Anthropogenic chemicals and their impacts on microbes living in buildings

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Summary
Humans spend the vast majority of their time indoors where complex interactions occur among indoor anthropogenic chemicals, indoor microbiomes and human occupants. This paper summarizes previous work addressing interactions between anthropogenic chemicals associated with indoor household products and building materials, and microorganisms found within the built environment. Water availability seems to determine the extent to which microbes are impacted by anthropogenic chemicals, since desiccation remains one of the primary stressors regulating microbial viability indoors. Several lines of evidence suggest that both fungi and bacteria are capable of transforming biodegradable ingredients originating from various products used indoors when water is present. Previous research also establishes positive and significant correlations between anthropogenic chemicals that are antimicrobial and antibiotic resistance gene abundance. As researchers move towards understanding complex indoor environments as well as the role of anthropogenic chemicals in shaping microbiomes, in situ activities associated with the viable indoor microbial population merit more attention.

What we know about microbes living in buildings
The chemistry of indoor environments has rapidly changed since the 1950s as a result of innovations in indoor building materials and household consumer product formulations (Weschler, 2009). The omnipresence of plastics, composite wood, carpets, polymeric flooring, vinyl, and scented and antimicrobial cleaning agents introduces a wide range of synthetic anthropogenic chemicals into the built environment. The chemicals found indoors are associated with different matrices (e.g. air, surface, dust) and various levels of volatilities (volatile, semi-volatile and non-volatile). Evaluations of settled floor dust and indoor air revealed the presence of endocrine-disrupting compounds such as polybrominated diphenyl ethers (Rudel et al., 2003; Hwang et al., 2008; Vishwanath et al., 2011; Whitehead et al., 2011), polychlorinated biphenyls (Whitehead et al., 2011), polycyclic aromatic hydrocarbons (Whitehead et al., 2011), pyrethroids (Hwang et al., 2008) and phthalates (Rudel et al., 2003). Many of them come from various additives used in indoor products, such as disinfectants, detergents, adhesives, flame retardants and emulsifiers (Rudel et al., 2003). In addition, the built environment is inhabited by various microorganisms that may affect occupant health in both positive and negative ways. Taken together, both indoor anthropogenic chemicals and indoor microorganisms play an important role in constituting a healthy indoor environment. Furthermore, potential chemical–microbe interactions add additional complexities to this already complex system. The role of anthropogenic chemicals in shaping the indoor microbiome, and the ways in which anthropogenic chemicals associated with product use affect microbes living in buildings, are not fully understood.

Many microorganisms across all domains of life have been identified from indoor environments, including bacteria, fungi, archaea and viruses. Past indoor biome studies have primarily focused on bacteria and to a lesser degree fungi. Bacteria represent perhaps the most intensively studied microorganism present indoors, although specific functions of non-pathogenic species are unknown but of great interest. Dampness and mould
issues have dominated the discussions on indoor fungi (e.g. *Alternaria* and *Aspergillus*) and fungal metabolites (e.g. mycotoxins) as allergens. Although archaea have long been thought to be widely associated with extreme environments (e.g. deep-sea hydrothermal vents), a recent study demonstrated the presence of archaea within the built environment (Pakpour et al., 2016). Archaea were found to be unevenly distributed in floor dust samples (e.g. living rooms, bedrooms and common rooms) with an abundance lower than that of bacteria (Pakpour et al., 2016). The authors observed that areas with high traffic tend to have higher archaea abundance.

In addition to bacteria and fungi, the study of viruses within indoor spaces is gaining traction (Prussin et al., 2020), particularly the transmission of airborne viruses that cause respiratory tract infections (Lim et al., 2011). Occurrences of Human Parainfluenza Virus 1 (HPIV1; Boone and Gerba, 2010), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; Liu et al., 2020) and respiratory syncytial virus (RSV; Foster et al., 2003) have been demonstrated on indoor fomite surfaces and in indoor air. While viruses are not metabolically active and unlikely to have a direct impact on indoor chemistry, the chemistry used to disinfect viruses indoors may incidentally impact other indoor microorganisms (Velazquez et al., 2019). Furthermore, phage may play a role in the survival and metabolic capabilities of indoor bacteria, for example aerobic methane oxidation (Chen et al., 2020) and antibiotic resistance (Zhang and Buckling, 2012). Since there is a relatively small body of literature that is concerned with archaea and viruses, this paper will summarize previous work on anthropogenic chemicals and their impacts on indoor bacteria and fungi.

