Development of Cellulose Aerogel as a New Material for the Reduction of Harmful Substances in Cigarette Smoke

Hashem Rahamin1 · Mehdi Jonoobi1,2 · Nooshin Abzan3 · Sima Sepahvand1 · Alireza Ashori4 · Tizazu H. Mekonnen2

Accepted: 22 June 2022 / Published online: 14 July 2022
© The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2022

Abstract
The current study proposes a novel and improved cigarette filtration design comprising cellulose nanofibers (CNFs) and powdered activated carbons (PACs) with different dry matter contents. The proposed filter samples were primarily analyzed to verify their applicability as cigarette filters via measurements and standard tests, such as SEM, BET, DSC, and airflow permeability analysis. The results were compared with the cellulose acetate (CA) sample used as a conventional cigarette filter. The preliminary results indicated noticeable improvement compared to the reference CA. Also, the cigarettes were tested using a smoking machine, and the filtered smoke was analyzed using GC–MS to evaluate the filters’ performance in reducing the harmful substances present in the smoke. The results showed that the filters made of CNF and PAC significantly decreased the toxic substances compared with the reference but did not affect the nicotine substantially and therefore will not negatively impact the trance level of smokers.

Keywords Cellulose nanofibers · Nicotine · Alkanes · Activated carbon · Cigarette smoke

Introduction
Cigarette smoke is a concentrated aerosol comprising thousands of chemical compounds, which are dynamically dispersed among the aerosol particles and the adjacent gaseous phase [1]. According to a study by Rodgman and Perfetti [2], more than 6000 substances have been recognized in cigarette smoke. Although the number of distinct chemical compositions in cigarette smoke is unidentified, Wright [1] estimates that it might be as many as 100,000. These chemicals could have different harmful and destructive effects on human health. The studies show that the chemical composition of cigarette smoke could be strongly affected by either cigarette design or the smoking conditions [3]. Many studies claim that cigarette smoke could seriously threaten human health [4]. Statistics show that the number of deaths related to smoking is increasing each year, and in some regions, it has even surpassed the number of deaths due to road accidents or alcohol consumption. Smoking cigarettes will not stop in society anytime soon despite all these conditions. Thus, practical actions, including technology that could reduce the smoking risk level and its negative health impacts while not significantly affecting the satisfaction level of smokers, will be essential.

Currently, mechanisms that help reduce toxic cigarette emissions mainly emphasize modifying the tobacco blend or improving the cigarette filtration mechanism. Two primary blending techniques have been previously introduced by Liu et al. [5], and McAdam et al. [6], known as blend treated tobacco (BTT) and tobacco sheet substitute (TSS), respectively. The literature has also investigated combining these blending methods [7]. The primary purpose of these modifications was to reduce the amino acids and proteins in
cigarettes because they are the main elements of the precursors of toxins in cigarette smoke.

In recent years, nanotechnology has inspired many researchers to provide more efficient methods and solutions to the existing challenges. Like other fields, the tobacco industry also benefits from nanotechnology to improve its products [8]. Nanotechnology has opened a new window in the science of smoke purification resulting from the combustion of tobacco products, especially cigarettes. In this regard, many filtration methods were introduced to trap harmful chemicals [9]. Reviewing the existing literature shows that utilizing efficient filters in tobacco products inhibits more than 80% of hydrogen cyanide, 92% of formaldehyde, and more than 95% of acrolein and acetaldehydes [10]. Therefore, the risk of lung cancer from smoking filtered cigarettes compared to unfiltered cigarettes can be reduced by 20% to 50%.

