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Review

Removal of Tobacco Specific Carcinogenic Nitrosamines in Mainstream Cigarette Smoke and Aqueous Solution—A Review

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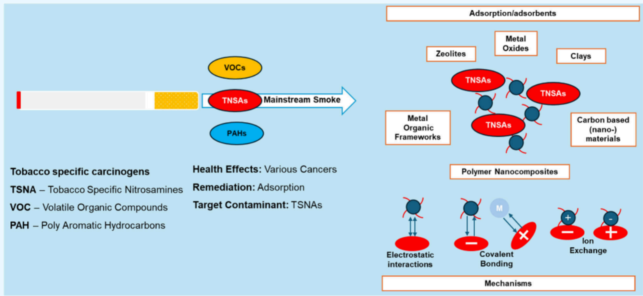
ABSTRACT: Tobacco-specific N-nitrosamines (TSNAs), which are associated with several cancers, are formed during the processing of tobacco alkaloids. Since tobacco smoking poses serious health risks, scientists, governments, and health regulators globally have denounced it and categorized its constituents according to their carcinogenicity. Tobacco smoke investigations are guided by standardized methods (ISO). With the help of standardized smoke-generating machines, precise quantification of TSNAs and other smoke constituents is now possible thanks to advancements in analytical techniques. This information supports initiatives to reduce the amount of TSNAs that smoking exposes people to. This review covers the occurrence, formation pathways, precursors, and control strategies through removal technologies, providing thorough analysis of the state of science today regarding TSNAs. The adsorption characteristics of different materials as possible filter additives or modifiers are critically discussed, emphasizing important elements like porosity, layering, acidity/alkalinity, and surface area that affect their performance for capturing TSNAs from smoke. While scientific understanding of these areas is still evolving, this review intends to provide for the first time research progress on the adsorption properties of various materials, including zeolites, silica, few-layer black phosphorus, metal−organic frameworks, and molecularly imprinted polymers, among others, for reducing TSNAs present in both cigarette smoke and aqueous solutions.



1. INTRODUCTION

Tobacco use is the leading cause of preventable disease and premature death in the world, accounting for approximately 5 million deaths annually. This number is expected to double by 2025, according to the World Health Organization (WHO).[1] Cigarette smoking is the most common form of tobacco consumption in the world, and approximately 20% of the world's population smoke cigarettes.[1,2] CThe global cigarette market value increased from USD 4.96 trillion in 1980 to USD 5.5 trillion in 2016, with the number being expected to reach USD 9 trillion by 2025.[3,4] Cigarettes, described by manufacturers as modern "drug administration delivery systems" of nicotine, are a complex physicochemical mixture containing several types of tobacco and numerous chemical additives.[5] Meanwhile, it has been estimated that the cigarette smoke (CS) resulting from the combustion of tobacco products during smoking contains over 7000 chemical compounds, which are present in both particulate and vapor phases.[6,7] It was approximated that more than 50 of these compounds are carcinogens, including the following classes of compounds: polycyclic aromatic hydrocarbons (PAH), aromatic amines (AA), and tobacco-specific nitrosamines (TSNAs).[6−8] Among the latter, the TSNAs, mainly N′-nitrosonornicotine (NNN), 4-methylnitrosamino-1,3-pyridyl-1-butanone (NNK), N′-nitrosoanatabine (NAT), and N′-nitrosoanabasine (NAB) are deemed as strong carcinogens.[9−11]

TSNAs are usually generated from the curing and combustion of tobacco products.[5,9] Although their content in tobacco and tobacco products is in the range of $\mu g\ g^{-1}$ (ppm) or $ng\ g^{-1}$ (ppb), TSNAs can cause various cancers or tumors in laboratory animals and possess the potential carcinogenicity in humans.[12−15] Given the health implications of TSNAs, considerable efforts have been dedicated to reducing the health effects of TSNAs in people who continue to use tobacco through cigarette smoking.[16−20] Currently, the primary methods for reducing harm to the tobacco industry include tobacco cultivation, leaf and cigarette processing, and cigarette filters.[21]

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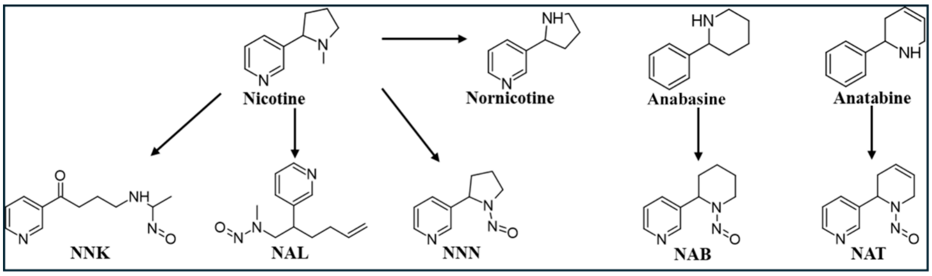

Figure 1. Chemical structures of major and minor alkaloids in tobacco and tobacco-specific N-nitrosamine formation pathway.

Although some carcinogens, such as TSNAs, are formed during the curing and aging process of tobacco, most of these compounds are generated by pyrosynthesis in the combustion of the cigarette. Consequently, cigarette filter use has been the main strategy for reducing the TSNAs from mainstream cigarette smoke.[12,20] The cigarette butt is mostly made from cellulose acetate, which is passive to the gaseous components of mainstream cigarette smoke. This has resulted in scientists developing a variety of filters that can actively trap some of the mainstream cigarette smoke toxins, TSNAs, in particular.[12,16−20,22−24] The materials used range from zeolites, metal oxide nanoparticles, carbonaceous materials, metal−organic frameworks, silica, and clays, among other types of materials.

Measuring the components of mainstream cigarette smoke is a standardized field. This is because the generation of smoke is a critical aspect of analytically measuring mainstream cigarette components as it determines the reliability of the obtained results. Some of the organizations that have approved methods of generating smoke for analytical measurements include the Federal Trade Commission (FTC), the Cooperation Centre for Scientific Research Relative to Tobacco (CORESTA) and the European Standards.[25]

Since 2010, there have been several review articles focused on TSNAs. Some of these reviews are focused on the analysis of TSNAs in biological matrices,[26] the chemical mechanisms of TSNAs from smoking and smokeless tobacco and cancer prevention,[27] while others delved into the reduction of TSNAs in smokeless tobacco products.[27,28] One of the reviews on the subject published in the last 10 years that the authors found to be interesting and informative was published by Konstantinou et al., who reviewed TSNAs holistically. Some of the key points highlighted in this review are as follows: Cigarette smoke contains harmful chemicals called TSNA, linked to various cancers. Most TSNA forms in tobacco before smoking, some during burning.[29] E-cigarettes also contain TSNA, but at much lower levels. The U.S. Food and Drug Administration (FDA) plans to regulate TSNA in e-cigarettes and other tobacco products. Research is needed to track TSNA exposure from new tobacco technologies.[29] Although the authors of this review do an excellent job at documenting the dangers of TSNAs and demonstrating that these dangers may be alleviated by consuming tobacco via smokeless devices, they do not cover options for those who still prefer consuming tobacco by smoking cigarettes and the high cost related to smokeless tobacco delivery systems. One review that was published in the past decade that attempted to address this problem by reviewing how zeolites can be used to filter N-nitrosamines and other cigarette smoke carcinogens, was published by Li et al.[30] Of the key findings, the authors highlighted that while the zeolite-like calcosilicate CAS-1 effectively removed 30−60% of TSNAs from cigarette smoke, orthodox zeolites displayed a struggle to capture TSNAs due to their large particle size and small pores.[30]

This review is, however, focused on the various types of materials that could be used to reduce TSNAs in mainstream cigarette smoke. This is usually done by modifying the cigarette butts or by incorporating additional adsorbents into already existing filters. In a recent review by Zeng et al.,[21] the authors provide a systematic summary of adsorption materials, published before 2022, for capturing hazardous compounds from cigarette smoke, including nicotine, PAHs, TNSAs, hydrogen cyanide, carbon monoxide, and formaldehyde. Their study highlights the research progress and overview on the adsorption effects and mechanisms of various advanced materials for various cigarette smoke contaminants adsorption, which is a fundamental core subject within the field. While these studies serve as an insightful reference, a critical analysis for each cigarette smoke compound and their studied advanced adsorption materials has not been drawn.

This we find to be the knowledge gap that differentiates this review and other relevant reviews, particularly, those published in the past decade. Furthermore, this review gives comprehensive details on what cigarette smoke generation for analytical work entails. This is important for scientists working in this field, so they know what the experiments entail for their results to be significant globally. This is especially important as there are standards and guidelines on how to analyze mainstream smoke components qualitatively and quantitatively. However, evaluating the effectiveness of materials used to modify cigarette butts for the removal of cigarette toxins, liquid-to-solid adsorption methods have been used in the literature, and this review covers literature that has employed this method. Therefore, this review aims to provide the existing knowledge on the formation and analysis of TNSAs present in tobacco-related products in the first aspect. Moreover, various materials have been assessed as adsorbents or cigarette filter modification agents for the removal of these TSNAs from tobacco smoke yields and aqueous environments.

2. TOBACCO SPECIFIC NITROSAMINES (TSNAs)

Tobacco contains the primary alkaloid and most active component, nicotine, which accounts for 96−98% of the total alkaloid content in tobacco.[31] Structurally like nicotine are nornicotine, anatabine, and anabasine, which form the minor alkaloids in tobacco (Figure 1). Nornicotine is also a metabolite of nicotine, formed through the demethylation reaction.[12,20,32] Tobacco alkaloids are precursors of TSNA, formed through their reaction with nitrosating agents during air cure, storage, and tobacco combustion.[33−35] The nitrosating agent mostly active during air-curing is nitrite, originating from the reduction of leave nitrates by microbes,

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Table 1. Tobacco-Specific N-Nitrosamine (TSNA) Levels in Cigarette Smoke[a]

Cigarette brand	TSNA ng/g cigarette				
	NAB ± SD	NNK ± SD	NAT ± SD	NNN ± SD	Total ± SE
Marlboro Red 100s	16.4 ± 1.0	80.7 ± 7.1	125.7 ± 11.8	134.9 ± 14.0	357.6 ± 5.8
Marlboro Red	15.3 ± 1.5	84.4 ± 11.1	114.1 ± 11.8	129.6 ± 21.8	343.1 ± 6.8
Marlboro Red 100s	17.2 ± 1.3	71.5 ± 5.2	121.9 ± 9.5	131 ± 9.1	341.5 ± 5.0
Marlboro Green	13.4 ± 1.4	76.9 ± 10.7	124 ± 8.0	112.3 ± 12.8	326.6 ± 5.7
Marlboro Red	15.3 ± 1.1	72.1 ± 10.6	117.1 ± 11.1	118.7 ± 10.1	323.2 ± 5.7
B&H Green 100s	16.2 ± 1.1	72.3 ± 6.3	117.7 ± 7.4	109.6 ± 6.9	315.8 ± 4.7
Newport Green 100s	14.7 ± 2.3	57.4 ± 8.2	103.2 ± 14.1	125 ± 12.1	300.3 ± 6.1
Marlboro Red Label	13.3 ± 0.9	62.7 ± 9.6	96.2 ± 8.2	101 ± 9.6	273.2 ± 5.3
Basic Green 100s	12.7 ± 1.8	68.4 ± 8.8	86.1 ± 11.4	99.1 ± 16.7	266.3 ± 6.2

[a]Adapted from ref 12. Copyright 2017 American Chemical Society.

while during combustion, nitrite and other NOx gases formed during the combustion process. During storage, the nitrosating agents are mostly nitrates and nitrites. Figure 1 shows the pathway for the formation of TSNAs, where N═O bonds replace N—H bonds in nicotine and carbon−nitrogen bonds are oxidatively cleaved in nornicotine, anatabine, and anabasine. The main TSNAs formed include 4-(methylnitrosamino)-a-butanone (NNK), N′-nitrosonornicotine (NNN), N′-nitrosoanatabine (NAT), N′-nitrosoanabasine (NAB), 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL), iso-NNAL and 4-(methylnitrosamino)-4-(3-pyridyl) butanoic acid (iso-NNAC).[3,12,15] Among the prominent TSNAs, NNN and NNK have been classified as the main carcinogens of tobacco smoke.[35−37]

A summary of the levels of these TSNAs in some cigarette brands was analyzed for their TSNA content using the Canadian standardized method of smoke generation, which is given in Table 1. The team reported that the concentration of carcinogenic nitrosamines, particularly NNN and NNK, differed considerably across some of the different American cigarette brands.[12,38] These results were obtained under a standardized method, which makes them credible for commercial and regulatory purposes. This truth necessitates that a significant portion of this review is on the standard methods of generating cigarette smoke for the quantitative and qualitative measurements of the components of cigarette smoke. Furthermore, the authors took care to ensure the statistical significance of their data. To generate representative averages, three packs of each commercial cigarette variety were purchased. For most measurements, one cigarette was randomly selected from each pack of a particular variety and analyzed separately, resulting in triplicate data for each analysis.

3. METHODS OF STUDYING TOBACCO-SPECIFIC N-NITROSAMINES IN MAINSTREAM CIGARETTE SMOKE

Analytical methods have been critical in awakening society to the dangers of smoking and regulating smoking. This means that the applied analytical methods need to be validated, accurate and precise. The key part in all of this is sample preparation, which is cigarette smoke generation. Literature on how analytical chemistry is used in determining the properties and composition of cigarette smoke is divided into at least two. In some reports, the analytical methods are designed such that they can be used for product comparison. In other instances, analytical methods are set up, so it is possible to use the data for regulatory purposes, such as estimating the maximum smoke emissions. The extensive work that goes into developing these kinds of analytical methods is dictated by the complexity of the nature of cigarette smoke and the possible changes that can occur during smoke collection and analysis. The following sections are constructed in a way that starts with defining cigarette smoke, leading to a discussion on the analytical techniques used to analyze TSNAs.

3.1. Standardized Smoke Generation Methods.

3.1.1. Tobacco Smoke Classification. Tobacco smoke is an aerosol mixture consisting of solid and liquid droplets and gaseous molecules all suspended in the air. This is created through an intertwined, complicated process of burning, pyrolysis, pyrosynthesis, distillation, sublimation, and condensation processes.[6,12,39] The smoke that is generated at the end of the cigarette butt when puffing is known as the mainstream smoke, which is the focus of this review. As a side note, the side stream smoke is the smoke that goes into the atmosphere from the lit end of the cigarette between puffs, while the exhaled stream is the mainstream smoke that the respiratory system had filtered.[5] Mainstream smoke is characterized by a highly saturated vapor that is formed in the endothermic pyrolysis and distillation region of the burning zone. In the process of puffing (inhalation of cigarette smoke), this smoke is drawn through the length of the cigarette to form mainstream smoke.

