

# Advances in Research on the Analysis and Detection of Chemical Components in Heated Tobacco Aerosols

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**Abstract.** Compared with traditional cigarettes, heated cigarettes have higher advantages in tar reduction, harm reduction, environmental impact and safety. This article provides an overview of the structure of heated tobacco products and the main chemical components in their aerosols. It also elaborates on methods for detecting these chemical components in aerosols. Furthermore, it discusses potential issues and offers suggestions for quality control in heated tobacco product research. The aim is to provide valuable insights and references for the continued research and development of heated tobacco products.

**Keywords:** Heated tobacco products; aerosol; chemical components; analysis and detection.

## 1. Introduction

Against the backdrop of increasing global efforts to control smoking and growing consumer health concerns, the development of low-harm tobacco products has become a focal point in the tobacco industry's current development. Presently, the market features three major categories of new tobacco products: smokeless tobacco products, heated tobacco products, and electronic cigarettes [1-2]. Among these, Heated Tobacco Products (HTPs) are a type of low-temperature tobacco product that heats tobacco flakes or tobacco leaves below 500°C using a specialized heat source without igniting the leaves. This process allows most of the aroma components and nicotine, which have boiling points below 300°C, to be vaporized. Due to the gentle heating conditions, the smoke from HTPs is primarily derived from the inherent tobacco flavors [3]. Compared to traditional cigarettes, the reduction in harmful substances in the aerosol produced by HTPs exceeds 90%, while maintaining a usage method and flavor characteristics closest to traditional cigarettes, making them highly favored by consumers [4].

The composition of aerosols in heated tobacco products not only affects consumers' smoking experience but also influences the research, development, and sales of these products. This article provides a review of the analytical and detection technologies for the aerosol components of heated tobacco products in recent years, aiming to offer effective references for the research and development of such products.

## 2. Introduction to Heated Tobacco Products

Heated tobacco products combine the characteristics of traditional cigarettes and electronic cigarettes. They consist of two main components: the tobacco stick and the heating device, with a variety of types available. IQOS by Philip Morris International has consistently held a leading position in this market. Marlboro, as the dedicated tobacco stick for IQOS, operates at a heating temperature below 350°C and is suitable for most heating devices [5], which structure is shown in Figure 1. The tobacco stick consists of four parts: the tobacco heating plug, the hollow acetate tube, the cooling polymer-film filter, and the mouthpiece filter. During use, the tobacco stick is simply inserted into the heating device. The gas generated by heating the tobacco flakes passes through the

hollow acetate tube to cool down, then goes through the filter section before being inhaled by the consumer.

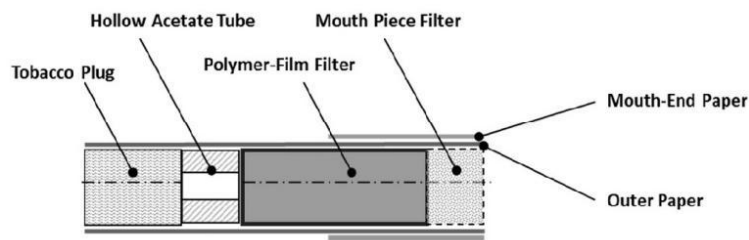


Fig. 1 Marlboro Structural Schematic Diagram [5].

### 3. Heated Tobacco Aerosol and its Component Analysis

Heated tobacco aerosol is produced when the core material is thermally distilled under low-temperature heating conditions. Due to the absence of combustion, the types and quantities of released components are lower than those in traditional cigarettes. Research in this area indicates that when the heating temperature is in the range of 100 to 200°C, the released nicotine mainly comes from evaporation and initial thermal decomposition. At around 300°C, the primary components in the aerosol are water, propylene glycol, glycerol, and nicotine. It's only when the temperature rises to around 350°C that the types and quantities of smoke-related flavor compounds (such as phenol and cresols) in the aerosol significantly increase [6-7].