Today, cigarette companies across the globe use cellulose (cellulose acetate, CA) as a cigarette filter substance. The main task of CA in cigarettes is to cool the cigarette smoke and remove or reduce harmful chemicals [11]. There are excellent studies published in the literature on the wood-derived biopolymers' applications in energy, electronics, biomedicine, and water treatment [12]. Recently, much attention has been placed on implementing cellulose nanofibers (CNFs) in the filters due to their low-cost, sustainability, and broader availability compared to other nanoparticles [13]. The CNF has unique features including high aspect ratio, renewability, nontoxicity, sustainability, high stiffness, high surface reactivity, good reinforcing effect, and high potential. These features can be tailored for intended use along with the CNF's biodegradability, biocompatibility, the ability to form a three-dimensional nanoporous network, thermal properties, low environmental issues during production and disposal steps, and so on [14–17]. Moreover, since nanofiber membranes have a porous structure with a high surface area and low initial weight, they are considered ideal candidates for filtering particles with micron dimensions and smaller than microns. Reviewing the literature confirms that in cigarette filters, CNF can be used alone or in combination with other materials, such as coarse fibers, paper, and activated carbon, AC [18, 19]. AC is often used in conventional cigarette filters to remove volatile organic compounds and adsorb vapors and fumes from the combustion of cigarettes up to its weight [20]. It was shown that utilizing AC filters results in significant elimination (up to 93%) of volatile organic compounds, including acrolein, acetaldehyde, benzene, and styrene, from tobacco combustion [21]. The findings also indicated that filters containing AC compared to conventional filters remove more toxic substances from cigarette smoke. Rafieian et al. [22] investigated hexadecyl trimethoxysilane (HDTMS) modified CNF aerogels with concentrations of 0.6, 0.9, and 1.2 wt% and evaluated their applicability for the adsorption removal of oils and organic pollutants from the water. They concluded that the oil adsorption increased as the concentration of modified CNF increased. The highest oil adsorption in this study was related to CNF 1.2 wt% of about 162.2 g g⁻¹. Sepahvand et al. [23] studied CNF aerogels modified with phthalimide to adsorb carbon dioxide (CO₂). The study found that modified CNF aerogels, due to the amine groups on the surface, high specific surface area, and small pore diameter, had the superior capability to adsorb CO₂.

Zeng et al. [24] investigated the ultrahigh adsorption of toxic substances from cigarette smoke using CNF–SiO₂ hybrid aerogels. They prepared a CNF–SiO₂ hybrid aerogel cigarette (CSG) filter based on the skeletal material of CNFs with the help of simple directional frozen technology. The results showed that the adsorption capacity of the CSG filter tip was higher against toxic substances caused by cigarette smoke compared to conventional CA filters. The adsorption efficiencies of the CSG filter tip for tar, total particulate matter (TPM), nicotine, and CO from cigarette smoke were found to be 92.2, 90.2, 95, and 20.6%, respectively. Most importantly, CSGs do not require additional chemical agents, indicating an eco-friendly process. Overall, the results indicated that CSGs show high potential as an ideal candidate for the adsorption of cigarette smoke toxicants. Bio-aerogels from bacterial cellulose (BC) are prepared by freeze-drying. Aside from having multifunctional properties such as high porosity, low density, and large specific surface area, they have superhydrophilic properties, excellent water absorption, and swelling properties. In addition, the bioaerogel film is very compact, flexible, and has good mechanical properties. In general, the BC bioaerogels are mainly used as green, stable, and degradable cigarette filter tips, which show a good absorption effect for the main components of the smoke [25].

This research has investigated the design and implementation of a novel improved cigarette filter containing CNF and AC. The applicability of the proposed filter is evaluated and compared with the conventional counterparts. The investigation also involves the analysis of independent and simultaneous effects on applicability and improvement of the filters.

Materials and Methods

Materials

Nanonovin Polymer Company (Iran) supplied the CNFs dispersion with a 2.2 wt% concentration in water used to prepare the sample filters. The powdered AC (PAC) with a surface area of 800–1800 m² g⁻¹ and dry bulk density of 360–740 kg m⁻³ was purchased from Sigma Aldrich (USA).
All solutions and dispersions were prepared using distilled water. The morphology of CNF, such as the diameter and distribution, was observed from transmission electron microscopy (TEM) EM 208S (Philips). Figure 1 shows the TEM image of isolated CNF, indicating that the CNF has a diameter of 20 to 50 nm.

**Fabrication of Cigarette Filters**

CNF suspensions were prepared from dried CNF with 1, 2, and 3 wt% concentrations and stirred at 500 rpm for 3 h at room temperature. Then, PAC with 5, 10, and 15 wt% were added to the CNF suspensions at room temperature and stirred for an additional 12 h using a magnetic stirrer to fabricate novel improved filters. Syringe molds with a 3 cm length and 1.5 cm diameter were mounted on a solid copper cylinder with a 2 cm diameter and 10 cm height. The prepared sample suspensions were poured into the syringe’s mold and placed on the copper base. The bottom 40 mm of the copper base was immersed in liquid N2 at a temperature of −196 °C. The copper base helps generate a homogeneous structure and prevents cracking and fracture of the samples during the freezing process. Finally, the frozen samples were freeze-dried in a lyophilizer (Christ Alpha 1–2 LD plus, Germany) at a temperature of −50 °C and reduced pressure (1 mbar) for 48 h. Figure 2 shows a schematic summary of the experimental steps employed in this work.