3.1.2. Nitrosamines Artifacts from Mainstream Cigarette Smoke. The different classes of compounds found in unaged cigarette smoke have been reviewed and listed by Borgerding et al.[40] It shows a range of components, such as water, carbon monoxide, carbon dioxide and nicotine, which are present in the milligram (mg) scale per cigarette to trace chemicals present in the pg scale per cigarette, such as heterocyclic amines and heavy metals. To a trained eye, just by looking at the table presented by Borgerding et al. (Table 3 in ref 40), it is easy to imagine the vast number of different reactions that could occur between the components of fresh mainstream cigarette smoke as it ages.[40] The interactions and chemical reactions between these components result in the generation of new compounds and the disappearance of some of the fresh smoke compounds. Artifact formation is common when cigarette smoke is collected and sampled and could potentially result in bad data during analytical testing. Artifact formation in cigarette smoke analysis refers to the generation of additional or altered chemical compounds during the process of collecting, handling, or analyzing cigarette smoke. These unintended products can distort the true chemical profile of cigarette smoke, leading to inaccurate data about its composition and the concentration of harmful substances.

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Table 2. Removal of N-Nitrosamines from Mainstream Cigarette Smoke Using Modified Butts and Analytical Techniques Used to Detect N-Nitrosamines

Cigarette type	Adsorbent	N-nitrosamine reduction %	Sampling method	Analytical technique	Refs.
Virginia type	HZSM-5	82.4	Standard ISO machine smoking regime	UV−vis spectrophotometry	11
	KA	59.6			
	NaA	19.2			
	NaZSM-5	74.1			
	NaY	83.9			
	MCM-48	30.1			
	SBA-15	83.9			
	SiO_2	10.9			
	AC	8.8			
Virginia type	5% CuO/NaY	35	Standard ISO machine smoking regime	Gas chromatography-thermal conductivity detector	49
Virginia type	MCM-41	18 (NPYR)	Glass made chamber[45]	Gas chromatography-flame ionization detector	23
	AM-773	37			
	AM-873	36			
	AM-973	28			
	AM-1073	19			
Virginia type	10% MgO	58	Standard ISO machine smoking regime	UV−vis spectrophotometry	10
	3% CuO/SBA-15	65			
Virginia type	SiO_2	34	Standard ISO machine smoking regime	UV−vis spectrophotometry	16
	AS5	38			
	AS10	42			
Chinese-blended type	NaY	82	Standard ISO machine smoking regime	UV−vis spectrophotometry	18
	NaA	21			
	AC	10			
Virginia type	CaS	73 (NNN)	Standard ISO machine smoking regime	Liquid chromatography-tandem mass spectrometry	50
		16.5 (NNK)			
		72.2 (NAT+NAB)			
		55.2 (TSNA)			
		32.6 (TPM)			
	NaA	19 (NNN)			
		4.1 (NNK)			
		16.7 (NAT+NAB)			
		10.8 (TSNA)			
		3.3 (TPM)			

This is important to consider when designing an analytical method for studying the (nitrosamines) components of mainstream cigarette smoke. An example typifying this phenomenon was reported by Caldwell and Conner,[41] who endeavored to design an experiment to investigate the extent of artifact formation during cigarette smoke N-nitrosamines trapping and device a method of preventing artifact formation.[41]

This was achieved using a nitrosation inhibitor, ascorbic acid, which competes with amines for nitrite.[42] The duo designed a sampling system that was used to collect mainstream smoke samples. The systems contain 4 midget impingers, each containing 15 mL citrate phosphate buffer at pH 4.5 and 53 mg of ascorbic acid. To these midget impingers, a Cambridge filter treated with 50 mg was attached. In the case of the control experiment, the Cambridge filter was not treated with ascorbic acid.[42]

The artification of N-nitrosamines on the Cambridge filter during mainstream smoke collection, the team compared the concentrations of N-nitrosamines on the treated and untreated Cambridge filter.[41] A variation in the distribution of the N-nitrosamines between the treated and untreated Cambridge filter and the buffer solutions was found. The team found that the concentration of most of the N-nitrosamines, NAB, NAT and NNK were double on the untreated Cambridge filter than on the untreated Cambridge filter.[41]

Several other studies were conducted to study the artification that occurs during experiments that are aimed at quantifying or qualifying N-nitrosamines in mainstream smoke.[5,12,20,32,41−43] For instance, Wu et al., citing the work done by Caldwell et al., conducted experiments to test mainstream cigarette smoke particulate matter for N-nitrosamine artifacts.[41,44] The mainstream cigarette smoke was collected from 5 cigarettes, each of whom was filtered through 5 Cambridge filter pads treated with ascorbic acid and 5 Cambridge filter pads untreated.[44] The team found that the cigarette smoke trapped on untreated Cambridge filter pads was 25−35% higher in TSNAs than the treated Cambridge filter pads.[44] Furthermore, they found that the concentration of N-nitrosamines trapped on untreated Cambridge filter pads had a large standard variation between the 5 replicate cigarettes, showing how the formation of N-nitrosamines artifacts during sample preparation can damage analytical data.

Mahanama and Daisey had some important considerations to make when endeavoring to study the artifact formation of N-nitrosamines in cigarette mainstream smoke.[32] The authors stated that because the ascorbic acid-treated Cambridge filters are placed upstream of the impinger solutions to prevent artifact formation, the method does not provide sufficient air flow.[32] Furthermore, they stated that using water-based ascorbic acid solutions was not an easy sampling medium, especially in field studies.[32] Issues with the aqueous ascorbic acid solution sampling technique mainly involve the labor-intensive sampling process. This entails liquid-to-liquid extraction that is often hampered by emulsion formation.[32] Alternative methods of preventing the formation of N-nitrosamine artifacts were reported in several other studies, although many others reported no observation of N-nitrosamines artifact formation.[20,24,45,46] The report that is under discussion by Mahanama and Daisey, who used Themosorb/N cartridges that are reputedly immune to the problems associated with water-based trap medium.[32] Regardless of the inconsistencies reported in the literature, it is important that scientists who work in this field account for ratification or even lack thereof. Nevertheless, artifaction is a major concern when sampling for N-nitrosamines, as these potent carcinogens can be formed during the sampling process itself. This can lead to an overestimation of the true levels of N-nitrosamines in the sample, posing a significant public health risk. Factors such as temperature, light, and pH are to be taken into consideration when sampling as both temperature and light can promote artifaction occurring while acidic conditions can promote the formation of nitrosamines by artifaction.

3.1.3. Cigarette Smoke Composition: N-Nitrosamines. There are many reports exploring the chemical composition of mainstream cigarette smoke, many of which reported results on N-nitrosamines. Currently, 7000 chemicals have been identified in cigarette smoke.[7,47] It is largely accepted that the toxicity of cigarette smoke is dependent on the nature of the chemicals in the cigarette smoke and their concentrations. The specific cigarette smoke chemicals that are commonly studied are called Hoffman analytes.[5,20,24] However, unlike the analytical methods for studying tobacco smoke yield and quantifying nicotine, tar and carbon monoxide, there are no analytical methods that have been validated and standardized for tobacco composition, including N-nitrosamines.

Furthermore, studies in different laboratories suggest that the empirical data on quantifying the composition of cigarette smoke is not comparable in interlaboratory trials.[25,48] For instance, the coefficient variation obtained when 6 laboratories quantified 4 TSNAs in cigarette smoke using different analytical methods was as high as 18%. However, reputable organizations such as ISO, CORESTA, and several independent laboratories have proposed methods of studying the components of cigarette smoke. These methods are often referenced by the FDA and are validated for good practice. However, they have not been recognized for regulatory purposes and neither does the FDA have a prescribed method for the analyses of TSNAs in mainstream cigarette smoke.[25]

The absence of standardized methods for the determination of cigarette smoke composition has not stalled the work done on identifying and quantifying chemicals in cigarette smoke. In relation to TSNAs, a lot of work has been done attempting to design cigarette butts with specialized adsorbents for the adsorption of N-nitrosamines in mainstream smoke. The most widely used method of sampling in these kinds of reports is the International Organization for Standardization (1991) ISO 3308: Routine analytical cigarette-smoking machine — Definition and standard condition. A random sampling of the reports on the removal of N-nitrosamines from mainstream cigarette smoke using modified butts shows that most of the experiments were conducted with the ISO cigarette smoking machine. It is important to note that, while the ISO and CORESTA methods are referenced by the FDA for TSNA analysis, they are not as tightly regulated as pharmaceutical testing. Pharmaceutical methods require higher validation, precision, and sensitivity due to the critical nature of drug testing. The key differences between the two fields are the complexity of the sample matrices, regulatory goals, and the level of regulatory scrutiny applied. Despite these differences, both industries prioritize accurate, reproducible data to ensure product safety and efficacy. This commitment is essential whether evaluating the safety of tobacco products or the purity of pharmaceutical drugs.

The summary is given in Table 2. However, there are some other nonstandardized smoking machines like the one designed by Miyake and Shibamoto.[48] More on the actual adsorbents and their efficiencies in removing N-nitrosamines will follow in the subsequent paragraphs. It is also interesting that the Virginia type of cigarettes is the one most used in such experiments (Table 2). This is not by coincidence, as it is the most smoked blend. This is because it has the mildest taste with elevated natural sugar amounts and a sweet taste and lights and burns easily.

3.1.4. Analytical Techniques in the Detection of N-Nitrosamines in Mainstream Cigarette Smoke. In the case of the analytical techniques, it is noteworthy that the authors identifying the individual N-nitrosamines from mainstream cigarette smoke opted for chromatographic techniques while those focused on quantifying the total N-nitrosamines content preferred modified spectrophotometric measurements. The concept of using spectrophotometric methods was described in this reference.[11] They stated that the recovery of N-nitrosamines using traditional spectrophotometric methods is incredibly low, in the range of 0.3% to 8%. This is because nitrosyl bromide (NOBr) that is formed from the selectively denitrosated N-nitrosamines with acetic acid and bromic acid is decomposed during the purging process, forming NO that is spectrophotometrically inactive. To counteract this drawback, based on the work done by Saltzman.[51] The team used an oxidation tube filled with chromium trioxide and incorporated it into the analysis setup to convert the nitric oxide to spectrophotometrically active NO. This was reported to have increased the recovery of the N-nitrosamines for analysis.[51]

Other than the above-mentioned spectrophotometric methods, most of the published articles used chromatography techniques (Table 2). Chromatography has an obvious advantage over spectrophotometric techniques because the individual N-nitrosamines in a sample can be identified and quantified rather than measuring the total N-nitrosamines content. Chromatography instruments, either gas chromatography or liquid chromatography coupled to a mass spectrometer (GC-MS or GC-MS-MS or LC-MS or LC-MS-MS), have high selectivity and low detection limits. Also, other detectors such as thermal energy Analyzer (TEA) and flame ionization detectors, when coupled to GC, have provided good selectivity for N-nitrosamines.

As science and technology improve, analytical instruments become more sophisticated, better, and more sensitive methods are developed for the detection of N-nitrosamines. For instance, Zhang and co-workers,[52] designed a sophisticated 2D online system that consisted of a solid phase extraction (SPE) coupled with liquid chromatography−tandem mass spectrometry. This was used for the automated analysis of N-

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nitrosamines in mainstream cigarette smoke.[52] A schematic representation of the online system is shown in Figure 2. This

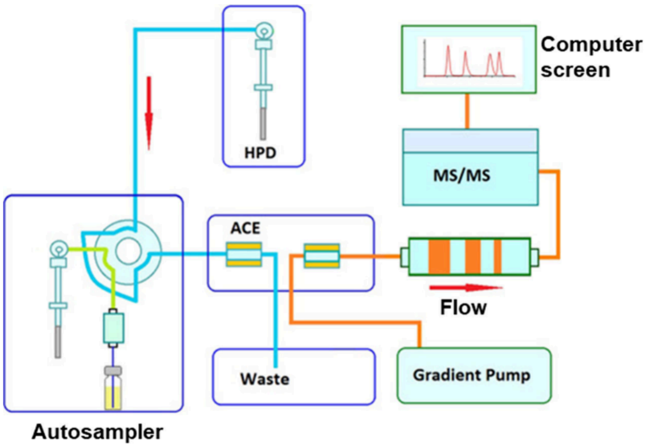

Figure 2. Scheme representing the elution part of the online solid phase extraction (SPE) system. Reproduced with permission from ref 52. Copyright 2016 Elsevier.

system setup consisted of two integrated units, (i) a refrigerated ALIAS autosampler equipped with two binary LC pumps and an Automated Cartridge Exchange (ACE) module that holds two trays of 96 extraction cartridges each and includes a high-pressure dispenser module (HPD) for handling solvents using a 2 mL high-pressure syringe (Figure 2).[52]

It is important to note that the team used the SM450 linear smoking machine permitted by ISO 3308:2000 to create mainstream smoke. The mainstream cigarette smoke was collected on a Cambridge filter pad. Virginia-type cigarettes were used. In this 2D online SPE coupled to LC-MS/MS setup, the SPE was conducted using two cartridges. The two cartridges used in this step had different extraction mechanisms; thus, they used an orthogonal cleanup method. The samples first went through the PRS cartridge and subsequently to a C18 HD cartridge for cleanup. The idea of the two-step cleanup at different polarities was to minimize the matrix effect since mainstream cigarette smoke has such a complicated matrix. The separation of the peaks was carried out using a UPLC C18 reversed-phase analytical column coupled to an MS/MS detector under optimum conditions.