Currently, global research on the aerosol components of heated tobacco products mainly focuses on toxicological evaluations and systematic assessments of potential harmful component release levels. There is relatively limited literature available on the analysis of aerosol components. The composition of aerosols is heavily influenced by puffing patterns and collection methods. Most of the detection of aerosol components is optimized and validated based on traditional cigarette smoke detection techniques. The following discussion will revolve around puffing patterns, collection methods, and component analysis.

#### 3.1 Impact of Puffing Patterns on Aerosol Components

Canadian Intense (HCI) and International Organization for Standardization (ISO) puffing regimes. Mcadam (2019) [8] examined the influence of puffing parameters (puff volume, puff duration, and puffing curve) on the total aerosol release from heated tobacco products and found that puff duration had the most significant impact on aerosol release.

Roal (2019) [9] investigated the release of various components in IQOS heated tobacco aerosol under HCI and ISO puffing patterns. The results revealed that, under the ISO puffing pattern, both total particulate matter and nicotine release were lower compared to the HCI puffing pattern.

Zhang Hongfei (2018) [10] studied the release of harmful components in the aerosols of GLO and IQOS under two different puffing patterns and found significant differences in the release of harmful components in the smoke under different puffing patterns. For example, the average tar release in IQOS samples was 1.3 mg under ISO and 9.8 mg under HCI, while GLO samples showed tar releases of 2.9 mg under ISO and 7.0 mg under HCI.

Miguel (2019) [11] compared the release of smoke components in 3R4F and IQOS cigarettes under the HCI puffing pattern. The results showed that IQOS emitted only 12 out of 37 components detected in 3R4F. This difference may be attributed to the fact that heated tobacco products do not involve the combustion of tobacco, preventing the release of substances from the tobacco plug.

### 3.2 Impact of Collection Methods on Aerosol Components

Various collectors, such as Cambridge filters, solid adsorbents, impactors, and electrostatic precipitators, have been used to collect mainstream smoke. However, due to the complex nature of smoke, even the best collectors are effective for only certain types of compounds or within specified volatility ranges. No single collector can capture all components of smoke. The choice of collection method depends on the specific target analytes. For instance, total particulate matter, nicotine, propylene glycol, glycerol, phenols, menthol, and tobacco-specific Nitrosamines (TSNAs) in aerosols are often collected using Cambridge filters. However, this method still leaves some volatile gas-phase compounds uncollected. Volatile organic compounds and polycyclic aromatic hydrocarbons are collected using adsorption tubes. Carbonyl compounds and ammonia are collected using absorption bottles. Ammonia, propylene glycol, nicotine, and water can also be collected using electrostatic collection methods [12-15].

Wei Weiwei (2021) [16] conducted a comparative analysis of the chemical components of fresh heated tobacco aerosol collected using vacuum cold trapping and Cambridge filters. The results showed that Cambridge filters captured only 36 components, mainly solid-phase components and semi-volatile substances. In contrast, vacuum cold trapping collected 70 components, primarily highly volatile compounds, suggesting that this collection method is better suited for analyzing highly volatile components in heated tobacco aerosol.

Dusautoir (2021) [17] used absorption bottles to collect carbonyl compounds in the smoke of heated tobacco products and traditional cigarettes. Their analysis revealed that heated tobacco products released 84.7% fewer carbonyl compounds compared to 3R4F cigarettes. Due to the low concentration of compounds in the aerosol produced by heated tobacco products, it is challenging to achieve complete collection.

Uchiyama (2018) [18] used a novel single adsorbent filter consisting of glass fiber pads and CX572 filter cartridges to collect mainstream smoke components generated by heated tobacco products. They found that the CX572 single cartridge method could collect both gas-phase and particulate-phase compounds in heated tobacco product aerosols, developing a simpler and more sensitive extraction method.

### 3.3 Analysis and Detection of Aerosol Chemical Components

The composition of aerosols released from heated tobacco products differs significantly from the smoke produced by combustion in traditional cigarettes. It primarily includes conventional components (glycerol, propylene glycol, water, and nicotine) and harmful components (CO, NNN, NNK, benzo[a,h]anthracene, crotonaldehyde) and volatile components. Analytical detection of these different compounds in aerosols often involves the combined use of separation instruments (LC, GC) and detection instruments (MS, MS/MS). Commonly used combinations include LC-MS, GC-MS, LC-MS/MS, and GC-MS/MS.