To investigate the effectiveness of the novel improved filters in reducing the harmful substances present in smoke, two available cigarette filter brands, “Mond Super Slim Blue” and “Royal Black Slim” were used as references. Table 1 presents the codes for the formulations and compositions of the CNF and PAC as well as references. In addition, to examine the properties of the manufactured filters, they were placed inside Mond Super Slim Blue and Royal Black Slim cigarettes (Fig. 3). As can be seen, to put the prepared sample filters in each cigarette, one-third of the main filter (CA) was removed and replaced with the filters presented in Table 1. All the sample cigarettes were placed in a Vötsch temperature and humidity controlled chamber and were conditioned before testing.

**Cigarette Filter Characterization**

**Scanning Electron Microscopy (SEM)**

The distribution of the cigarette filter compositions (CNF–PAC) and porous structure was evaluated by SEM. The SEM observations were carried out using a DSM-960A (Zeiss) operated at an accelerating voltage of 15 kV. The samples were sputtered-coated with a gold layer before the SEM evaluation.

**Brunauer–Emmett–Teller (BET) Analysis**

The liquid N2 adsorption of the various formulations was measured at a constant temperature of −196 °C on a BELSORP-mini II (BEL Japan, Inc., Japan) after degassing under a vacuum at 300 °C for 20 h. The pore size and volume of the prepared cigarette filter were determined via the BET equation with the 0.01–0.10 relative pressure range.

**Differential Scanning Calorimetry (DSC)**

DSC measurements were performed on a DSC TA Instruments Q100 (USA). In this study, a certain amount (about 5 mg) of each sample was weighed into a high-pressure gold-plated steel crucible, sealed, and transferred to the DSC apparatus. Analysis was conducted in the temperature range of 20 to 360 °C at a heating rate of 10 °C min−1 under a nitrogen atmosphere.

**Airflow Permeability**

The airflow permeability of the cigarette filters with suction flow provided by a vacuum pump at a specific time (1 min) and a pressure of 25 kPa with Air Permeability Tester model SDLAtlas, M021S (USA) according to the method specified in EN ISO 9237 standard was conducted. Finally, the airflow permeability of the samples was calculated using Eq. (1).

\[
R = \left( \frac{D_n}{A} \right) \times 0.167, \tag{1}
\]

where R is airflow permeability (m s⁻¹), Dₙ is average airflow rate (dm³ s⁻¹), and A is sample cross-section (m²).

**The Efficiency of Filters by Machine Smoking**

The sample cigarettes fitted with the fabricated fillers were smoked following the standardized ISO 8250 using a smoking machine to investigate the efficiency of the filters. The process...
was carried so that the smoking machine examined each pack of cigarettes (20). Throughout the standard smoking tests, the cigarette condensates were analyzed.

**Measurement of Chemicals in Cigarette Filters**

The amount of CO and condensate adsorption in the cartridges (considered smokers’ lungs) and the puff number of any cigarette were directly measured for each sample. Also the amount of nicotine, tar, phenol and alkanes (heptadecane, pentadecane, hexadecane) of the smoked cigarettes were analyzed using GC–MS GC (7890)-MSD (5975C) (Agilent Technologies, Germany) on the methanol solutions, which contained the cartridges for 24 h. The amount of condensate is determined using Eq. (2):

\[
\text{Condensate (g)} = \frac{\text{Weight of cartridge after smoking test} - \text{weight of cartridge before smoking test}}{\text{Quantity of burned cigarettes (20)}} \times 1000.
\]
In addition, the tar shall be obtained using Eq. (3):

\[
\text{Tar (g)} = \text{Condensate (g)} - (\text{water amount of cartridge (g)} + \text{nicotine (g)}). \quad (3)
\]