The usefulness of the two-step cleanup process is evident when examining the results that they obtained and are shown in this review in Figure 3. Here we see that the chromatogram of NNN when injected the sample was injected directly into the analytical column, is plagued with a lot of noise and other undefined peaks in Figure 3a-1. A similar case is observed on samples that underwent only one cleanup cartridge, either the PRS cartridge in Figure 3a-2 or C18 HD cartridge in Figure 3a-3, except in the case of these two, the intensity of the matrix components is lower. The benefit of using the orthogonal cleanup process is laid bare in Figure 3a-4, the chromatogram

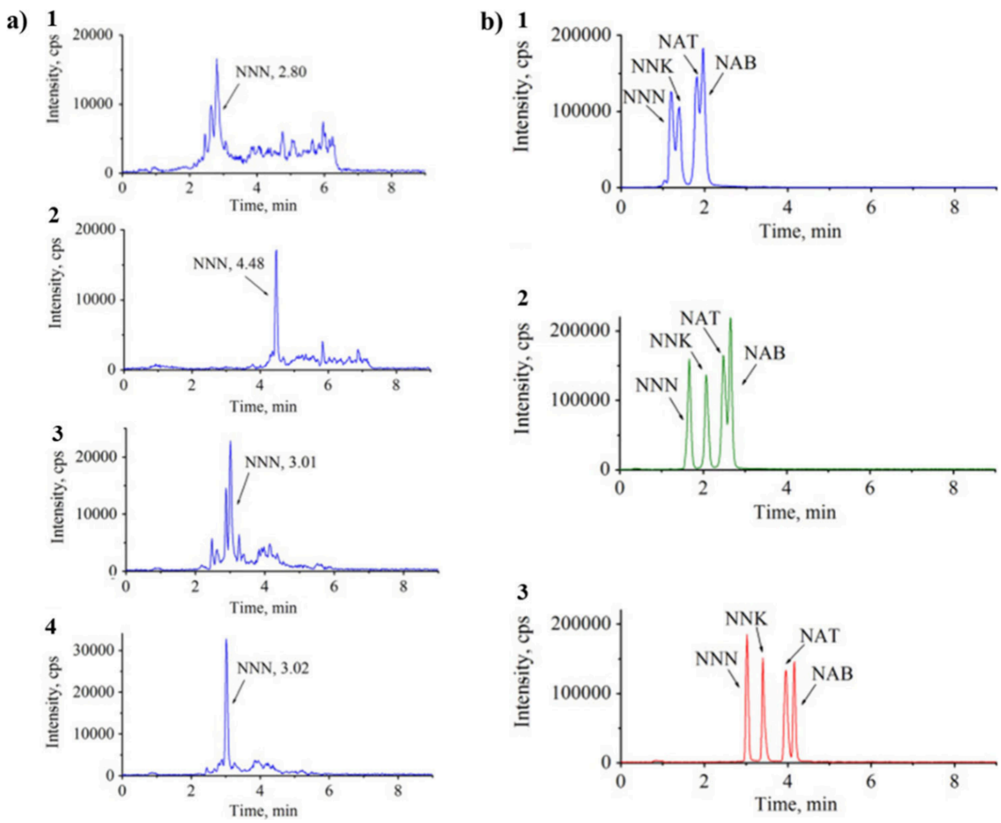

Figure 3. (a) Chromatogram of NNN: (1) directly injected into the analytical column without online SPE cleanup, (2) underwent only the PRS cartridge cleanup, (3) underwent only the C18 HD cartridge cleanup, and (4) underwent both PRS and C18 HD cartridges for cleanup. (b) Total ion chromatogram of mainstream smoke NNK, NAT, NNN, and NAB with different LC columns. (1) Xterra MS C18 (2.1 mm × 50 mm, 2.5 μm). (2) SHISEIDO MGII (2 mm × 50 mm, 3 μm). (3) ACQUITY UPLC CSH C18 (3.2 mm × 100 mm, 1.7 μm). Reproduced with permission from ref 52. Copyright 2016 Elsevier.

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is a whole lot cleaner with fewer interferences from the matrix, and the intensity of the peak has at least 10000 more counts.[52] As part of their chromatographic method development, the team tried several different columns and found that the ACQUITY UPLC CSH C18 (3.2 mm × 100 mm, 1.7 μm) was best suited for their application. This was adjudged by examining the peak separation quality, as shown in Figure 3b-3.[52] The team claimed that when their report was published, it was the most sensitive method for quantifying the 4-TSNAs in mainstream cigarette smoke. They reported limits of detection for the 4-TSNAs as low as 0.6 pg/cigarette.

Furthermore, they reported that the method had an accuracy that ranged between 93 and 107.3%. More importantly, although not enough for regulatory purposes, the coefficient of variation in intra and interday analysis were 5.4% and 7.5%, respectively. This shows that with more ingenuity and creativity a lot can be done to get to a point where the quantification of N-nitrosamines (and other chemicals) in mainstream smoke can get to a point where it can be standardized.

Some of the measures that could be undertaken to improve the detection and quantifying TSNAs in mainstream cigarette smoke include the following: Technique improvements such as concentrating the mainstream smoke samples would result in improved precision and accuracy in measurements. Column chemistry could be improved to be better suited for the separation of TSNAs from each other and other mainstream cigarette smoke components. Zhang et al. demonstrated how sampling techniques can improve separation and minimize the matrix effect. Other, more complicated techniques such as isotope dilution methods can also be applied to improve the accuracy and precision of TSNAs analyses.[52] By continually exploring these advancements and others, tailoring them to specific needs, researchers can significantly improve the application of chromatographic techniques for studying TSNAs in mainstream smoke, leading to a more comprehensive understanding of their presence and potential health risks.

4. TSNA HEALTH EFFECTS

Cigarette smoke has numerous adverse effects on human health due to the multiple chemicals it releases.[53] Although it is well documented that nicotine in cigarettes causes addiction, there are other chemical compounds in tobacco products which have an impact on health. The chemical mixture found in cigarette smoke that causes it to be highly toxic may be due to the reason that the compounds belong to almost every class of chemicals which are toxic and protective, antagonistic and agonist, carcinogenic as well as anticarcinogenic and occur in gaseous and particulate phases.[54] Some of the TSNAs (and other classes of compounds found in cigarette smoke) are carcinogens, also referred to as tumor promoters. The complex chemical composition of cigarette smoke makes it difficult to determine the constituent that is responsible for tobacco-related adverse health effects and disease. However, it is established that TSNAs specifically play a significant role in tobacco-smoke-mediated cancer initiation.[54−57]

N-nitrosonornicotine (NNN) and 4-methyl-N-nitrosamino-1-(3-pyridyl)-1-butanone (NNK) are two of the most carcinogenic TSNAs found in tobacco and tobacco smoke. TSNAs are carcinogens which are linked to several cancers, i.e., oral cancer, esophageal cancer, liver cancer, pancreatic cancer and most commonly, lung cancer.[54−57] The risk of developing cancer increases with exposure to TSNAs, the number of cigarettes that are smoked daily, the age at which smoking was started and the lifetime duration of smoking.[57,58] Gupta et al. reported a rising incidence of cervical cancer being associated with TSNAs wherein nitrosamine carcinogens were found in the cervical mucus of women who smoke.[59] High exposure to TSNAs in cigarette smoke is the main cause of lung cancer in individuals, accounting for approximately 90% of cases in males and 79% in females. Smoking may also increase the risk of developing liver, kidney, anal, prostate, uterine cervix cancer and several forms of acute leukemia.[54]

Furthermore, TSNAs have been found to be mutagenic.[54−57] This means they can induce mutations in an organism's DNA, potentially leading to genetic disorders or cellular dysfunction. This differs from their aforementioned carcinogenic effects, which refer to their ability to promote cancer development by inducing uncontrolled cell growth. While some mutagens are also carcinogens, this is not always the case. For instance, evidence suggests that NNN and NNK can induce carcinogenesis through multiple mechanisms: by causing DNA adducts and mutations, as well as by promoting tumor growth through receptor-mediated effects involving nicotinic acetylcholine receptors (nAChR) and β-adrenergic receptors (β-AR).[57]

Exposure to TSNAs from cigarette smoke may also be implicated in other chronic diseases, such as chronic bronchitis and pulmonary emphysema. Cardiovascular diseases and chronic obstructive pulmonary diseases (lung diseases) are often also reported as the main health impediments associated with TSNAs from tobacco smoke inhalation.[60] Smoking accounts for about 10% of all cardiovascular diseases.[61] Apart from cardiovascular diseases, exposure to TSNAs contributes greatly to stroke and other atherosclerotic disease of the circulatory system.[62] To curb the development of disease or serious health effects due to frequent and high exposure to tobacco and/or cigarette toxins, TSNAs, in particular, technological strategies such as mixing of tobacco species, tobacco treatment and substitutes, as well as filter adsorbents are being developed to reduce smokers' exposure to TSNAs toxicants. These methods, however, do not reduce every toxicant smoke constituent uniformly.

This necessitates further research into removing or reducing the TSNAs from mainstream cigarette smoke. This has important implications, no less reducing the risk factor posed by these chemicals, i.e., substantial decrease in cancer diagnoses and deaths among smokers. Furthermore, this has the potential for broader impact. It is possible, perhaps, that when smokers see and appreciate efforts going into reducing the harm of cigarettes might encourage more smokers to quit, further decreasing smoking-related deaths. There are also benefits to public health such that should there be reduced harm to cigarette smoking, the burden on the healthcare system can be alleviated significantly. The economic benefits of this would be astronomical. This leads to a discussion of the efforts that scientists all over the world have undertaken to reduce the TSNAs in cigarette smoke, making all the aforementioned benefits a realistic possibility.

Furthermore, given the extent of the dangers associated with exposure to N-nitrosamines by smoking cigarettes, it is necessary that the same standards used to regulate nitrosamines in food and drugs be used for cigarettes. In the pharmaceutical industry, nitrosamines are considered contaminants in drug products and must be controlled to prevent

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exposure. The FDA has set strict limits for nitrosamines in drug products, often in the range of ng to μg per dose depending on the drug's therapeutic use. In the food industry, regulations are more about preventing their formation during processing, with strict allowable limits. The levels of nitrosamines in cigarette smoke are much higher, often in the ppm range, far exceeding the limits seen in food or pharmaceuticals, reflecting tobacco's higher risk of carcinogenic exposure.

5. STRATEGIES FOR THE REMOVAL OF N-NITROSAMINES FROM MAINSTREAM SMOKE

The WHO has devised a plan for mitigating the universal cigarette smoking problem. These plans are largely centered around preventing people from taking up smoking, assisting those who are smoking with quitting, reducing the visibility of tobacco products, and awareness of the dangers of tobacco smoking. There is some merit in tackling the issues associated with smoking this way, but we have seen that more and more people are taking up smoking. The next best way to assist those who consume tobacco by smoking is to reduce the toxicity associated with smoking cigarettes. The four major ways that have been shown to have some success at achieving this goal include conventional methods of tobacco leaves cultivation and processing, cigarette processing and modifying existing cigarette butts (filters).[21]

5.1. Conventional Treatment Limitations. The growth and development processes of a tobacco plant affect the chemical composition of the leaf and, therefore, the usability of the leaf. Accordingly, the cultivation and curing processes of tobacco leaves have been widely considered as a means of reducing the potential of the leaf to generate some of the smoke toxicants, considerably reducing the levels of TSNAs. Strategic intervention considerations include genetic engineering, fertilization, and nutrition of tobacco plants, and planting methods, harvesting variables, and curing and aging of tobacco.

However, these methods have some constraints, including a limited range of chemical and agronomic regulations to reduce nicotine content in tobacco leaves. The inhibition or knockout of the key genes of nicotine synthesis can effectively reduce nicotine synthesis and content in tobacco leaves to levels of near zero. Still, it is difficult to apply this in production due to the impact on quality and restrictions on genetically modified organisms. Moreover, industrial methods, such as chemical extraction and different types of curing, can reduce nicotine content in tobacco leaves to very low levels, but they also have adverse effects, such as the decrease of aroma components. Nonetheless, although these agricultural and processing practices are important, we limit our discussion here to the reduction of TSNAs during the manipulations that are part of the manufacture of cigarettes, and more relevant to this review is the modification of cigarette filters for tobacco smoke harm reduction.

5.2. Modification of Cigarette Butt Filters. Efforts on modifying and/or designing new materials for cigarette butt filters have been a subject of research with great interest from scientists. These efforts have been primarily aimed at designing filters with active adsorbents capable of removing harmful components of mainstream smoke. The most important requirement in designing these materials is that the filter should be porous, loose, and have gas permeation and be able to remove the targeted toxins without interfering with the smoke-ability of the cigarettes and the nicotine content. Many of these materials have been tested for the removal of N-nitrosamines in mainstream smoke. The following sections focus on the filters meant to reduce N-nitrosamines in mainstream cigarette smoke.

However, as it will be seen, there are two critical aspects not covered in literature concerning the use of the reviewed and other active adsorbents for the removal of TSNAs and other toxins from mainstream cigarette smoke. These are crucial for advancing this field of research, they are (1) the integration of adsorbents into cigarettes and whether these additives might leach during smoking. (2) If they do leach, understanding the health consequences of such exposure is essential. The safety and efficacy of filter modifications should account for the potential release of chemicals during smoking, which could introduce new risks for smokers. Addressing these issues will be pivotal for ensuring both the effectiveness and safety of the proposed solutions in reducing TSNAs and other harmful components in cigarette smoke.

5.2.1. Modified Cellulose Acetate-Based Cigarette Filters. Modification of traditional cigarette filter butts' materials, particularly cellulose acetate filters, has been considered for prior discussion as a widely used material cigarette filter butts, and owing to its abundance, sustainability and low-cost properties, many efforts have even been focused on recycling cigarette butts for cellulose acetate recovery.[59,63] Dittrich et al. examined the modifications to filter cellulose acetate filter through the addition of split-tipping filter paper design, that allows for main-stream air dilution.[53] They also looked at varying the filter length and composition through the incorporation of active charcoal and resin.

Mainstream cigarette smoke experiments were conducted using three accredited smoking machine regimes, where results showed that the modified filter was able to remove TSNAs up 50% more than a compared commercial modified filter with 80% more removal obtained for NNN specifically. An existing cellulose acetate cigarette filter can be modified in various ways to enable it to work as an active filter for some toxins. For instance, Pandey et al. reported a unique cigarette filter where they sandwiched a thin and flexible membrane made from multiwalled carbon nanotubes (MWCNTs) into the middle of an orthodox cellulose acetate cigarette butt (Figure 4a).[64] The idea here is that, as a puff is taken, the toxins in cigarettes pass through the first half of the cellulose acetate onto the MWCNTs where the toxins are removed.