In addition, some newer techniques such as comprehensive two-dimensional gas chromatography (GC×GC), electron paramagnetic resonance (EPR), and proton nuclear magnetic resonance spectroscopy (1H-NMR) have also been gradually applied to the analysis of aerosol chemical components. GC×GC, when combined with time-of-flight mass spectrometry (TOF/MS), offers significant advantages in identifying complex compounds, making it suitable for qualitative and semi-quantitative non-target analysis [19].

As the methods for detecting conventional components in aerosols have been covered in the core material, the following discussion will primarily focus on the harmful components and volatile components in aerosols.

#### 3.3.1 Harmful Components

Although the harmful components in aerosols from heated tobacco products are reduced by 92% compared to those in smoke from traditional cigarettes, there are still some potentially harmful constituents that can be released through distillation and simple heat reactions. For example,

TSNAs are present in tobacco due to the widespread distribution of nitrate and amine compounds, which can generate TSNAs. As a result, TSNAs are commonly found in food, water, soil, and tobacco. In addition, some carbonyl compounds, especially formaldehyde, acetaldehyde, and crotonaldehyde, are toxic to cilia. When inhaled along with hydrogen cyanide and ammonia, they can suppress the clearance of lung secretions, leading to lung diseases. Furthermore, if aerosols contain a high concentration of free radicals, they can deplete the body's antioxidants, resulting in oxidative stress. This oxidative stress can lead to the modification of unsaturated fatty acids, proteins, DNA, and other molecules through free radical attacks, causing them to undergo structural changes and contributing to the development of diseases [20]. Ishizaki (2019) [21] established a solid-phase microextraction-LC-MS/MS method to study TSNAs in heated tobacco products. This method does not require pre-processing and offers high selectivity and sensitivity. Uchiyama (2021) [17] analyzed carbonyl compounds in IQOS aerosols using HPLC and found that substances such as formaldehyde, acetaldehyde, and acetone were present in small amounts. Shein (2021) [22] used EPR (electron paramagnetic resonance) technology to compare the types and quantities of free radicals in 3R4F cigarette samples and mainstream smoke from heated tobacco products. Their research showed that the level of free radicals in aerosols from heated tobacco products did not exceed 1% of that in traditional cigarette smoke, indicating a lower free radical content in heated tobacco product aerosols and reduced harm to the human body.

### 3.3.2 Volatile Components

Volatile components are essential aroma constituents in tobacco and serve as the primary factors for creating favorable flavors in aerosols from heated tobacco products. They are also crucial for evaluating product quality. Consequently, research on volatile components has been a significant focus of tobacco researchers. Yang Ji (2015) [23] employed headspace gas chromatography-mass spectrometry (HS-GC/MS) to investigate volatile components in tobacco materials from electrically heated cigarettes and smoke from traditional cigarettes at different temperatures. The results revealed that at 200°C, the highest number of components were detected in the smoke from both types of tobacco materials, primarily consisting of formic acid, acetic acid, hydroxyacetone, and propylene glycol. Schwanz (2020) [24] utilized comprehensive two-dimensional gas chromatography coupled with time-of-flight mass spectrometry (GC×GC-TOFMS) to study the impact of different heating temperatures on the volatile compounds produced by two reconstituted tobacco leaves. They found that with increasing heating temperature, the volatile substances in RTB1 and RTB2 increased by 9.6% and 18.5%, respectively. Building upon Schwanz's work, Savareear (2019) [25] established a TD-GC×GC-TOFMS/FID dual detection method to analyse the volatile substances released from heated tobacco product (THP1.0) and 3R4F samples. Their research indicated that compared to 3R4F, THP1.0 produced fewer volatile components, amounting to less than one-tenth of the release in 3R4F cigarette smoke.