Table 1  The CNF and PAC content percentage for each treatment

| Treatment codes | Codes of cigarettes with different filters | Dry matter CNF content (%) | PAC content (%) | Number of samples |
|-----------------|--------------------------------------------|----------------------------|----------------|------------------|
| Royal           | Mond                                      |                            |                |                  |
| A1              | R1  MO1 1                                | 0                          | 60             |                  |
| A2              | R2  MO2 2                                | 0                          | 60             |                  |
| A3              | R3  MO3 3                                | 0                          | 60             |                  |
| A11             | R11 MO11 1                               | 5                          | 60             |                  |
| A21             | R21 MO21 2                               | 5                          | 60             |                  |
| A31             | R31 MO31 3                               | 5                          | 60             |                  |
| A12             | R12 MO12 1                               | 10                         | 60             |                  |
| A22             | R22 MO22 2                               | 10                         | 60             |                  |
| A32             | R32 MO32 3                               | 10                         | 60             |                  |
| A13             | R13 MO13 1                               | 15                         | 60             |                  |
| A23             | R23 MO23 2                               | 15                         | 60             |                  |
| A33             | R33 MO33 3                               | 15                         | 60             |                  |
| CAFa            | RRb RMc                                  | 0                          | 60             |                  |

aCellulose acetate filter (CAF) (based on commercial cigarettes)
bReference of Royal cigarette (with conventional cellulose acetate filter)
cReference of Mond cigarette (with conventional cellulose acetate filter)

Results and Discussion

SEM

The morphological properties of the fabricated pure CNF and CNF–PAC-based cigarette filters are shown in Fig. 4a, b. The samples have a highly porous structure and an integrated cellulose network, indicating that the CNF is autonomously connected to a 3D network via hydrogen bonds. Figure 4a shows that the surface of the CNF has a porous matrix with relatively good dispersion. On the contrary, the addition of PAC has slightly changed the surface morphology of the CNF, as noted in Fig. 4b, while maintaining an integrated CNF surface. The CNF–PAC structure is more compact and tightly interconnected [16, 22]. It is observed that the pore diameter in CNF is larger than the pore diameter in CNF–PAC. The larger the diameter of the pores, the lower the pores’ volume, which decreases the filters’ air permeability [23]. Generally, the CNF seems to be arranged in the longitudinal direction due to the gradual freeze-drying provided by the copper metal conduction from the liquid nitrogen. Such positioning can positively impact the filter’s applicability and ease an appropriate airflow passage through the filters.

BET Characteristics

The results of the BET analysis presented in Table 2, indicated that the average pore diameter size and pore volumes were 8.81 nm and 0.031 cm$^3$ g$^{-1}$, respectively, suggesting that the prepared filter samples have less porosity compared to the typical (conventional) filter for cigarettes (CA). In general, it was observed that with increasing the concentration of CNF and the amount of PAC, the average pore diameter and pore volume decrease due to the compaction that results in higher density cigarette filters [21, 26, 27].

DSC Thermal Properties

The DSC results are shown in Table 3. As can be seen, the DSC analysis indicated that average glass transition temperature ($T_g$) and melting temperature ($T_m$) for the prepared sample filters were 85.2°C and 158°C, respectively, which are higher than the temperatures for the CA filters (CAF). Therefore, the prepared filters could have a broader range of temperature applicability than cigarette filters, which is essential because smoking could generate higher heat and stability of the filter under such temperature will have great interest.
Figure 5 shows the airflow permeability of cigarette filters. The average filter samples’ air permeability was 3270 (dm min\(^{-1}\)), which is about 11% less than the air permeability for the CAF reference sample. The decreased air permeability in the prepared filter samples can be due to the fibers’ small diameter and pores compared to the reference CAF sample. The small pore diameter in the fabricated filters reduces the air flow rate, which allows the smoke to interact intimately with the filter material. On the contrary, the large pore diameter of the CAF provides little resistance to airflow, which leads to a drop in pressure [23, 27].

### The Absorption of CO and Condensate

The amount of condensate, the estimated CO, and condensate absorption in the simulated lungs was measured for each sample cigarette using a smoking machine throughout the standard smoking tests. The analysis results for “Royal1 black slim” and “Mond super slim blue” cigarette samples are presented in Fig. 6a and b, respectively. As can be seen in Fig. 6a, the highest amount of CO and condensate absorption in the lung was related to the
reference sample with 6.2 mg and 7.19 mg, respectively, but the lowest amount of CO and condensate absorption was associated with R13 sample, which was 1.04 mg and 0.975 mg, respectively. Figure 6b shows that the lung's highest amount of CO and condensate absorption amount was related to the reference sample with 3.6 mg and 4.27 mg, respectively. Still, the lowest CO and condensate absorption were associated with the M23 sample at 0.7 mg and 0.76 mg, respectively. Based on the results, for both cigarette brands, the smoking of the commercial reference samples resulted in the highest estimated CO absorption in the smoking machine filter lungs. In comparison, utilizing the prepared filters led to a substantial reduction in the inhaled CO level. The same goes for the condensate level, which indicates the PAC’s significant positive impact of the PAC. Due to its high specific surface area and high absorption capacity, PAC can absorb considerable amounts of CO and condensate [28].