The cleaner smoke then goes through the second half of the acetate cellulose filter to be inhaled by the smoker. The scanning electron microscopy (SEM) analysis of the MWCNT membrane after smoking experiments was conducted. Here, they reported that before smoking, the morphology of the MWCNTs was clear with entangled randomly angled nanotubular structures. Conversely, the membrane structure after smoking experiments was observed to be covered with particulate matter with a jelly like structure forming on the surface of the nanotubes.[64]

The Fourier Transform Infrared Spectroscopy spectra of the membrane before and after smoking were even more telling as the difference between them was night and day (Figure 4b). The spectrum of the membrane before smoking virtually had no peaks, while that of the membrane after smoking was characterized by many peaks. Some of the notable peaks that appeared on the FTIR spectrum of the MWCNTs membrane, as reported by the authors, included peaks at 3002 cm^{-1}, 2886 cm^{-1}, 2828 cm^{-1}, and 1731 cm^{-1}, which were attributed to the aromatic hydrogen stretch, alcohol dimers, aliphatic carbon

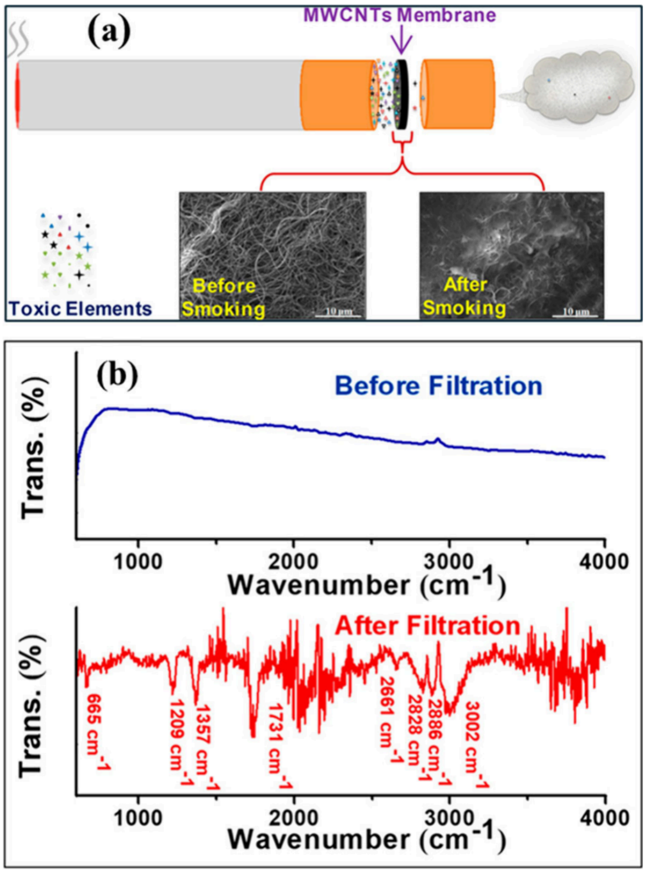

Figure 4. (a) Sandwiched multiwalled carbon nanotubes membrane showing the removal of toxins and the SEM of the filter before and after smoking. (b) The FTIR spectra of the membrane before and after smoking. Reproduced from ref 64. Copyright 2020 American Chemical Society.

and hydrogen bond stretches and carbonyl vibrations, respectively. The appearance of the absorption peaks on the FTIR spectrum of the MWCNTs after smoking showed that the material adsorbed a whole host of compounds from the mainstream cigarette smoke. More to the point of this review, peaks associated with N-nitrosamines were also observed, including the N−O symmetric stretch at 1357 cm^{-1} and the C−O stretch at 1209 cm^{-1}. The team did not measure the concentration of N-nitrosamines; instead, they reported ca. 99% reduction in particulate matter.[64]

An alternative to sandwiching a filter in between the cellulose acetate filter was proposed by Zeng et al., who synthesized cellulose nanofibers and silicon dioxide hybrid aerogel cigarette butt for the ultrahigh removal of toxins from mainstream cigarette smoke.[65] The cigarette filter was synthesized using the directional frozen method. The authors described the process as follows: A homogeneous suspension of cellulose nanofibers and silica nanoparticles in water was freeze-dried, at which point it turned into a 3D network structure aerogel. The high aspect ratio cellulose nanofibers with an interconnected porous structure served as a skeleton, whereas the high surface area silica nanoparticles served as a filler (Figure 5a).[65] Herewith, silica nanoparticles were precipitated on the surface of the cellulose nanofibers through hydrolyzation and condensation chemical reactions. It was also observed via SEM that mainstream smoke contaminants accumulated on the surface of the fibrous cellulose nanofibers and silica nanoparticles network (Figure 5b).[65] The method is a little more complicated, but it is interesting and worth exploiting. The authors implore the reader to be mindful of these two examples of how cellulose can be modified to create a functional filter when reading the sections below on the different types of materials that have been used to adsorb N-nitrosamines.

5.2.2. Carbon-Based Cigarette Filters. Carbon materials, particularly carbon nanomaterials, have been shown to be capable adsorbents for a wide variety of organic compounds, ranging from gas to solid adsorption,[66−71] to liquid to gas adsorption.[72−77] This is because of their porous nature and tunable properties. A few articles exist on the use of carbonaceous (nano)materials for modifying the cellulose acetate filters or as a replacement toward the removal of N-nitrosamines. Some of the literature is found in these references.[64,78−83] Li et al. developed a novel hierarchical porous carbon materials from recycled cigarette filters.[81] The carbon materials were further doped with Fe_xO salts to

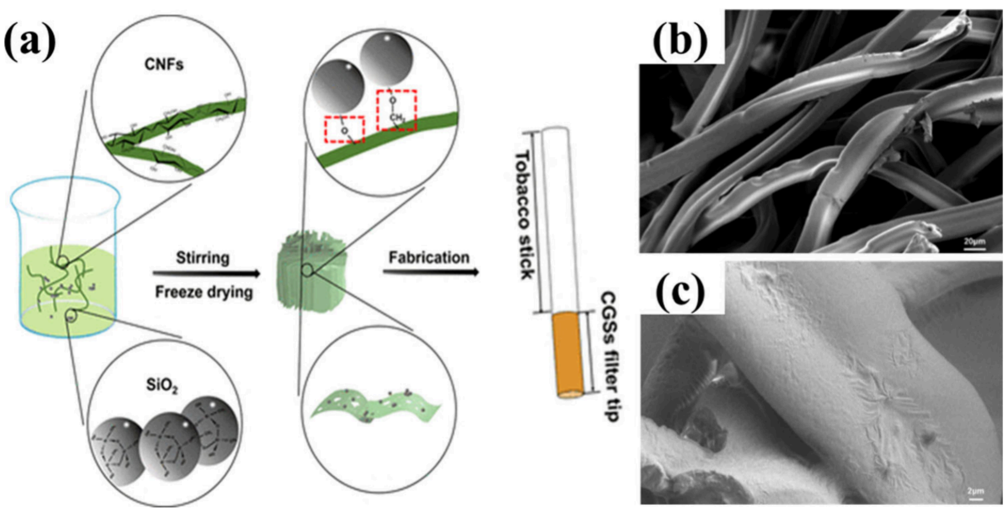

Figure 5. (a) Synthesis of the cellulose nanofiber-silica cigarette butt. SEM images of the cigarette butt (b) before smoking experiments and (c) after smoking experiments. Reproduced from ref 65. Copyright 2022 American Chemical Society.

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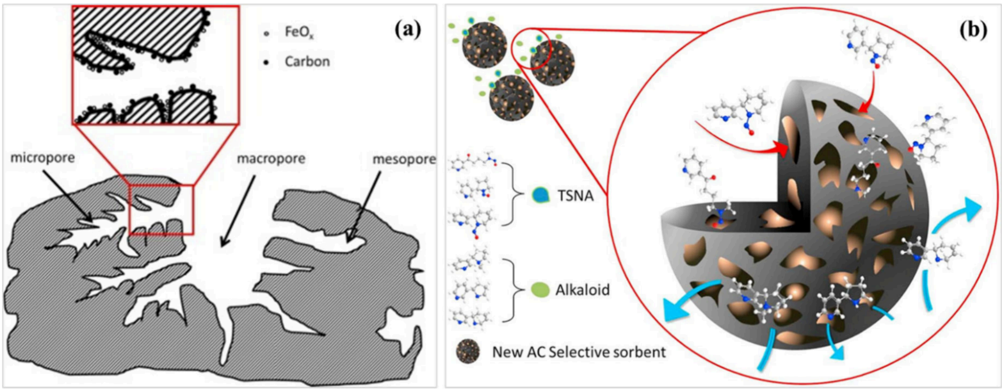

Figure 6. (a) Incorporation of FeOx into the AC pores to promote the adsorption of TSNAs. (b) Coconut shell AC with FeO_x mimicking a zeolite-like structure. Reproduced with permission from ref 89. Copyright 2018 Elsevier.

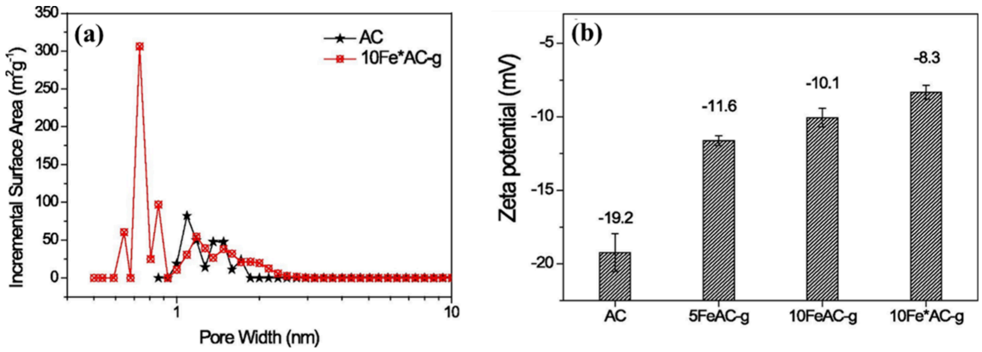

Figure 7. (a) Pore size spread and (b) zeta potential of AC and AC modified with 10% FeO_x (10Fe*AC-g). Reproduced with permission from ref 89. Copyright 2018 Elsevier.

increase their selectivity for TSNAs in solution. The adsorbents were able to remove up to 33.8% of TSNAs and 93% of NNK in tobacco solution containing a variety of compounds. It is clear from the aforementioned references that a lot of work still needs to be done to take advantage of the tunable and filtering properties of carbonaceous materials for the removal of N-nitrosamines in mainstream smoke. It is also noteworthy that a lot of the experiments covered were done in a solution, which is not ideal. Still, it should provide an indication of the affinity of the various materials toward TSNAs. However, a mathematical study performed by Mehdi Yoosefan theorized that single-walled carbon nanotubes loaded with Pd and Ni could potentially have high filtration efficiency for the removal of NNK from tobacco smoke using first-principles calculations.[84]

An experimental version of this work was reported by Sun et al., who explored the selectivity of the structure and surface state of graphene and carbon nanotubes.[85] These two adsorbents were reported to have trapped only 3% of N-nitrosonornicotine in solution. Graphene demonstrated a 6.9% higher adsorption capacity than zeolites (HZSM-5) for the removal of NNK, with a significantly shorter equilibrium time of 5 min compared to 20 min required by the zeolites. The adsorption was due to electrostatic interactions between graphene and TSNA in solution. However, the hydrophobicity of the sp^2 hybridized carbonaceous meant that the affinity of the adsorbents was not sufficient. Similarly, in another study a recyclable graphene aerogel was utilized for the adsorption of NNK in aqueous solution and adsorption mechanism was attributed to cation-π staking interactions. They also reported that a solution pH of up to 8 was conducive for the adsorption of NNK using the graphene aerogel.[86]

Activated carbon (AC) has been widely used for the removal of organic contaminants due to the functional groups in its structure that allow for adsorption, large surface area and robustness.[87] Because of these properties, activated carbon is used as an absorber, depending on the structure of the pollutant. In the tobacco industry, AC was first included in the cigarettes to form an AC filter cigarette in 1954. Unfortunately, the resultant cigarettes had a charcoal flavor, which affected sales effectively.[88] In recent years, commercially available cigarettes have included charcoal as a form of toxins purification.[88] Therefore, AC has gained much traction in research and development toward the adsorption of TSNAs and other toxins from tobacco/cigarettes. The hydrophobic nature of AC, however, compromises its adsorption capability of AC for TSNAs and other nonpolar organic compounds. To improve the adoption capacity and kinetics, researchers have modified AC with metal oxides such as CuO, ZnO, Al_2O_3 and FeO_3.[88]

A study by Shi et al. attempted to afford AC the capacity to adsorb like zeolite selectively for the first time.[89] Activated carbon was made from coconut shells by carefully modifying it with ferric acetate. This was achieved via impregnation of the coconut shell with ferric acetate followed by carbonization, thereby yielding a generous amount of ferric oxide fine particles mixed with carbon nanoparticles that reduced the pore size of the activated carbon and increased the surface roughness of the pore walls (Figure 6a). This meant that the modified AC adsorbent kept its naturally ordered porous structure. In addition, the funnel-like pores were modified to

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have the ideal slender grooves incorporated with metal ions, thus resulting in an environment mimicking that of zeolites without the complications associated with the diffusion and the of N-nitrosamines into the zeolite channels (Figure 6b).[89] The material was shown to selectively capture TSNAs while discriminating against alkaloids.[89]

Effectively, upon exposing the activated carbon to tobacco toxins in the tobacco extract solution of 1796 ng/mL, 60% of TSNAs were adsorbed, resulting in a staggering adsorption capacity of 222 mg/g. Interestingly, the zeolite-like adsorbent showed selectivity and managed to adsorb *ca*. 98% of 4-methylnitrosamino-1,3-pyridyl-1-butanone (NNK) due to the lanky shape of this strong carcinogen (Figure 6b).[89] The concentrations of the TSNAs were analyzed by gas chromatography coupled to a flame ionization detector (FID). The evidence for the formation of the zeolite-like porous structure was determined by measuring the porosity of the modified AC.

Here, it was observed that the virgin AC had a probable large microporous structure of between 11 and 14 Å, whereas that of the modified AC was between 0.73 and 0.86 Å, similar to that of NaY zeolites (Figure 7a).[89] The change in zeta potential of AC modified with 10% FeO_x (10Fe*AC-g) to −8.3 mV from −18.3 mV for the virgin AC was deemed to be important for the adsorption of the negatively charged N-NO functional group present in TSNAs (Figure 7b).[89] This is because TSNAs are conventionally neutral or slightly positively charged molecules. AC, on the other hand, often presents a negative surface charge due to the presence of oxygen-containing functional groups such as carboxylic and phenolic functional groups. This inherent negative charge can lead to electrostatic repulsion between the activated carbon and TSNAs, hindering their adsorption. Therefore, modifying the surface charge of activated carbon to be more neutral or slightly positive can be beneficial for improving TSNA adsorption.

5.2.3. Metal Oxide-Based Cigarette Filters.

In the previous example of carbonaceous nanomaterials being used to reduce the N-nitrosamines, it was clear that carbon nanomaterials alone were inefficient at filtering TSNAs, mainly due to their hydrophobicity. The efficiency of the carbon nanomaterials was often aided by depositing metal and metal oxide nanoparticles. Therefore, it was natural that other scientists investigated metal oxides as active materials for the removal of N-nitrosamines in mainstream cigarette smoke. It is important to note that in the case of metal oxide particles, the mode of removing TSNAs is not adsorption; it is rather a degradation.

A prime example of this kind of work was reported by Deng et al.[90] who synthesized nanostructured titanates in the morphology of sheets, wires and tubes and were used as additives for the reduction of TSNAs.[90] This study followed the recommended methods of quantifying components (TSNAs) in mainstream smoke, refer to Section 3. Briefly, they added the titanates to the tips of the cigarette butts and then smoked them using an ISO-4387 smoking machine where the condensates were trapped on Cambridge filter pads.[90] The samples were analyzed for N-nitrosamines (NNN, NAB, NNK and NAT) concentration using LC-MS/MS. They reported that the titanate nanowires were the most efficient at reducing TSNAs, reporting a 60.84% reduction, followed by titanate nanotubes and titanate nanospheres with a reduction efficiency of 54.87% and 38.93%, respectively.[90] Furthermore, the team explained that because the titanates were synthesized using ion-exchange in hydrochloric acid, the materials were heavily positively charged; thus, they could attract the N-NO functional groups of the N-nitrosamines.[93] The superior efficiency of the titanate nanowires was attributed to their aspect ratio, that their long length ensured prolonged contact of the smoke with the nanowires.[90] Their studies also investigated the selectivity of the titanate additives had toward TSNAs against tar. They found that titanate nanowires were the most selective toward TSNAs over tar by 41%, while nanospheres and nanotubes registered efficiency values of 8.56 and 23.76%.[90] This meant that the titanate nanosphere and titanate nanotubes were also removing tar. The authors made the argument that tar contains aromatics that give cigarettes their characteristic flavor; thus, removing it may be a disadvantage to smokers.[90]

In another study involving the reduction of TSNAs using metal oxides, the same group led by Deng et al. developed microporous titania mesocrystals for the removal of TSNAs via degradation.[91] The team reported a high degradation efficiency of up to 97%, citing the trapping of NNN, NAT and NAB into the pores of the mesocrytals, ensuring prolonged exposure of the TSNAs to the photocatalyst.[91] Cao et al. investigated metal oxides to address the geometric limitations of zeolites and mesoporous silica.[16] A metal oxide layer of copper oxide or alumina was applied on amorphous support to form a functional composite.[16] Nitrosamines can be very easily trapped by the copper-modified zeolite because of their unique interaction with the N—N═O group of nitrosamines; this occurs prior to or as the initial step in the catalytic reaction.