## 4. Conclusion and Outlook

Currently, there is a considerable amount of foreign research on the analysis of aerosol chemical components. However, most studies couple separation instruments with detection instruments, and the use of new instruments for analysis is relatively limited. Furthermore, conventional detection methods often require expensive equipment, demanding sample pre-processing, and reliance on specialized technical personnel. These factors limit the analysis process. Developing a fast, efficient, and convenient detection method for the precise analysis of chemical components in heated tobacco products could significantly reduce both the testing cycle and costs.

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## References

- [1] Z. ZOI, A. MOHAMED, F. KONSTANTINOS, et al. Effects of exposure to tobacco cigarette, electronic cigarette and heated tobacco product on adipocyte survival and differentiation in vitro[J]. *Toxics*, 8(1), 9 (2020)
- [2] Z. T. BITZER, R. GOEL, N. TRUSHIN, et al. Free radical production and characterization of heat-not-burn cigarettes in comparison to conventional and electronic cigarettes[J]. *Chemical Research in Toxicology*, 33(7), 1882-1887 (2020)
- [3] I. PETRACHE, E. D. BOER. Cooling off the heated controversy of a safer cigarette: heat-not-burn no better than traditional combustion cigarettes Comment[J]. *Thorax*, 76(6), 536 (2021)
- [4] LI X, LUO Y, JIANG X, et al. Chemical analysis and simulated pyrolysis of tobacco heating system 2.2 compared to conventional cigarettes.[J]. *Nicotine & Tobacco Research : Official Journal of the Society for Research on Nicotine and Tobacco*, 21(1), 111-118 (2019)
- [5] Fu Y, Ma Z, Yuan Q, Xia Q, Jing D, Liu G. Overviews of Electrical Heated Non-burned Cigarette Bomb and Core Material Products development[J]. *SHANDONG HUAGONG*, 49(7), 72-76 (2020)
- [6] [6] YANG J, YANG S, DUAN Y, TIAN Y, ZHAO Wei, YANG L, TANG J, ZHU D, CHEN Y, MIAO M. Investigation of thermogravimetry and pyrolysis behavior of tobacco material in two heat-not-burn cigarette brands[J]. *Acta Tabacaria Sinica*, 21(6):7-13 (2015)
- [7] M. Forster, C. Liu, M. G. Duke, K. G. McAdam, C. J. Proctor. An experimental method to study emissions from heated tobacco between 100-200 degrees C[J]. *Chemistry Central Journal*, 9 (2015)
- [8] K. MCADAM, P. DAVIS, L. ASHMORE, et al. Influence of machine-based puffing parameters on aerosol and smoke emissions from next generation nicotine inhalation products[J]. *Regulatory Toxicology And Pharmacology*, 101, 156-165 (2019)
- [9] R. SALMAN, S. TALIH, R. EL-HAGE, et al. Free-base and total nicotine, reactive oxygen species, and carbonyl emissions from iqos, a heated tobacco product.[J]. *Nicotine & Tobacco Research : Official Journal of the Society for Research on Nicotine and Tobacco*, 21(9), (2019)
- [10] ZHANG H, JIANG X, PANG Y, LI X, LUO Y, ZHU F, YAN R, MA T, CHEN X. Analysis of mainstream aerosol emissions of heat-not-burn tobacco products under two puffing regimes[J]. *Tobacco Science & Technology*, 51(9), 40-48 (2018)
- [11] P. MIGUEL, M. DANIEL, G. G. ALICIA, et al. A comparative study of non-volatile compounds present in 3r4f cigarettes and iqos heat sticks utilizing gc-ms[J]. *American Journal of Analytical Chemistry*, 10: 76-85 (2019)
- [12] G. JACCARD, M. BELUSHKIN, C. JEANNET, et al. Investigation of menthol content and transfer rates in cigarettes and tobacco heating system 2.2[J]. *Regulatory Toxicology and Pharmacology*, 101, 48-52 (2019)
- [13] J. SCHALLER, D. KELLER, L. POGET, et al. Evaluation of the tobacco heating system 2.2. Part 2: Chemical composition, genotoxicity, cytotoxicity, and physical properties of the aerosol[J]. *Regulatory Toxicology and Pharmacology*, 812: S27-S47 (2016)
- [14] B. D. ILIES, S. P. MOOSAKUTTY, N. M. KHARBATIA, et al. Identification of volatile constituents released from IQOS heat-not-burn tobacco heat sticks using a direct sampling method[J]. *Tobacco Control*, (2020)
- [15] [15] P. B. STÃ, G. DIDIER, H. JULIA, et al. State-of-the-art methods and devices for the generation, exposure, and collection of aerosols from heat-not-burn tobacco products:[J]. *Toxicology Research and Application*, 4 (2020)
- [16] WEI W, LI Y, DENG T, DING S, FU J, DENG C, GONG S, YANG H. Capture and Analysis of Fresh Smoke from Heated Tobacco Product[J]. *FLAVOUR FRAGRANCE COSMETICS*, (02):25-30 (2021)