**Absorption of Alkane (Heptadecane, Pentadecane, Hexadecane) and Phenol**

Figure 7a, b showed the absorption rates of the alkanes) heptadecane, pentadecane, and hexadecane) and phenol for Royal black slim and Mond super slim blue cigarette samples. As can be seen, in cigarette filters made with CNF and PAC, fewer alkanes)heptadecane, pentadecane, hexadecane) and phenol passes through them than in the reference sample. Especially when cigarette filters made of 3 wt% CNF and 5 wt% PAC are used, they can easily absorb alkanes) heptadecane, pentadecane, hexadecane) and phenol before reaching the lungs, which can be due to the high specific
surface area and small diameter of their pores allowing intimate interaction with the AC and CNF for adsorption.

**Absorption of Nicotine and Tar**

The tar and nicotine yields of the cigarettes were analyzed and compared with the reference cigarettes using a GC–MS method. The results of GC–MS analysis for “Royal black slim” and “Mond super slim blue” cigarette samples are shown in Fig. 8a, b. As seen, the amount of tar has significantly decreased in comparison to the reference cigarette. However, after applying the proposed filters for the Royal1 black slim and Mond super slim blue cigarette samples, the tar levels decreased by 63.3% and 55.8%, respectively. Tar comprises most cancer-causing chemicals within cigarette smoke [29]. Once the cigarette smoke is inhaled, the tar may form an adhesive film on the inside of the lungs, damaging them and leading to lung-related problems such as emphysema or cancer [30]. Therefore, the proposed sample filters performed very well in filtering harmful chemicals.

Moreover, the nicotine levels decreased after applying the proposed filters for the Royal1 black slim and Mond super slim blue cigarette samples, which implies excellent applicability for the filters since the nicotine level in the cigarettes is one of the critical factors in the satisfaction level of the users [31, 32]. Therefore, although the filters significantly prevent smokers from inhaling most harmful chemicals, they do not substantially decrease their satisfaction level.

**Conclusions**

Health concerns related to smoking have prompted a significant research and development effort to improve cigarette filtration efficiency in conjunction with efforts to reduce smoking habits. To this aim, a novel improved cigarette filtration comprising both CNF and PAC was introduced in the present work. Primarily, sample filters with different dry matter contents of CNF (1, 2, and 3 wt%) and PAC (0, 5, 10, and 15%) were prepared. SEM analysis indicated a proper distribution of CNF in the sample filters. BET analysis showed that the average pore diameter size and volume were 8.81 nm and 0.031 cm³ g⁻¹, respectively, less than the typical cigarette filters. Furthermore, DSC analysis on the sample filters showed that the average glass transition and melting temperatures were increased to 85.2 °C and 158 °C, respectively, confirming that the modified filters have higher thermal stability providing a broader temperature range of applicability. More importantly, the air permeability test for the prepared samples according to EN ISO 9237 standard showed a reduction compared to the reference CA sample due to the less porosity of the prepared samples. Since the primary analysis confirmed the applicability of the prepared samples as cigarette filters, their performances were investigated using a smoking test machine. The reduction in the CO levels, as well as heptadecane, pentadecane, hexadecane, phenol, nicotine, and the tar yields of the cigarettes, were noted using a GC–MS method. Overall, the fabricated filter samples have significantly reduced the amount of harmful chemicals, leading to better filtration of cigarette smoke.

**Acknowledgements** The authors wish to acknowledge the University of Tehran for the financial support of this research and the Iranian Tobacco Company for allowing to use their smoking machine. M. Jonoobi and T.H. Mekonnen acknowledge the financial support of NSERC and the University of Waterloo.

**Funding** The authors have not disclosed any funding.

**Declarations**

**Conflict of interest** The authors declare that they have no conflict of interest.
Human and Animal Rights Statement  This article does not contain any studies involving animals or human participants performed by any of the authors.