Furthermore, this study showed that altering the copper oxide allowed the enzyme to break down the nitrogen compound NPYR at lower temperatures.[16] Results of coating alumina on silica on in situ IR spectra showed that the strength of the distinctive bands increased together with the amount of alumina coated on the silica, demonstrating the favorable effect of alumina on the adsorption of volatile nitrosamines in silica. This was explained to be because the N—N═O functional group of volatile nitrosamines has a negative charge, that the tervalent aluminum ion may have an attraction function for it to promote the adsorption steaming from results of more than 80% trapping of NNN by different types of silica which were more than that of the parent silica.[95] These two studies conclude that the coating of copper oxide and alumina greatly increases the selective adsorption and catalytic degradation of volatile nitrosamines, which helps remove nitrosamines from cigarette smoke. More on the roles of zeolites and silica in the reduction of N-nitrosamines will follow in the subsequent sections. However, it is evident that metal oxides make these kinds of materials better.

5.2.4. Zeolites and Other Silicate-Based Cigarette Filters.

Zeolites are aluminosilicates with group alkali and alkaline earth metals as counterions. The network that composes their structure consists of silicates and aluminates arranged in a tetrahedral geometry.[15,92] The two are connected via the corners of a tetrahedron, linked through an oxygen atom. The resulting 3-D structure with cavities and voids is responsible for the most desirable characteristics of zeolites and, thereby, their application.[15] Some of the most common applications of zeolites include catalysis, adsorbents, and support materials. These properties and applications are exactly what scientists are looking for when designing materials for the removal of TSNAs from cigarette smoke.

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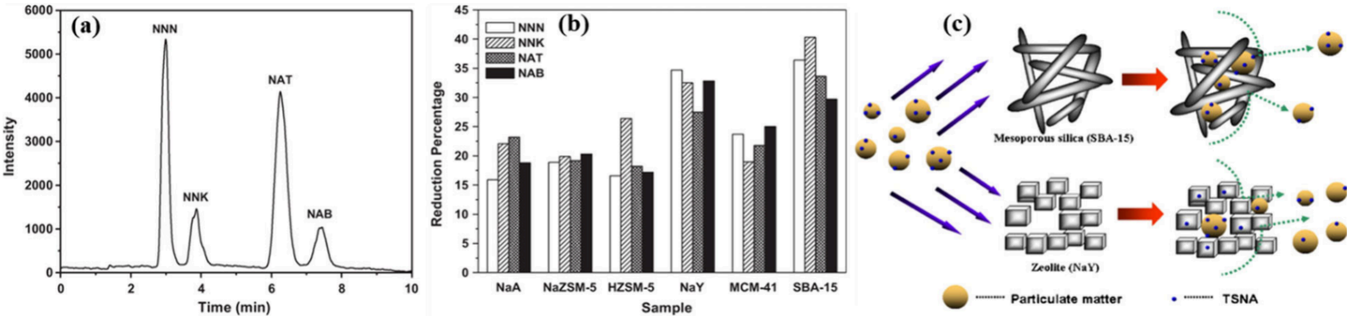

Figure 8. (a) LC chromatogram of TSNAs without additives, (b) reduction percentage of TSNAs with different additives, and (c) probable TSNA reduction mechanism by NaY and SBA-15. Reproduced with permission from ref 15. Copyright 2013 Elsevier.

Lin et al. provided one such example of the application of zeolites and mesoporous silica in the removal of TSNAs in cigarette smoke.[15] This team took an interesting approach when incorporating these materials; they included them in the cigarette rod instead of the filtering butt. The team tested a series of zeolites, including NaA, NaZSM-5, NaY, HZSM-5, mesoporous silica MCM-41 and SBA-15.[98] This was done to investigate the influence of the materials' pore size, the concentration of Al, morphological properties, and acidity/alkalinity on the reduction of N-nitrosamines in mainstream cigarette smoke. The team used the SM450 smoking machine (Borgwaldt) under ISO standard conditions to generate smoke, and the samples were analyzed for NNN, NNK, NAT and NAB content using LC-MS/MS (Figure 8a). They reported that the zeolites and mesoporous reduced the TSNAs in the hot zone after they had been vaporised, measuring up to 35% reduction in TSNA concentration, with SBA-15 reducing the largest concentration of TSNAs (Figure 8b and Table 3).[15]

Table 3. Summation of the Removal of TSNAs Using Zeolites and Mesoporous Silica

Material	TSNAs	Reduction %	Adsorption mechanism	Refs.
NaA	Total TSNAs	19.8	Gas to solid	15
NaZSM-5	- NNN	19.2		
NaY	- NNK	31.3		
HZSM-5	- NAT	18.32		
MCM-41	- NAB	22.4		
SBA-15		35.4		

The observed superiority of SBA-15 and the somewhat modest efficiency of MCM-41 was attributed to the low framework density; thus, they could easily be distributed along the cigarette rod resulting in the fiber-like morphology of the materials easily intercepting the TSNAs in cigarette smoke. They referred to this method of TSNAs removal by low-density materials as straw spreading.[15] Furthermore, they reported that the mesoporous SiO_2 additives mainly filtered the particulates in smoke to remove N-nitrosamines, while zeolite-based additives removed significantly higher levels of total particulate matter at the expense of removing TSNAs (Figure 8c).

In other studies, for instance, the one by Zhu et al. evaluated the use of zeolite for N-nitrosamines adsorption in aqueous solutions.[22] In their study, three commonly used zeolites, NaY, ZSM-5 and NaA, were evaluated for the removal of NDMA, NPYR and N-nitrosohexamethylenimine (NHM) from methylene chloride or aqueous solution at high concentrations. Their findings confirmed that zeolites can effectively remove nitrosamines from aqueous solutions, along with the influence of the adsorbent structure involving surface area on adsorption capacities and equilibrium isotherms. Among the used adsorbents, the NaY zeolite exhibited the highest sorption capacity for all the N-nitrosamines, which increased with increasing adsorbate concentrations. Sun et al. attempted to control TSNAs pollution caused by smoking through liquid adsorption of TSNA in tobacco-extract solution using zeolites and other porous materials.[93] They modified zeolite by impregnating it with ZnAC, which effectively adsorbed 73% of TSNA; Similarly, they modified Zeolite with Za to afford Zeolite CaA, which again was efficient in removing more than 40% of TSNAs.

There is a lot of potential in the use of zeolites and other silicates to modify existing cigarette filters for the removal of TSNAs. The potential stems from the high porosity of the materials, which allows them to capture TSNAs in their pores. In addition, their tunable porosity and surface chemistry, particularly, surface charge, is important for the selective adsorption of TSNAs from mainstream cigarette smoke. There is also a potential for catalytic decomposition of TSNAs into less harmful products. However, issues such as cost and scalability and regeneration, has prompted scientists to investigate other types of materials. The following section delves into other unorthodox and innovative materials that could be used to save lives by reducing TSNAs from mainstream cigarette smoke.

5.2.5. Miscellaneous Materials for Filtering TSNAs from Cigarette Smoke. In recent history, several newish materials have gotten a lot of attention for their adsorption properties. In this regard, it is not easy to look beyond a few-layers of black phosphorus,[74,94−97] metal−organic frameworks,[98−101] and molecularly imprinted polymers.[102−104]

5.2.5.1. Few-Layer Black Phosphorus. To the best of our knowledge, there are no reports in the literature that describe the use of a few-layers of black phosphorus for the removal of TSNAs. These materials are mentioned in this review because they have properties, such as high surface area, tunable thickness and spacing between their layers, suitable for this purpose. All these properties make for an excellent adsorbent.[95,105,116] Two main factors hamper its widespread use. The first disadvantage of this material is that (when exfoliated into a few-layers) it is not stable in ambient conditions as oxygen in the air easily reacts with it, damaging its crystal structure.[95,106] However, with advancements in synthetic methods and strategies for stabilizing a few-layers black phosphorus, widespread use of this material, including in the removal of TSNAs in mainstream cigarette smoke, is imminent. An example of efforts that have been made to stabilize a few-layers black phosphorus was reported by Ryder et al., who proposed covalently functionalizing a few-layers black phosphorus with 4-nitrobenzene-diazonium and 4-methoxybenzenediazonium tetrafluoroborate salts.[107] The team observed a stable morphology of the modified few-layers black phosphorus in more than 10 days, citing the introduction of the covalently bound aryl-phosphorus, which effectively rendered the few-layers black phosphorus inactive toward oxygen and moisture in the environment.[107]

Improvements on the instability of few-layers black phosphorus in ambient conditions, the challenges associated with its synthesis and processing hamper the widespread use of this very promising material. In addition, there are concerns with the toxicity of few-layers black phosphorus as its degradation products whose long-term health effects are not fully understood. Therefore, safer, and more viable materials are sought after.

5.2.5.2. Molecularly Imprinted Polymers. In the case of molecularly imprinted polymers (MIPs), which are synthetic molecules that can be made to specification of the targeted molecule to be adsorbed or classes of structurally related compounds.[108−111] This definition immediately shows how MIPs could be ideal for modifying the cellulose acetate-based filters for the removal of TSNAs, i.e., polymers can be imprinted with TSNAs templates and incorporated into the existing cigarette butts.

One such example was reported by Li et al., who synthesized MIPs by grafting nicotinamide as a template onto the surface SiO_2 gel to yield MIP@SiO_2, which was used as an additive to cellulose acetate cigarette butts for the adsorption of TSNAs in mainstream cigarette smoke (Figure 9).[111] A Cerulean SM450 smoking machine was used to generate cigarette smoke, and the mainstream smoke was collected using Cambridge filter pads, and the TSNAs were analyzed by LC-MS/MS.[117] They found that both cigarettes that were smoked using filters with the MIP@SiO_2 additives had reduced TSNAs levels when compared to those that were smoked without any additive and those smoked with silica additives.[111] In addition, they observed no discernible change in the amount of total particulate matter in mainstream smoke generated with filters modified with MIP@SiO_2 (15.37 mg/cig) when compared to cigarettes smoked without additives (15.92 mg/cig) and those smoked with SiO_2 as an additive (12.37 mg/cig).[111] This meant that the MIP@SiO_2 additive reduced the carcinogenic TSNAs without changing the cigarette flavor.

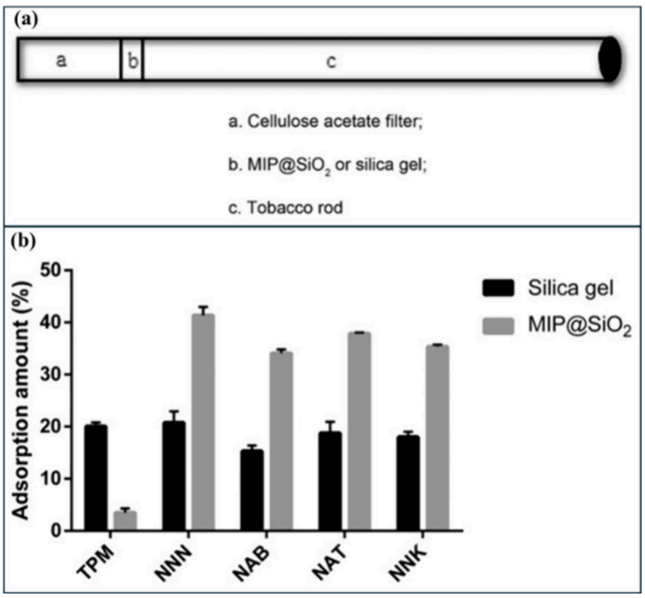

Figure 9. (a) Schematic of the cigarette with the additives and (b) concentration of the TSNAs and total particulate matter removed from the mainstream smoke. Reproduced with permission from ref 111. Copyright 2015 John Wiley and Sons.

Similarly, in a study by Zheng et al., they reported unique hollow MIPS microspheres imprinted with nicotinamide that used the two-stage dispersion polymerization and swelling seed polymerization method.[112] The adsorption experiments were done in solution, and they demonstrated an increased mass transfer rate and an adsorption capacity of 1.7 mg/g, thrice that of experiments conducted with nonimprinted hollow polymers.[112]

The evidence suggests that these MIP materials could be useful in lowering TSNAs in mainstream smoke. Their widespread use could be mainly affected by the fact that they are still emerging, and not much research has been done on incorporating them in the modification of cigarette filters. Furthermore, their synthesis is a little complicated as it is hampered by low yields and diminished binding sites due to the damage caused by grinding, along with the struggle of etching out the template from the interior part of the MIP particles.[113]

5.2.5.3. Metal−Organic Frameworks. Metal−organic frameworks (MOFs) are another class of emerging materials that have the potential to revolutionize separation science. MOFs, or porous coordination polymers (PCPs), are a class of emerging porous materials made from nodes containing metals linked by organic linkers.[114,115] They are formed through the self-assembly of their building units, organic ligands and metal ions, to form highly crystalline and periodic 3D network structures.[122]

MOFs have several advantageous characteristics, including adjustable pore size, large surface area, flexibility in pore size and skeletal structure, high porosity, and tunable pore surface functional groups with unsaturated metal coordination sites.[116−120] Additionally, MOFs have high adsorption capacities for different toxic pollutants, such as organic pollutants and toxic gases.[22,69,116] To the best of our knowledge, there is limited reporting on the use of MOFs to aid the removal of TSNAs from cigarette smoke, despite the exciting properties of MOFs, mainly their porosity, tuneability and adsorption properties.[117,118] Zhu et al. reported for the first time on the removal of TSNAs in aqueous solutions using ZIF-8.[119] Adsorption mechanism occurred through cation-π staking interactions between the pyridine rings of the TSNAs and imidazole rings of the adsorbent, rather than the expected geometric confinement effect. In addition, ZIF-8 promoted synergistic adsorption between TSNA compounds, where the presence of NNK enhanced the adsorption of NNN. A study by Wan et al. demonstrated the potential of modifying cellulose acetate with MOFs for filtering mainstream cigarette smoke.[120] It is important to note that this study focused on the removal of nicotine, which is outside the scope of this review, but it demonstrates the use of MOFs in filtering mainstream cigarette smoke. The study entailed modifying cellulose fibers with six types of MOFs that varied in porosity and particle size.