**Interactions between anthropogenic chemicals and the indoor microbiome**

Anthropogenic chemicals can be introduced into the built environment unintentionally through the use of building materials that emit semi-volatile organic chemicals (SVOC) and volatile organic chemicals (VOC). Given the concern with disease transmission from infectious microorganisms, many indoor household products are formulated to be antimicrobial, including but not limited to hand soap, inanimate surfaces and fabrics. However, preliminary evidence indicates that exposure to certain microorganisms can be beneficial, such as early-life exposures to diverse microbes associated with indoor pets (Stein et al., 2016; Tun et al., 2017). Therefore, traditional notions that microorganisms are considered solely as a source of disease need to change.

Human exposure to indoor anthropogenic chemicals and the indoor microbiome lead to many fundamental questions regarding potential interactions between them (NASEM, 2017; NASEM, 2018). A recent study demonstrated that geography and location are the primary drivers of office microbiome composition, while indicating that the impact of three testing surface materials (drywall, ceiling tile and carpet) on bacterial communities is insignificant (Chase et al., 2016). In pair-wise community dissimilarity comparisons, carpet samples that were installed on the ceiling were more similar to carpet samples installed on the wall, than they were to the carpet samples on the floor. The impacts of occupant interactions on surface microbiome appear more prominent than the impacts of testing surface materials, while other studies conducted under various defined conditions (predetermined testing relative humidity levels, presence of antimicrobials, etc.) identified (i) biotransformation of anthropogenic chemicals under certain environmental conditions; and (ii) associations between antimicrobials and bacterial resistome.

**Biotransformation of anthropogenic chemicals**

The biotransformation of many indoor pollutants has been demonstrated in wastewater, sludge, freshwater, sediments, soil and in vitro (Liang et al., 2008), but has remained unexplored within the built environment because indoor surfaces and settled dust have long been thought of as microbial ‘wastelands’ for lack of water and nutrients (Gibbons, 2016). While fungi have been known to contribute to indoor pollutants as allergenic mycotoxins (Bennett and Inamdar, 2015), their contribution to non-allergenic processes, such as direct transformation of anthropogenic chemicals (e.g. phthalate esters; Boll et al., 2020), was demonstrated only recently. A chamber study revealed that dust-associated fungi found in worn carpets were capable of degrading phthalate esters presumably via beta-oxidation and hydrolysis under elevated relative humidity (≥80% equilibrium relative humidity; Bope et al., 2019). Such biotransformation activity was shown to be largely limited by available water (Bope et al., 2019). As a result, anthropogenic chemicals like phthalates, although capable of serving as a carbon source for microbial growth, are unlikely to be transformed by indoor microorganisms under humidity levels that are of realistic relevance in the absence of severe water damage.

While some indoor environments, such as carpets and building materials, are optimally not subject to frequent or prolonged wetting, water is a permanent or recurring feature of other indoor environments, such as sinks and dishwashers (Raghupathi et al., 2018). There have been several in vitro studies focusing on the impacts of hand soap on sink-associated bacteria. These studies have used classic model microorganisms and carbapenemase producing *Enterobacteriaceae* (CPE) and non-CPE
isolates cultured from hand washing sinks (e.g. *Escherichia coli*, *Klebsiella oxytoca* and *Klebsiella pneumoniae*, *Citrobacter freundii* and *Enterobacter cloacae*; Boyle et al., 2020). One soap containing sodium laurel ether sulfate (SLES), an anionic surfactant widely used in liquid detergents and cosmetic products (Khleifat, 2006), resulted in a significant growth for all clinical and model strains tested except for *E. coli*, whereas another soap investigated in the study, containing both SLES and an antimicrobial preservative (DMDM hydantoin), led to an average of one log reduction after 72 h (Boyle et al., 2020). Aerobic degradation of SLES facilitated by *Citrobacter braakii* (Dhouib et al., 2003) and a consortium of *Acinetobacter calcoaceticus*, *Klebsiella oxytoca* and *Serratia odorifera* (Khleifat, 2006) indicate that uses of SLES, and other biodegradable ingredients, may contribute to the persistence of sink-associated species, particularly those capable of utilizing SLES for growth.