- [17] R. DUSAUTOIR, G. ZARCONI, M. VERRIELE, et al. Comparison of the chemical composition of aerosols from heated tobacco products, electronic cigarettes and tobacco cigarettes and their toxic impacts on the human bronchial epithelial BEAS-2B cells[J]. *Journal of Hazardous Materials*, 401 (2021)
- [18] S. UCHIYAMA, M. NOGUCHI, N T. Simple determination of gaseous and particulate compounds generated from heated tobacco products[J]. *Chemical Research in Toxicology*, 7(31), 585-593 (2018)
- [19] DING Y, ZHU L, LIU S, et al. Analytical method of free and conjugated neutral aroma components in tobacco by solvent extraction coupled with comprehensive two-dimensional gas chromatography-time-of-flight mass spectrometry[J]. *Journal of Chromatography A*, 1280: 122-127 (2013)
- [20] G. JACCARD, D. D. TAFIN, O. MOENNIKES, et al. Comparative assessment of hphc yields in the tobacco heating system ths2.2 and commercial cigarettes[J]. *Regulatory Toxicology and Pharmacology*, 90 (2017)
- [21] I. ATSUSHI, K. HIROYUKI. A sensitive method for the determination of tobacco-specific nitrosamines in mainstream and sidestream smokes of combustion cigarettes and heated tobacco products by online in-tube solid-phase microextraction coupled with liquid chromatography-tandem mass spectrometry[J]. *Analytica Chimica Acta*, 1075 (2019)
- [22] M. SHEIN, G. JESCHKE. Comparison of free radical levels in the aerosol from conventional cigarettes, electronic cigarettes, and heat-not-burn tobacco products[J]. *Chemical Research in Toxicology*, 32(6): 1289-1298 (2019)
- [23] YANG J, TANG J, SHANG S, YANG L, ZHENG X, DUAN Y, TIAN Y, ZHAO W, CHEN Y, MIAO M. Comparative Analysis of Volatile Components in Novel and Traditional Cigarettes by HS-GC/MS[J]. *Tobacco Science & Technology*. 48(11), 33-39 (2015)
- [24] T. G. Schwanz, M. G. Nespeca, J. C. Dias, L. V. Vieira Bokowski, M. C. A. Marcelo, D. H. Maximiano, L. S. Canova, P. B. de S. Cruz, O. F. S. Pontes, S. Kaiser. GC×GC-TOFMS and chemometrics approach for comparative study of volatile compound release by tobacco heating system as a function of temperature[J]. *Microchemical Journal*, 159: 105578 (2020)
- [25] B. SAVAREEAR, J. ESCOBAR-ARNANZ, M. BROKL, et al. Non-targeted analysis of the particulate phase of heated tobacco product aerosol and cigarette mainstream tobacco smoke by thermal desorption comprehensive two-dimensional gas chromatography with dual flame ionisation and mass spectrometric detection[J]. *Journal of Chromatography A*, 1603, 327-337 (2019)