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They observed that all the cellulose filters modified with different MOFs were better adsorbents for nicotine than the virgin cellulose filter, as was measured by GC and the color of the solutions (Figures 10a and b).[120]

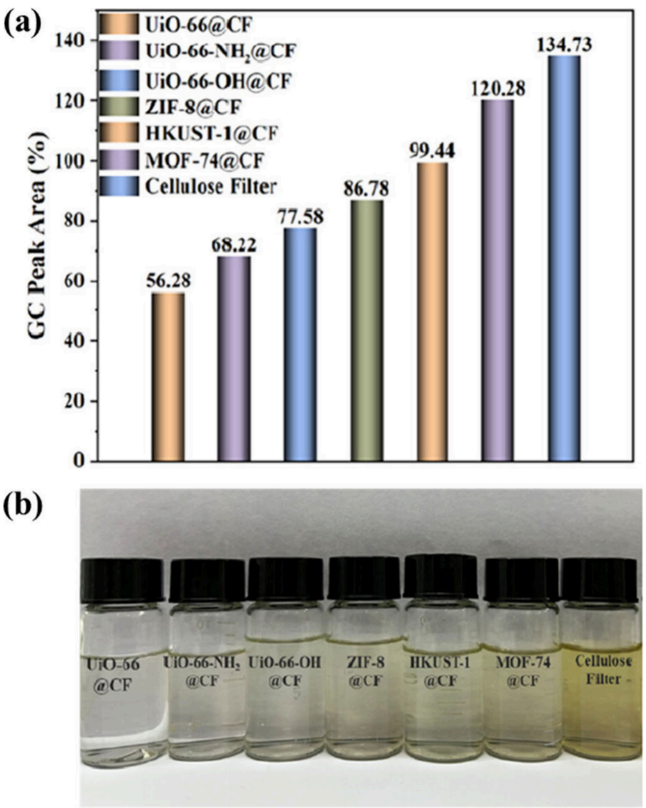

Figure 10. (a) Gas chromatography peak areas and (b) solution color of unadsorbed nicotine after adsorption experiments using cellulose filter modified with various MOFs. Reproduced from ref 120. Copyright 2023 American Chemical Society.

These examples demonstrate that MOFs can be fine-tuned to target certain chemicals, including TSNAs in cigarette smoke. The limited use of MOFs for the removal of specifically TSNAs in mainstream cigarette smoke could be attributed to several reasons: MOFs are new and emerging materials, there are concerns with their cost, scalability, and their regeneration. However, like it was the case with graphitic carbon nitride, advancements in synthetic procedures and the use of waste materials to synthesize MOFs, as was demonstrated by Dyosiba et al., can go a long way toward addressing the aforementioned reservations.[121]

5.2.5.4. Porous Organic Polymers. Porous organic polymers (POPs) are organic macromolecules that have gained popularity as emerging materials for a wide range of applications including adsorption and catalysis. This is attributed to their high specific surface areas, tunable porosities, lightweight, high thermal and chemical stabilities, modifiable compositions, convenient postfunctionalization, and hydrophobicity/hydrophilic characteristics.[122,123] Thus, making them plausible material for the adsorption of toxic compounds found in mainstream cigarette smoke. Lu et al. developed a reusable porous organic polymer with a nitrosamine receptor for the adsorption of TSNAs in both aqueous solutions and tobacco extracts.[124] They determined that the addition of the tungsten-calix[4]arene imido complex nitrosamine receptor led to increased adsorption selectivity for NNK over nicotine, where a 203 mg/g adsorption capacity was obtained for NNK. Zhang et al. in their study utilized covalent organic frameworks (COFs) functionalized with nanotitania for the adsorption of N-nitrosamines in drinking water.[125] There determined that they could synthesis the COF to have different structural arrangements, including single roll-up, double roll-up and clover shaped by increasing the adsorbent synthesis reaction time. Results showed that the clover-shaped COF had the highest adsorption efficiency for N-nitrosamines, where they proposed that adsorption mechanisms occurred through hydrogen bonding interactions, hydrophobic/hydrophilic interactions. Although POPs are promising materials in both catalysis and adsorption they have several drawbacks that hinder their widespread application. Namely, their synthesis requires large volumes of solvent, the use of metal catalysts and cumbersome postfunctionalization procedures leading to high costs.[126]

6. CONCLUSIONS AND FUTURE PERSPECTIVES

In this review, we have highlighted the existing literature on the dangers of cigarette smoking to human health. The health risks of consuming tobacco through smoking are directly linked to the thousands of chemicals found in cigarette smoke. Among these, tobacco-specific nitrosamines (TSNAs) stand out as some of the most dangerous, with several identified as carcinogenic. This has alerted stakeholders, including regulators, scientists, and governments, to the urgent need for interventions to protect the public from the harmful effects of cigarette smoke. Consequently, significant research efforts have been directed toward quantifying and qualifying the components of cigarette smoke, revealing issues such as the artifactual formation of nitrosamines during sampling.

Given the life-threatening nature of these toxins, regulations and standardized methods have been established to study cigarette smoke composition in a reproducible manner, exemplified by the Standard ISO smoking regime machine. This tool has been pivotal for smoke sampling applications, particularly for mainstream cigarette smoke. Analytical techniques, notably chromatographic methods, continue to improve alongside advancements in technology, enabling more precise measurements.

Current research in this field is largely focused on reducing toxins in mainstream smoke, including TSNAs, through filtration strategies. Various materials, such as zeolites, silica, carbonaceous materials, and metal oxides, have been investigated for this purpose. These materials exhibit desirable characteristics, including high porosity and surface area, making them potential additives or modifying agents for cigarette filters. While promising results demonstrate varying degrees of TSNA filtration efficiency, much work remains to be done to optimize and scale these solutions. Researchers must continue exploring advanced materials that offer high adsorption capacities and excellent selectivity at low costs to mitigate the harmful effects of cigarette smoke on human health.

However, even with these advancements, significant challenges remain in creating materials that can effectively reduce harmful compounds in cigarette smoke without detracting from the smoking experience. Most in the tobacco control community agree that eliminating tobacco-related deaths and diseases should be the ultimate goal. Achieving this requires a unified and cohesive approach to harm reduction

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strategies, addressing not only TSNAs but also other toxicants, such as polycyclic aromatic hydrocarbons (PAHs) and volatile organic compounds (VOCs). A strategic dialogue focusing on the evolving science, identifying research gaps, and fostering consensus on effective harm reduction approaches is urgently needed.

A critical component of achieving these goals lies in standardizing data collection and reporting. While standardized analytical techniques provide a foundation, true standardization requires that all scientists report data in a uniform manner, facilitating direct comparison of results across studies. Currently, the literature reflects diverse methods for measuring the removal of TSNAs from mainstream cigarette smoke, resulting in inconsistencies and reduced comparability. Establishing clear guidelines for reporting metrics such as reduction percentages, adsorption capacities, equilibrium times, and detection limits, alongside uniform experimental conditions, will enhance the reproducibility and utility of research findings. Collaborative efforts among researchers, regulators, and industry stakeholders are essential to achieve this level of standardization.

Ultimately, the findings and strategies discussed in this review represent foundational steps toward reducing the morbidity and mortality caused by tobacco smoking. Advancing the development of selective materials capable of targeting carcinogenic compounds while minimizing nicotine uptake offers an important pathway to harm reduction. Such efforts are expected to complement current prevention and treatment strategies, alleviating the public health burden and fostering broader societal and economic benefits.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) WHO report on the global tobacco epidemic, 2013: enforcing bans on tobacco advertising, promotion and sponsorship; World Health Organization: Geneva, Switzerland. Available online: http://www.who.int/tobacco/en/ (Accessed on July 11, 2013).

(2) Tobacco Free Ireland Programme 2013. Available online: https://www.hse.ie/eng/about/who/tobaccocontrol/ (Accessed on July 11, 2013).

(3) Mozafarinia, R.; Assarian, M.; Ziaaddini, A. Prevalence of Substance Abuse among Students of Tehran University of Medical Sciences, Iran. *Addict. Health* **2017**, *9*, 103−109.

(4) Ng, M.; Freeman, M. K.; Fleming, T. D.; Robinson, M.; Dwyer-Lindgren, L.; Thomson, B.; Wollum, A.; Sanman, E.; Wulf, S.; Lopez, A. D.; Murray, C. J. L.; Gakidou, E. Smoking Prevalence and Cigarette Consumption in 187 Countries, 1980−2012. *JAMA* **2014**, *311*, 183−92.

(5) Brunnemann, K. D.; Yu, L.; Hoffmann, D. Assessment of Carcinogenic Volatile N-Nitrosamines in Tobacco and in Mainstream and Sidestream Smoke from Cigarettes. *Cancer Res.* **1977**, *37*, 3218−22.

(6) Rodgman, A.; Green, C. Toxic Chemicals in Cigarette Mainstream Smoke - Hazard and Hoopla. *Beiträge zur Tabakforschung International/Contributions to Tobacco Research* **2003**, *20*, 481−545.

(7) Rodgman, A.; Perfetti, T. A. *The Chemical Components of Tobacco and Tobacco Smoke*, 1st ed.; CRC Press Taylor & Francis Group: Boca Raton, FL, 2008; p 1840.

(8) Beauval, N.; Antherieu, S.; Soyez, M.; Gengler, N.; Grova, N.; Howsam, M.; Hardy, E. M.; Fischer, M.; Appenzeller, B. M. R.; Goossens, J. F.; Allorge, D.; Garçon, G.; Lo-Guidice, J.-M.; Garat, A. Chemical Evaluation of Electronic Cigarettes: Multicomponent Analysis of Liquid Refills and Their Corresponding Aerosols. *J. Anal. Toxicol.* **2017**, *41*, 670−678.

(9) Yershova, K.; Yuan, J. M.; Wang, R.; Valentin, L.; Watson, C.; Gao, Y. T.; Hecht, S. S.; Stepanov, I. Tobacco-Specific N-Nitrosamines and Polycyclic Aromatic Hydrocarbons in Cigarettes Smoked by the Participants of the Shanghai Cohort Study. *Int. J. Cancer* **2016**, *139*, 1261−1269.

(10) Xu, Y.; Jiang, Q.; Cao, Y.; Wei, Y. L.; Yun, Z. Y.; Xu, J. H.; Wang, Y.; Zhou, C. F.; Shi, L. Y.; Zhu, J. H. The Synthesis of Novel Porous Functional Materials for Use as Nitrosamine Traps. *Adv. Funct. Mater.* **2004**, *14*, 1113−1123.

(11) Xu, Y.; Zhu, J. H.; Ma, L. L.; Ji, A.; Wei, Y. L.; Shang, X. Y. Removing Nitrosamines from Mainstream Smoke of Cigarettes by Zeolites. *Micropor. Mesopor. Mater.* **2003**, *60*, 125−138.

(12) Edwards, S. H.; Rossiter, L. M.; Taylor, K. M.; Holman, M. R.; Zhang, L.; Ding, Y. S.; Watson, C. H. Tobacco-Specific Nitrosamines in the Tobacco and Mainstream Smoke of U.S. Commercial Cigarettes. *Chem. Res. Toxicol.* **2017**, *30*, 540−551.

(13) Zhou, J.; Bai, R.; Zhu, Y. Determination of Four Tobacco-Specific Nitrosamines in Mainstream Cigarette Smoke by Gas Chromatography/Ion Trap Mass Spectrometry. *Rapid Commun. Mass Spectrom.* **2007**, *21*, 4086−4092.

(14) Wu, M. J.; Dai, Y. H.; Tuo, S. X.; Hu, N. N.; Li, Y.; Chen, X. M. Analysis of Four Tobacco-Specific Nitrosamines in Mainstream Cigarette Smoke of Virginia Cigarettes by LC-MS/MS. *J. Cent. South Univ. Technol. (Engl. Ed.)* **2008**, *15*, 627−631.

(15) Lin, W. G.; Zhou, Y.; Cao, Y.; Zhou, S. L.; Wan, M. M.; Wang, Y.; Zhu, J. H. Applying Heterogeneous Catalysis to Health Care: In Situ Elimination of Tobacco-Specific Nitrosamines (TSNAs) in Smoke by Molecular Sieves. *Catal. Today* **2013**, *212*, 52−61.

(16) Cao, Y.; Shi, L. Y.; Zhou, C. F.; Yun, Z. Y.; Wang, Y.; Zhu, J. H. Novel Amorphous Functional Materials for Trapping Nitrosamines. *Environ. Sci. Technol.* **2005**, *39*, 7254−9.

(17) Li, Y. Y.; Cao, Y.; Yue, M. B.; Yang, J.; Zhu, J. H. Hierarchical Composites to Reduce N-Nitrosamines in Cigarette Smoke. *Materials* **2015**, *8*, 1325−1340.

(18) Zhou, C. F.; Cao, Y.; Zhuang, T. T.; Huang, W.; Zhu, J. H. Capturing Volatile Nitrosamines in Gas Stream by Zeolites: Why and How. *J. Phys. Chem. C* **2007**, *111*, 4347−4357.

(19) Gu, F. N.; Zhuang, T. T.; Cao, Y.; Zhou, C. F.; Zhu, J. H. Effect of Copper Cation on the Adsorption of Nitrosamines in Zeolite. *Solid State Sci.* **2008**, *10*, 1658−1665.

(20) Hoffmann, D.; Adams, J. D.; Brunnemann, K. D. A Critical Look at N-Nitrosamines in Environmental Tobacco Smoke. *Toxicol. Lett.* **1987**, *35*, 1−8.

(21) Zeng, T.; Liu, Y.; Jiang, Y.; Zhang, L.; Zhang, Y.; Zhao, L.; Jiang, X.; Zhang, Q. Advanced Materials Design for Adsorption of Toxic Substances in Cigarette Smoke. *Adv. Sci.* **2023**, *10*, 2301834.

(22) Zhu, J. H.; Yan, D.; Rong Xai, J.; Ma, L. L.; Shen, B. Attempt to Adsorb N-Nitrosamines in Solution by Use of Zeolites. *Chemosphere* **2001**, *44*, 949−56.

(23) Yang, J. Y.; Yang, J.; Zhou, Y.; Lin, W. G.; Wang, H. J.; Zhu, J. H. Effective Nitrosamines Trap Derived from the in Situ Carbonized Mesoporous Silica MCM-41. *J. Hazard. Mater.* **2010**, *176*, 602−608.

(24) Prokopczyk, B.; Hoffmann, D.; Cox, J. E.; Djordjevic, M. V.; Brunnemann, K. D. Supercritical Fluid Extraction in the Determination of Tobacco-Specific N-Nitrosamines in Smokeless Tobacco. *Chem. Res. Toxicol.* **1992**, *5*, 336−340.