Ethical Approval  This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent  None.

References

1. Wright C (2015) Trends Anal Chem 66:118–127
2. Rodgman A, Perfetti TA (2013) The chemical components of tobacco and tobacco smoke. CRC Press, Boca Raton
3. Naidu SK (2001) Chem Technol Crop Sci 41:255–255
4. Stratton K, Shetty P, Wallace R, Bondurant S (2001) Tob Control 10:189–195
5. Liu C, DeGrandpré Y, Porter A, Griffiths A, McAdam K, Voisine R, Cote C, Proctor C (2011) Food Chem Toxicol 49:1904–1917
6. McAdam KG, Gregg EO, Liu C, Dittrich DJ, Duke MG, Proctor CJ (2011) Food Chem Toxicol 49:1684–1696
7. Crooks I, Scott K, Dalrymple A, Dillon D, Meredith C (2015) Regul Toxicol Pharmacol 71:507–514
8. Xie L, Liu Q, Wu MJ, Hu RR (2007) Guangdong Chem Ind 11:40–42
9. Cao J, Xiaolong M, Yang A, Xu W (2006) Polym Polym Compos 14:65–71
10. Aufderheide M, Scheffler S, Ito S, Ishikawa S, Emura M (2015) Exp Toxicol Pathol 67:407–411
11. Wang B, Sain M, Oksman K (2007) Appl Compos Mater 14:89–103
12. Liu C, Luan P, Li Q, Cheng Z, Xiang P, Liu D, Hou Y, Yang Y, Zhu H (2021) Adv Mater 33(28):2001654
13. Thomas D, Cebe P (2017) Therm J Anal Calorim 127:885–894
14. Alemdar A, Sain M (2008) Compos Sci Technol 68:557–565
15. Shatkin JA, Wegner TH, Bilek ET, Cowie J (2014) TAPPI J 13:9–16
16. Sepahvand S, Jonoobi M, Ashori A, Gauvin F, Brouwers HJH, Yu Q (2020) Polym Compos 41:219–226
17. Hu F, Zeng J, Cheng Z, Wang X, Wang B, Zeng Z, Chen K (2021) Carbohydr Polym 254:117474
18. SSG MJ (2005) US Patent Application 0139223
19. Daneleviciute-Vaisniene A, Katunskis J, Buika G (2009) Fibres Text East Eur 6:40–43
20. Branton P, Bradley RH (2011) Adsorption 17:293–301
21. Polzin GM, Zhang L, Hear BA, Tavakoli AD, Vaughan C, Ding YS, Ashby DL, Watson CH (2008) Tob Control 17:i10–i16
22. Rafieian F, Hosseini M, Jonoobi M, Yu Q (2018) Cellulose 25:4695–4710
23. Sepahvand S, Jonoobi M, Ashori A, Gauvin F, Brouwers HJH, Oksman K, Yu Q (2020) Carbohydr Polym 230:115571
24. Zeng J, Wang T, Cheng Z, Liu L, Hu F (2022) ACS Appl Polym Mater 4(2):1173–1182
25. Cheng Z, Duan C, Zeng J, Wang B, Xu J, Gao W, Li J, Chen K (2021) Adv Mater Interfaces 8(7):2002101
26. Rafieian F, Mousavi M, Yu Q, Jonoobi M (2019) Int J Biol Macromol 130:280–287
27. Sepahvand S, Bahmani M, Ashori A, Pirayesh H, Yu Q, Dafchahi MN (2021) Int J Biol Macromol 182:1392–1398
28. Dillon EC Jr, Wilton JH, Barlow JC, Watson WA (1989) Ann Emerg Med 18:547–552
29. Kaufman DW, Palmer JR, Rosenberg L, Stolley P, Warshauer E, Shapiro S (1989) Am J Epidemiol 129:703–711
30. Harris JE, Thun MJ, Mondul AM, Calle EE (2004) BMJ 328:372
31. Taghavi S, Khashyharmanesh Z, Moalemzadeh-Haghighi H, Nasirli H, Eshraghi P, Jalali N, Hassanzadeh-Khayyat M (2012) Addict Health 4:28
32. Benowitz NL, Jacob P III, Herrera B (2006) Clin Pharmacol Ther 80:703–714

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.