**Associations between antimicrobials and the bacterial resistome**

Unlike chemicals that are unintentionally introduced into the built environment with associated building materials (e.g. phthalates), many antimicrobial agents are intentionally incorporated into the formulation of household products. Antimicrobials are not only added to preserve product integrity, but also dedicated to kill microorganisms. It remains unclear to what extent household and non-essential uses of antimicrobial-containing products contribute to the widespread antimicrobial resistance crisis. Therefore, much of the current literature on indoor microbiomes pays particular attention to possible impacts of antimicrobial chemicals on bacterial community structure and antibiotic resistance (Velazquez et al., 2019). In one study, elevated concentrations of triclosan and triclocarban were shown to be associated with distinct indoor microbiomes. These indoor microbiomes are enriched for Gram-positive species with various genes responsible for biocide resistance, regulation of efflux pumps, lipid metabolism and material transport across cell membranes (Fahimipour et al., 2018). However, in another dust microbiome study, dust-associated anthropogenic chemicals had insignificant effects on the overall microbial community composition, possibly due to insufficient contact time (Hartmann et al., 2016) as well as the dominant role of desiccation in viability reduction compared with the range of triclosan concentrations observed in the study.

Despite having inconsistencies associated with microbial assembly, various studies have demonstrated correlations between antimicrobials and antibiotic resistance gene abundance. Accordingly, antimicrobials may have a stronger influence on the retention of antibiotic resistance genes, compared with their impacts on microbial structure. Hartmann et al. discovered that *ermX*, *tetK* and *vgaA*, which encode for rRNA methyltransferase, tetracycline efflux protein and ABC-F subfamily protein, respectively, were significantly and positively associated with triclosan concentration detected from dust samples (Hartmann et al., 2016). The *erm(33)*, *ermC* and *cmr* genes were associated with methylparaben concentration (Hartmann et al., 2016). Other genes related to fluoroquinolone and aminoglycoside resistance (*qnr*, *ftsH*, Fahimipour et al., 2018) and multidrug efflux pumps (*qacA*, *patAB*, *degP*, *dsbA*) were associated with elevated triclosan and triclocarban concentrations (Mahnert et al., 2019). Moreover, frequent and standardized cleaning procedures occurring in a confined indoor space were further shown to enrich for not only genes encoding multidrug efflux pumps (e.g. *mexA* and *mexB*), but also those responsible for intrinsic resistance (*katG*) that confers non-specific broad-spectrum antibiotic resistance (Mahnert et al., 2019). Bacterial communities exposed to anthropogenic cleaning agents are equipped with additional functions related to xenobiotic degradation (e.g. geraniol, limonene, pinene, naphthalene, bisphenol, chlorocyclohexane, chlorobenzene), virulence factors, oxidative stress, membrane transport, secretion, apoptosis and nutrient acquisition (Mahnert et al., 2019).

The chemistries that we use indoors have the potential to impact our microbial cohabitants, intentionally or not. Due to technical limitations, many of these interactions have been largely unexplored. However, the outlook is bright: researchers have begun to elucidate the ways in which the indoor chemicals may interact with or shape the indoor microbial community. The studies highlighted here illustrate the distinctions between indoor chemicals that are antimicrobial versus those with other uses and that both types can impact indoor microbes. Products designated for decontamination potentially apply additional stressors and selections to the already stressful microbial ‘wasteland’ (Gibbons, 2016), thereby favoring microorganisms that are able to persist under extreme conditions (e.g. antimicrobials, lack of nutrients, water scarcity). Use of antimicrobials correlates positively and significantly with elevated abundance of certain antibiotic resistance genes, but causal relationships within the built environment have not been observed. Therefore, plausible mechanisms for how environmental chemicals would be expected to influence microbial richness, diversity, composition and the spread of antibiotic resistance remain ambiguous. To unveil the true impacts of indoor chemistry on indoor microbiology, more studies are needed to discriminate the viable microbiome, responsible for *in situ* microbial activities, versus non-viable microorganisms that contribute little to chemical–microbe interactions.
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Conflict of interest

None declared.

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