(25) Wright, C. Standardized Methods for the Regulation of Cigarette-Smoke Constituents. *TrAC - Trend Anal. Chem.* **2015**, *66*, 118−127.

(26) Shah, K. A.; Karnes, H. T. A review of the analysis of tobacco-specific nitrosamines in biological matrices. *Crit. Rev. Toxicol.* **2010**, *40*, 305−327.

(27) Hecht, S. S.; Hatsukami, D. K. Smokeless tobacco and cigarette smoking: chemical mechanisms and cancer prevention. *Nat. Rev. Cancer* **2022**, *22*, 143−155.

(28) Gupta, A. K.; Nethan, S. T.; Mehrotra, R. Tobacco use as a well-recognized cause of severe COVID-19 manifestations. *Respir. Med.* **2021**, *176*, 106233.

(29) Konstantinou, E.; Fotopoulou, F.; Drosos, A.; Dimakopoulou, N.; Zagoriti, Z.; Niarchos, A.; Makrynioti, D.; Kouretas, D.; Lagoumintzis, G.; Poulas, K. Tobacco-Specific Nitrosamines: A Literature Review. *Food Chem. Toxicol.* **2018**, *118*, 198−203.

(30) Li, Y. Y.; Wan, M. M.; Zhu, J. H. Cleaning carcinogenic nitrosamines with zeolites. *Environ. Chem. Lett.* **2014**, *12*, 139−152.

(31) Huang, H. Y.; Hsieh, S. H. Analyses of Tobacco Alkaloids by Cation-Selective Exhaustive Injection Sweeping Microemulsion Electrokinetic Chromatography. *J. Chromatogr. A* **2007**, *1164*, 313−319.

(32) Mahanama, K. R. R.; Daisey, J. M. Volatile N-Nitrosamines in Environmental Tobacco Smoke: Sampling, Analysis, Emission Factors, and Indoor Air Exposures. *Environ. Sci. Technol.* **1996**, *30*, 1477−1484.

(33) Veena, S.; Rashmi, S. A Review on Mechanism of Nitrosamine Formation, Metabolism and Toxicity in in Vivo. *Int. J. Toxicol. Pharmacol. Res.* **2014**, *6*, 86−96.

(34) Li, G.; Saad, S.; Oliver, B. G.; Chen, H. Heat or Burn? Impacts of Intrauterine Tobacco Smoke and E-Cigarette Vapor Exposure on the Offspring's Health Outcome. *Toxics* **2018**, *6*, 43−64.

(35) Kim, H. J.; Shin, H. S. Determination of tobacco-specific nitrosamines in replacement liquids of electronic cigarettes by liquid chromatography-tandem mass spectrometry. *J. Chromatogr. A* **2013**, *1291*, 48−55.

(36) Nair, J.; Pakhale, S. S.; Bhide, S. V. Carcinogenic Tobacco-Specific Nitrosamines in Indian Tobacco Products. *Food Chem. Toxicol.* **1989**, *27*, 751−753.

(37) Hecht, S. S. It Is Time to Regulate Carcinogenic Tobacco-Specific Nitrosamines in Cigarette Tobacco. *Cancer Prev Res.* **2014**, *7*, 639−647.

(38) Jain, V.; Alcheva, A.; Huang, D.; Caruso, R.; Jain, A.; Lay, M.; O'Connor, R.; Stepanov, I. Comprehensive Chemical Characterization of Natural American Spirit Cigarettes. *Tob Regul Sci.* **2019**, *5*, 381−399.

(39) Intorp, M.; Purkis, S. W.; Wagstaff, W. Determination of Selected Volatiles in Cigarette Mainstream Smoke. The CORESTA 2009 Collaborative Study and Recommended Method. *Beitrage zur Tabakforschung International/ Contributions to Tobacco Research* **2011**, *24*, 243−251.

(40) Borgerding, M.; Klus, H. Analysis of Complex Mixtures - Cigarette Smoke. *Exp. Toxicol. Pathol.* **2005**, *57*, 43−73.

(41) Caldwell, W. S.; Conner, J. M. Artifact Formation During Smoke Trapping: An Improved Method for Determination of IV-Nitrosamines in Cigarette Smoke. *J. Assoc. Off. Anal. Chem.* **1990**, *73*, 783−789.

(42) Mirvish, S. S.; Wallcave, L.; Eagen, M.; Shubik, P. Ascorbate-Nitrite Reaction: Possible Means of Blocking the Formation of Carcinogenic N-Nitroso Compounds. *Science* **1972**, *177*, 65−68.

(43) Piadé, J. J.; Wajrock, S.; Jaccard, G.; Janeke, G. Formation of Mainstream Cigarette Smoke Constituents Prioritized by the World Health Organization - Yield Patterns Observed in Market Surveys, Clustering and Inverse Correlations. *Food Chem. Toxicol.* **2013**, *55*, 329−347.

(44) Wu, W.; Ashley, D. L.; Watson, C. H. Simultaneous Determination of Five Tobacco-Specific Nitrosamines in Mainstream Cigarette Smoke by Isotope Dilution Liquid Chromatography/ Electrospray Ionization Tandem Mass Spectrometry. *Anal. Chem.* **2003**, *75*, 4827−4832.

(45) Cucco, J. A.; Brown, P. R. Confirming the Presence of N-Nitrosamines in Ambient Air and Cigarette Smoke by Converting to and Photochemically Altering Their Corresponding n-Nitroamines. *J. Chromatogr. A* **1981**, *213*, 253−263.

(46) Sleiman, M.; Maddalena, R. L.; Gundel, L. A.; Destaillats, H. Rapid and Sensitive Gas Chromatography-Ion-Trap Tandem Mass Spectrometry Method for the Determination of Tobacco-Specific N-Nitrosamines in Secondhand Smoke. *J. Chromatogr. A* **2009**, *1216*, 7899−7905.

(47) Cooke, M. The Chemical Components of Tobacco and Tobacco Smoke. *Chroma.* **2010**, *71*, 977.

(48) Miyake, T.; Shibamoto, T. Quantitative Analysis by Gas Chromatography of Volatile Carbonyl Compounds in Cigarette Smoke. *J. Chromatogr. A* **1995**, *693*, 376−381.
(49) Xu, Y.; Liu, H. D.; Zhu, J. H.; Yun, Z. Y.; Xu, J. H.; Cao, Y.; Wei, Y. L. Removal of Volatile Nitrosamines with Copper Modified Zeolites. *New J. Chem.* **2004**, *28*, 244−252.
(50) Gao, L.; Cao, Y.; Zhou, S. L.; Zhuang, T. T.; Wang, Y.; Zhu, J. H. Eliminating Carcinogenic Pollutants in Environment: Reducing the Tobacco Specific Nitrosamines Level of Smoke by Zeolite-like Calcosilicate. *J. Hazard. Mater.* **2009**, *169*, 1034−1039.
(51) Saltzman, B. E. Colorimetric Microdetermination of Nitrogen Dioxide in Atmosphere. *Anal. Chem.* **1954**, *26*, 1949−1955.
(52) Zhang, J.; Bai, R.; Yi, X.; Yang, Z.; Liu, X.; Zhou, J.; Liang, W. Fully Automated Analysis of Four Tobacco-Specific N-Nitrosamines in Mainstream Cigarette Smoke Using Two-Dimensional Online Solid Phase Extraction Combined with Liquid Chromatography-Tandem Mass Spectrometry. *Talanta* **2016**, *146*, 216−224.
(53) Dittrich, D. J.; Fieblekorn, R. T.; Bevan, M. J.; Rushforth, D.; Murphy, J. J.; Ashley, M.; McAdam, K. G.; Liu, C.; Proctor, C. J. Approaches for the Design of Reduced Toxicant Emission Cigarettes. *Springerplus* **2014**, *3*, 1−23.
(54) Saha, S. P.; Bhalla, D. K.; Whayne, T. F.; Gairola, C. G. Cigarette Smoke and Adverse Health Effects: An Overview of Research Trends and Future Needs. *Int. J. Angiol.* **2007**, *16*, 77−83.
(55) Rodu, B.; Jansson, C. Smokeless Tobacco and Oral Cancer: A Review of the Risks and Determinants. *Crit. Rev. Oral Bio. Med.* **2004**, *15*, 252−263.
(56) Ramírez, N.; Özel, M. Z.; Lewis, A. C.; Marcé, R. M.; Borrull, F.; Hamilton, J. F. Exposure to Nitrosamines in Thirdhand Tobacco Smoke Increases Cancer Risk in Non-Smokers. *Environ. Int.* **2014**, *71*, 139−147.
(57) Sarlak, S.; Lalou, C.; Amoedo, N. D.; Rossignol, R. Metabolic Reprogramming by Tobacco-Specific Nitrosamines (TSNAs) in Cancer. *Semin. Cell Dev. Biol.* **2020**, *98*, 154−166.
(58) Branton, P. J.; McAdam, K. G.; Winter, D. B.; Liu, C.; Duke, M. G.; Proctor, C. J. Reduction of Aldehydes and Hydrogen Cyanide Yields in Mainstream Cigarette Smoke Using an Amine Functionalised Ion Exchange Resin. *Chem. Cent. J.* **2011**, *5*, 15−29.
(59) Gupta, P. C.; Murti, P. R.; Bhonsle, R. B. Epidemiology of Cancer by Tobacco Products and the Significance of TSNA. *Crit Rev. Toxicol.* **1996**, *26*, 183−198.
(60) Fu, Z.; Zhou, S.; Xia, L.; Mao, Y.; Zhu, L.; Cheng, Y.; Wang, A.; Zhang, C.; Xu, W. Juncus Effusus Fiber-Based Cellulose Cigarette Filter with 3D Hierarchically Porous Structure for Removal of PAHs from Mainstream Smoke. *Carbohydr. Polym.* **2020**, *241*, 116308.
(61) Gallucci, G.; Tartarone, A.; Lerose, R.; Lalinga, A. V.; Capobianco, A. M. Cardiovascular Risk of Smoking and Benefits of Smoking Cessation. *J. Thorac Dis.* **2020**, *12*, 3866−3876.
(62) Trofor, A. C.; Papadakis, S.; Lotrean, L. M.; Radu-Loghin, C.; Eremia, M.; Mihaltan, F.; Driezen, P.; Kyriakos, C. N.; Mons, U.; Demjén, T.; Nogueira, S. O.; Fernández, E.; Tountas, Y.; Przewoźniak, K.; McNeill, A.; Fong, G. T.; Vardavas, C. I. Knowledge of the Health Risks of Smoking and Impact of Cigarette Warning Labels among Tobacco Users in Six European Countries: Findings from the EUREST-PLUS ITC Europe Surveys. *Tob. Induc. Dis.* **2018**, *16*, 1−13.
(63) Afroz, F.; Mahmud, R. U.; Islam, R. Green Approach to Recover the Cellulose Acetate Fiber from Used Cigarette Butts, and Characterize the Filter Fiber. *AATCC J. Res.* **2023**, *10*, 311−320.
(64) Pandey, S. K.; Vishwakarma, P. K.; Yadav, S. K.; Shukla, P.; Srivastava, A. Multiwalled Carbon Nanotube Filters for Toxin Removal from Cigarette Smoke. *ACS Appl. Nano Mater.* **2020**, *3*, 760−771.
(65) Zeng, J.; Wang, T.; Cheng, Z.; Liu, L.; Hu, F. Ultrahigh Adsorption of Toxic Substances from Cigarette Smoke Using Nanocellulose-SiO_2Hybrid Aerogels. *ACS Appl. Polym. Mater.* **2022**, *4*, 1173−1182.
(66) Seow, Y. X.; Tan, Y. H.; Mubarak, N. M.; Kansedo, J.; Khalid, M.; Ibrahim, M. L.; Ghasemi, M. A Review on Biochar Production from Different Biomass Wastes by Recent Carbonization Technologies and Its Sustainable Applications. *J. Environ. Chem. Eng.* **2022**, *10*, 107017.
(67) Gopinath, K. P.; Vo, D. V. N.; Gnana Prakash, D.; Adithya Joseph, A.; Viswanathan, S.; Arun, J. Environmental Applications of Carbon-Based Materials: A Review. *Environ. Chem. Lett.* **2021**, *19*, 557−582.
(68) Ren, X.; Chen, C.; Nagatsu, M.; Wang, X. Carbon Nanotubes as Adsorbents in Environmental Pollution Management: A Review. *Chem. Eng. J.* **2011**, *170*, 395−410.
(69) Rahimi, M.; Singh, J. K.; Müller-Plathe, F. CO_2 Adsorption on Charged Carbon Nanotube Arrays: A Possible Functional Material for Electric Swing Adsorption. *J. Phys. Chem. C* **2015**, *119*, 15232−15239.
(70) Li, H.; Wen, C.; Zhang, Y.; Wu, D.; Zhang, S.-L.; Qiu, Z.-J. Accelerating Gas Adsorption on 3D Percolating Carbon Nanotubes. *Sci. Rep.* **2016**, *6*, 21313.
(71) Zhao, J.; Buldum, A.; Han, J.; Lu, J. P. Gas Molecule Adsorption in Carbon Nanotubes and Nanotube Bundles. *Nanotechnology* **2002**, *13*, 195−200.
(72) Muhammad, S.; Yahya, E. B.; Abdul Khalil, H. P. S.; Marwan, M.; Albadn, Y. M. Recent Advances in Carbon and Activated Carbon Nanostructured Aerogels Prepared from Agricultural Wastes for Wastewater Treatment Applications. *Agriculture* **2023**, *13*, 208.
(73) Sabzehmeidani, M. M.; Mahnaee, S.; Ghaedi, M.; Heidari, H.; Roy, V. A. L. Carbon Based Materials: A Review of Adsorbents for Inorganic and Organic Compounds. *Mater. Adv.* **2021**, *2*, 598−627.
(74) Machabaphala, M. K.; Hlekelele, L.; Dlamini, L. N. A Heterostructure of Black Phosphorus and Zirconium-Based MOF as a Photocatalyst for Photocatalytic Applications. *Mater. Lett.* **2020**, *281*, 128660.
(75) Huang, Y.; Chen, X. Carbon Nanomaterial-Based Composites in Wastewater Purification. *Nano Life* **2014**, *04*, 1441006.
(76) Gusain, R.; Kumar, N.; Ray, S. S. Recent Advances in Carbon Nanomaterial-Based Adsorbents for Water Purification. *Coord. Chem. Rev.* **2020**, *405*, 213111−213167.
(77) Mofokeng, L. E.; Hlekelele, L.; Moma, J.; Tetana, Z. N.; Chauke, V. P. Energy-Efficient CuO/TiO_2@GCN Cellulose Acetate-Based Membrane for Concurrent Filtration and Photodegradation of Ketoprofen in Drinking and Groundwater. *Appl. Sci.* **2022**, *12*, 1649−1668.
(78) Zhang, Y. K.; Gao, L.; Hong, Y.; Shen, W. J.; Wang, Y.; Zhu, J. H. New Environmental Selective Micro-Mesoporous Carbonaceous Sorbent for Eliminating Tobacco Specific Nitrosamines and Lead Ion. *Microporous Mesoporous Mater.* **2021**, *318*, 111037.
(79) Li, S. H.; Sun, X. D.; Wang, Y.-z.; Shi, C. L.; Gu, W.-b.; Wang, W.-m.; Yao, H.-m.; Wang, Y.; Zhu, J. H. Novel Mesoporous Composite with Zeolite-like Selectivity to Capture Tobacco Specific Nitrosamine NNK. *Chem. Eng. J.* **2018**, *332*, 331−339.
(80) Zhang, Y. K.; Gao, L.; Hong, Y.; Shen, W. J.; Wang, Y.; Zhu, J. H. Sustainable Sorbent Derived from Discarded Cigarette Butts for Elimination of Tobacco Specific Nitrosamines Carcinogen. *Environ. Technol. Innov.* **2021**, *24*, 101825.
(81) Li, S.; Shi, C. L.; Wang, Y.-z.; Sun, X. D.; Qi, D.-w.; Wu, D.; Wang, Y.; Zhu, J. New Efficient Selective Adsorbent of Tobacco Specific Nitrosamines Derived from Discarded Cigarette Filters. *Microporous Mesoporous Mater.* **2019**, *284*, 393−402.
(82) Widger, L. R.; Combs, M.; Lohe, A. R.; et al. Selective removal of nitrosamines from a model amine carbon-capture waterwash using low-cost activated-carbon sorbents. *Environ. Sci. Technol.* **2017**, *51*, 10913−10922.
(83) Wang, W.; Wang, J.; Guo, Y.; Zhu, C.; Pan, F.; Wu, R.; Wang, C. Removal of Multiple Nitrosamines from Aqueous Solution by Nanoscale Zero-Valent Iron Supported on Granular Activated Carbon: Influencing Factors and Reaction Mechanism. *Sci. Total Environ.* **2018**, *639*, 934−943.
(84) Yoosefian, M. A High Efficient Nanostructured Filter Based on Functionalized Carbon Nanotube to Reduce the Tobacco-Specific Nitrosamines, NNK. *Appl. Surf. Sci.* **2018**, *434*, 134−141.

