlations between the genotoxicity and water-soluble metals present in indoor PM_{2.5} of various workplaces in Greece. Among the targeted metals, Zn and Pb were found to be good predictors of the genotoxicity of water-soluble PM_{2.5}. Once again, the study of Kogianni et al. [114] only focused on the genotoxicity of the water-soluble metals of indoor PM_{2.5}, but the contribution of other water-soluble PM_{2.5} to the induced genotoxicity was not ruled out by the authors. It should also be emphasized that the studies of Xiang et al. [113] and Kogianni et al. [114] addressed workplace exposures whose magnitudes differed from that of the average indoor environment. Therefore, further investigations are needed, focusing not only on additional water-soluble PM_{2.5} constituents in indoor air, namely on its WSOC fraction, but also addressing other indoor environments (e.g., houses). Furthermore, the contribution and specific mechanisms underlying the role of the WSOC as a determinant of the cytotoxicity of PM indoors needs to be clarified. Moreover, assessing the content,

chemical composition, sources, and evolution of the WSOC present in indoor air particles is also key to a better understanding of the toxicity of daily exposure to PM components. The acquired data would be beneficial in epidemiologic studies indoors and, eventually, inform on more targeted air pollution measures.

Recently, the importance and possible role of a specific indoor WSOC constituents—the surface active substances (SAS)—in stabilizing respiratory aerosols in closed spaces has emerged in the context of the airborne transmission of SARS-CoV-2 [115]. The main assumption is that indoor generated SAS fraction of the WSOC could stabilize bio-aerosols by a reduction in surface tension of aerosol droplets, thereby increasing, stabilizing, and prolonging the lifetime of the cloud of respiratory droplets in the indoor air. This assumption on the possible role of water-soluble SAS in the viability of some virus inside of respiratory droplets deserves further attention, and can be put forward as another motivation for including the study of aerosol WSOC in indoor air quality measurements.

5. Conclusions

The outdoor studies have made a remarkable progress toward the understanding of the importance, composition, sources, and transformation of the WSOC present in ambient PM. Nevertheless, because of the complex nature of aerosol WSOC, which reflects into both the aerosol–climate and aerosol–health interactions, there still remain many open questions to be addressed by the outdoor air chemistry community [4,5,10]. One of these issues concerns the relationship between the oxidative and pro-inflammatory potential of aerosol WSOC and their atmospheric concentrations and structural characteristics. In indoor air, however, much remains to be uncovered on the physicochemical characteristics, sources, dynamics, and health effects of particulate WSOC. Indeed, this water-soluble OA fraction constitutes a new challenge for indoor air quality, for which the outdoor experience would assist in delineating and prioritizing research on this indoor OA component.

The water-soluble organic compounds including both the gas- and particulate-phases are clearly an important fraction of indoor environments. Based on the outdoor experience, one should expect a particularly complex chemical composition for the water-soluble OA indoors. In a similar vein, it is unlikely that a full representation of the state of all water-soluble organic species will be achieved throughout their lifetime in indoor environments. However, the progress reached in resolving the chemical complexity and impact of aerosol WSOC in outdoor scenarios will help to delineate a set of objectives for future research indoors including (but not limited to):

- (1) selection of the measurement location(s), considering the spatial intra- and interbuilding heterogeneity, which is ultimately closely linked to the purpose of investigation;
- (2) understanding the indoor WSOC composition and its dynamics at the structural or molecular level through the application of both online (e.g., AMS) and offline (e.g., NMR spectroscopy and HR-MS) sophisticated multidimensional analytical techniques;
- (3) ensure the collection of an adequate and representative amount of aerosol WSOC for subsequent offline structural and molecular characterization;
- (4) identification and quantification of indoor SOA components in either chamber experiments or field studies through the application of powerful analytical techniques (e.g., HR-ToF-AMS);
- (5) elucidation of indoor SOA formation pathways and OA aging processes using laboratory or chamber experiments;
- (6) apportionment of the indoor water-soluble OA among different sources based on the identification of unique source and process organic markers (i.e., source fingerprinting), and application of sophisticated statistical approaches for both data mining and source apportionment; and
- (7) establish a relationship between exposure to indoor water-soluble OA and oxidative and inflammation induction.

With the research goals previously outlined, it is expected to enhance clarity and encourage discussion within the indoor air chemistry community on the need to include the water-soluble OA as a key particle-phase component in indoor air quality studies.

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