(85) Sun, X. D.; Shi, C. L.; Li, S. H.; Wang, Y.-z.; Qi, D.-w.; Wang, W.-m.; Yao, H.-m.; Wang, Y.; Zhu, J. H. New Shape-Selectivity Discovered on Graphene-Based Materials in Catching Tobacco Specific Nitrosamines. *J. Hazard. Mater.* **2018**, *358*, 234−242.
(86) Xu, T.; Shi, R.; Lu, N.; Zhang, J.; Bai, R.; Yang, Z.; Zhou, J. Y. Adsorption of tobacco-specific nitrosamine 4-(methylnitrosamino) −1- (3-pyridyl)-1-butanone from aqueous solution with graphene aerogel. *IOP Conf. Ser. Mater. Sci. Eng.* **2018**, *324*, 012028.
(87) Leyva Ramos, R.; Ovalle-Turrubiartes, J.; Sanchez-Castillo, M. A. Adsorption of Fluoride from Aqueous Solution on Aluminum-Impregnated Carbon. *Carbon* **1999**, *37*, 609−617.
(88) Sun, X. D.; Li, Y. Y.; Wang, L. J.; Wu, D.; Zheng, S. J.; Wang, W. M.; Tong, Y. G.; Wang, Y.; Zhu, J. H. Capturing Tobacco Specific N-Nitrosamines (TSNA) in Industrial Tobacco Extract Solution by ZnO Modified Activated Carbon. *Microporous Mesoporous Mater.* **2016**, *222*, 160−168.
(89) Shi, C. L.; Li, S. H.; Sun, X. D.; Wang, Z. P.; Wang, Y.-z.; Xiong, J.-w.; Gu, W.-b.; Wang, W.-m.; Yao, H.-m.; Wang, Y.; Zhu, J. H. New Activated Carbon Sorbent with the Zeolite-like Selectivity to Capture Tobacco-Specific Nitrosamines in Solution. *Chem. Eng. J.* **2018**, *339*, 170−179.
(90) Deng, Q.; Huang, C.; Zhang, J.; Xie, W.; Xu, H.; Wei, M. Selectively Reduction of Tobacco Specific Nitrosamines in Cigarette Smoke by Use of Nanostructural Titanates. *Nanoscale* **2013**, *5*, 5519−5523.
(91) Deng, Q.; Hong, Z.; Liu, H.; Huang, C.; Xu, H.; Lan, H.; Xie, W.; Xie, J.; Wei, M. Highly Efficient Degradation of Tobacco Specific N-Nitrosamines by TiO_2 Mesocrystals with Robust and Tailored Microporous Structure. *ChemistrySelect* **2018**, *3*, 10266−10270.
(92) Hlekelele, L.; Franklyn, P. J.; Dziike, F.; Durbach, S. H. Novel Synthesis of Ag Decorated TiO_2 Anchored on Zeolites Derived from Coal Fly Ash for the Photodegradation of Bisphenol-A. *New J. Chem.* **2018**, *42*, 1902−1912.
(93) Sun, X. D.; Lin, W. G.; Wang, L. J.; Zhou, B.; Lv, X. L.; Wang, Y.; Zheng, S. J.; Wang, W. M.; Tong, Y. G.; Zhu, J. H. Liquid Adsorption of Tobacco Specific N-Nitrosamines by Zeolite and Activated Carbon. *Micropo. Mesopor. Mater.* **2014**, *200*, 260−268.
(94) Mayorga-Martinez, C. C.; Sofer, Z.; Pumera, M. Layered Black Phosphorus as a Selective Vapor Sensor. *Angew. Chem., Int. Ed.* **2015**, *54*, 14317−14320.
(95) Wang, J.; Zhang, Z.; He, D.; Yang, H.; Jin, D.; Qu, J.; Zhang, Y. Comparative Study on the Adsorption Capacities of the Three Black Phosphorus-Based Materials for Methylene Blue in Water. *Sustainability* **2020**, *12*, 8335−8354.
(96) Zhao, Q.; Ma, W.; Pan, B.; Zhang, Q.; Zhang, X.; Zhang, S.; Xing, B. Wrinkle-Induced High Sorption Makes Few-Layered Black Phosphorus a Superior Adsorbent for Ionic Organic Compounds. *Environ. Sci.: Nano* **2018**, *5*, 1454−1465.
(97) Machabaphala, K. M.; Hlekelele, L.; Dlamini, L. N. The Photoreduction of Selenite and Selenate on the Surface of Few Layer Black Phosphorus and a UiO-66 p-n Junction Heterostructure. *New J. Chem.* **2021**, *45*, 8467−8478.
(98) Zhou, H. C. J.; Kitagawa, S. Metal-Organic Frameworks (MOFs). *Chem. Soc. Rev.* **2014**, *43*, 5415−5415.
(99) Chernikova, V.; Shekhah, O.; Belmabkhout, Y.; Eddaoudi, M. Nanoporous Fluorinated Metal-Organic Framework-Based Membranes for CO_2 Capture. *ACS Appl. Nano Mater.* **2020**, *3*, 6432−6439.
(100) Firooz, S. K.; Armstrong, D. W. Metal-Organic Frameworks in Separations: A Review. *Anal. Chim. Acta* **2022**, *1234*, 340208.
(101) Tu, K.; Ding, Y.; Keplinger, T. Review on Design Strategies and Applications of Metal-Organic Framework-Cellulose Composites. *Carbohydr. Polym.* **2022**, *291*, 119539−119548.
(102) Pan, S.-D.; Shen, H.-Y.; Zhou, L.-X.; Chen, X.-H.; Zhao, Y.-G.; Cai, M.-Q.; Jin, M.-C. Correction: Controlled Synthesis of Pentachlorophenol-Imprinted Polymers on the Surface of Magnetic Graphene Oxide for Highly Selective Adsorption. *J. Mater. Chem. A* **2019**, *7*, 15451−15452.
(103) Sharma, G.; Kandasubramanian, B. Molecularly Imprinted Polymers for Selective Recognition and Extraction of Heavy Metal Ions and Toxic Dyes. *J. Chem. Eng. Data* **2020**, *65*, 396−418.
(104) Guan, G.; Pan, J. H.; Li, Z. Innovative Utilization of Molecular Imprinting Technology for Selective Adsorption and (Photo)Catalytic Eradication of Organic Pollutants. *Chemosphere* **2021**, *265*, 129077.
(105) Tian, Y.; Wang, H.; Li, H.; Guo, Z.; Tian, B.; Cui, Y.; Li, Z.; Li, G.; Zhang, H.; Wu, Y. Recent Advances in Black Phosphorus/Carbon Hybrid Composites: From Improved Stability to Applications. *J. Mater. Chem. A* **2020**, *8*, 4647−4676.
(106) Eswaraiah, V.; Zeng, Q.; Long, Y.; Liu, Z. Black Phosphorus Nanosheets: Synthesis, Characterization and Applications. *Small* **2016**, *12*, 3480−3502.
(107) Ryder, C. R.; Wood, J. D.; Wells, S. A.; Yang, Y.; Jariwala, D.; Marks, T. J.; Schatz, G. C.; Hersam, M. C. Covalent Functionalization and Passivation of Exfoliated Black Phosphorus via Aryl Diazonium Chemistry. *Nat. Chem.* **2016**, *8*, 597−602.
(108) Song, X.; Turiel, E.; He, L.; Martín-Esteban, A. Synthesis of Molecularly Imprinted Polymers for the Selective Extraction of Polymyxins from Environmental Water Samples. *Polymers* **2020**, *12*, 131−143.
(109) Liu, Z.; Xu, Z.; Liu, H.; Wang, D.; Yang, Y.; Duan, Y.; Ma, L.; Lin, T. A Review on Molecularly Imprinted Polymers Preparation by Computational Simulation-Aided Methods. *Polymers* **2021**, *13*, 2657−2675.
(110) Vasapollo, G.; Sole, R. D.; Mergola, L.; Lazzoi, M. R.; Scardino, A.; Scorrano, S.; Mele, G. Molecularly Imprinted Polymers: Present and Future Prospective. *Int. J. Mol. Sci.* **2011**, *12*, 5908−45.
(111) Li, M. T.; Zhu, Y. Y.; Li, L.; Wang, W. N.; Yin, Y. G.; Zhu, Q. H. Molecularly Imprinted Polymers on a Silica Surface for the Adsorption of Tobacco-Specific Nitrosamines in Mainstream Cigarette Smoke. *J. Sep. Sci.* **2015**, *38*, 2551−2557.
(112) Zheng, X.; Xu, T.; Shi, R.; Lu, N.; Zhang, J.; Jiang, C.; Zhang, C.; Zhou, J. Preparation of Hollow Porous Molecularly Imprinted Polymers for N-Nitrosamine Adsorption. *Mater. Lett.* **2018**, *211*, 21−23.
(113) Sajini, T.; Mathew, B. A Brief Overview of Molecularly Imprinted Polymers: Highlighting Computational Design, Nano and Photo-Responsive Imprinting. *Talanta Open* **2021**, *4*, 100072.
(114) Chaikittisilp, W.; Ariga, K.; Yamauchi, Y. A New Family of Carbon Materials: Synthesis of MOF-Derived Nanoporous Carbons and Their Promising Applications. *J. Mater. Chem. A* **2013**, *1*, 14−19.
(115) Stock, N.; Biswas, S. Synthesis of Metal-Organic Frameworks (MOFs): Routes to Various MOF Topologies, Morphologies, and Composites. *Chem. Rev.* **2012**, *112*, 933−969.
(116) Yu, F.; Bai, X.; Liang, M.; Ma, J. Recent Progress on Metal-Organic Framework-Derived Porous Carbon and Its Composite for Pollutant Adsorption from Liquid Phase. *Chem. Eng. J.* **2021**, *405*, 126960.
(117) Nasalevich, M. A.; Van Der Veen, M.; Kapteijn, F.; Gascon, J. Metal-Organic Frameworks as Heterogeneous Photocatalysts: Advantages and Challenges. *CrystEngComm* **2014**, *16*, 4919−4926.
(118) Guo, M.; Zhang, M.; Liu, R.; Zhang, X.; Li, G. State-of-the-Art Advancements in Photocatalytic Hydrogenation: Reaction Mechanism and Recent Progress in Metal-Organic Framework (MOF)-Based Catalysts. *Adv. Sci.* **2022**, *9*, 2103361.
(119) Zhu, W. B.; Gao, L.; Zhang, Y. K.; Zhang, Q.; Hong, Y.; Shen, W. J.; Wang, Y.; Zhu, J. H. Insight into the liquid adsorption of tobacco specific nitrosamines on ZIF-8. *Microporous Mesoporous Mater.* **2022**, *333*, 111730.
(120) Wan, L.; Liu, K.; Kirillov, A. M.; Fang, R.; Yang, L. Fabrication of Cellulose Filters Incorporating Metal-Organic Frameworks for Efficient Nicotine Adsorption from Cigarette Smoke. *Langmuir* **2023**, *39*, 5364−5374.
(121) Dyosiba, X.; Ren, J.; Musyoka, N. M.; Langmi, H. W.; Mathe, M.; Onyango, M. S. Preparation of Value-Added Metal-Organic Frameworks (MOFs) Using Waste PET Bottles as Source of Acid Linker. *Sustain. Mater. Technol.* **2016**, *10*, 10−13.

(122) Mohamed, M. G.; EL-Mahdy, A. F.; Kotp, M. G.; Kuo, S. W. Advances in porous organic polymers: Syntheses, structures, and diverse applications. *Mater. Adv.* **2022**, *3*, 707−733.
(123) Li, N.; Huo, L.; Shen, W.; Qiang, C.; Wu, M.; Sun, G.; Li, Q.; Shi, M.; Ma, J. Porous organic polymers for superefficient removal of pollutants from water: Design, synthesis and adsorption performance. *J. Clean. Prod.* **2023**, *396*, 136558.
(124) Lu, R. Q.; Yuan, W.; Feng, H.; Luo, S. X. L.; Wu, Y. C. M.; Etkind, S. I.; Kumar, M.; Swager, T. M. Porous Polymers Containing Metallocalix [4] arene for the Extraction of Tobacco-Specific Nitrosamines. *Chem. Mater.* **2022**, *34*, 10623−10630.
(125) Zhang, Y.; Zhao, Y. G.; Muhammad, N.; Ye, M. L.; Zhu, Y. Ultrasound-assisted synthesis of clover-shaped nano-titania functionalized covalent organic frameworks for the dispersive solid phase extraction of N-nitrosamines in drinking water. *J. Chromatogr. A* **2020**, *1618*, 460891.
(126) Lu, S.; Liu, Q.; Han, R.; Guo, M.; Shi, J.; Song, C.; Ji, N.; Lu, X.; Ma, D. Potential applications of porous organic polymers as adsorbent for the adsorption of volatile organic compounds. *J. Environ. Sci. (China)* **2021**, *105*, 184−203.

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