

Novel Aerogels Based on Citric Acid Crosslinked Bacterial Cellulose for Sustained Release of Nicotine in Oral Nicotine Products *

by

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SUMMARY

In this study we developed a novel carrier material that can be used to regulate nicotine release profile to provide a more constant release. Bacterial cellulose (BC) was produced by fermentation of tobacco waste, nicotine was derived from the backfilling of tobacco extracts. Citric acid (CA) has been used to react with bacterial cellulose to prepare an aerogel (CA-BC) which showed to possess sustained nicotine release by varying CA and its cross-linking ratio with BC. Aerogels prepared at 10% CA/BC ratios during crosslinking exhibited significant sustained nicotine release effects. Another notable finding was that the sustained-release of nicotine for the CA-BC aerogel with high nicotine contents significantly outperformed that of low nicotine contents. The Weibull model and Gallagher-Corrigan model were used to elucidate the mechanism of nicotine dissolution from CA-BC aerogels. Material characterization revealed that the CA-BC aerogel had an improved thermal stability and decreased water absorption, a 3D fiber network structure at the microscopic level with an optimal average pore size of 30 μm was used to explain this difference. [Contrib. Tob. Nicotine Res. 34 (2025) 135–147]

KEYWORDS

Bacterial cellulose, citric acid, aerogel, dissolution test, nicotine sustained release

ZUSAMMENFASSUNG

In dieser Studie wurde ein neuartiges Trägermaterial entwickelt, mit dem das Nikotinabgabeprofil reguliert werden kann, um eine gleichmäßigere Abgabe zu erzielen. Bakterielle Cellulose (BC) wurde durch Fermentation von Tabakabfällen hergestellt, Nikotin wurde aus rekonstituierten Tabakextrakten gewonnen. Zitronensäure (CA) wurde verwendet, um mit bakterieller Cellulose zu reagieren und ein Aerogel (CA-BC) herzustellen, das durch Variation des CA-Anteils und seines Vernetzungsverhältnisses mit BC eine anhaltende Nikotinabgabe zeigte. Aerogele, die bei einem CA/BC-Verhältnis von 10% während der Vernetzung hergestellt wurden, zeigten eine signifikante nachhaltige Nikotinabgabe. Eine weitere bemerkenswerte Erkenntnis war, dass die nachhaltige Nikotinabgabe des CA-BC-Aerogels mit hohem Nikotingehalt diejenige mit niedrigem Nikotingehalt deutlich übertraf. Das Weibull-

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Modell und das Gallagher-Corrigan-Modell wurden verwendet, um den Mechanismus der Nikotinabgabe aus CA-BC-Aerogelen aufzuklären. Die Materialcharakterisierung ergab, dass das CA-BC-Aerogel eine verbesserte thermische Stabilität und eine verringerte Wasseraufnahme aufwies. Zur Erklärung dieses Unterschieds wurde eine dreidimensionale Fasernetzwerkstruktur auf mikroskopischer Ebene mit einer optimalen durchschnittlichen Porengröße von 30 µm herangezogen. [Contrib. Tob. Nicotine Res. 34 (2025) 135–147]

RESUME

Cette étude a permis de mettre au point un nouveau matériau support pouvant être utilisé pour réguler le profil de libération de nicotine afin d'obtenir une libération plus constante. La cellulose bactérienne (BC) a été produite par fermentation de déchets de tabac, la nicotine a été extraite des résidus d'extraits de tabac. L'acide citrique (CA) a été utilisé pour réagir avec la cellulose bactérienne afin de préparer un aérogel (CA-BC) qui s'est révélé capable de libérer de la nicotine de manière prolongée en faisant varier la proportion de CA et son taux de réticulation avec la BC. Les aérogels préparés avec des rapports CA/BC de 10 % pendant la réticulation ont montré des effets significatifs de libération prolongée de nicotine. Une autre découverte notable est que la libération prolongée de nicotine pour l'aérogel CA-BC à forte teneur en nicotine était nettement supérieure à celle des aérogels à faible teneur en nicotine. Les modèles de Weibull et de Gallagher-Corrigan ont été utilisés pour élucider le mécanisme de dissolution de la nicotine à partir des aérogels CA-BC. La caractérisation des matériaux a révélé que l'aérogel CA-BC présentait une meilleure stabilité thermique et une absorption d'eau réduite. Une structure fibreuse tridimensionnelle au niveau microscopique, avec une taille moyenne optimale des pores de 30 µm, a été utilisée pour expliquer cette différence. [Contrib. Tob. Nicotine Res. 34 (2025) 135–147]

INTRODUCTION

Oral tobacco products, also known as non-combustible tobacco products, deliver nicotine through oral mucosal absorption. Nowadays, there are two major kinds of commercial oral tobacco products, namely traditional moist smokeless tobacco (MST) and oral tobacco-derived nicotine (OTDN) (1). These products are primarily consumed via oral dissolution and absorption so the pharmacological and sensory experiences provided by them are significantly affected by their nicotine and flavor release profiles (2). Combined with historical and regulatory reasons, such as free from “secondhand smoke” and privacy during use, oral tobacco and nicotine products are relatively popular in Nordic and North American markets. For inexperienced users, however, oral tobacco and nicotine products usually produce an exponential-shaped nicotine release kinetics which can be unfamiliar because the initial nicotine rush may be too strong (3–4). To tackle this difficulty, the ‘sustained release of nicotine’ has been extensively studied in recent years, as the constant release

of nicotine can be realized by altering product packaging or adjusting formulations (5–6). Nevertheless, thorough understanding of the structure-property relationship for the substrate materials used inside pouches are needed to improve the nicotine release for modern oral nicotine products.

Aerogels are ultraporous solid materials that have demonstrated broad application potential in the field of drug delivery because of their low thermal conductivity, high porosity, high specific surface area, and chemical stability (7–8). Research typically utilizes silica polymers, alginate biopolymers, or protein compositions to create aerogels (9–11). In addition, aerogels based on bacterial cellulose exhibit excellent biodegradability and mechanical performance and have been widely used in adsorption and biomedical fields (12–14). However, there is no report of bacterial cellulose aerogels being used as carrier materials for nicotine products intended for oral usage so far.

Bacterial cellulose is a polymer produced by bacterial fermentation of biomass materials. In recent years, to reduce the cost of raw materials in the production of bacterial cellulose, especially the cost of carbon sources, several waste materials have been shown to be potential substrates for the production of bacterial cellulose, such as tobacco waste, fruit juice, corn stover, beverage industry waste, corn cob acid hydrolysate, and spent brewery yeast (15). Among these, bacterial cellulose prepared using tobacco waste water extract as the fermentation substrate has been demonstrated that there is no significant difference in morphological structure compared with bacterial cellulose which was produced with traditional Hestrin-Schramm (HS) media (16), and that the bacterial cellulose produced contains natural nicotine components. In addition, there are plenty of hydroxyl groups on the surface of bacterial cellulose, which can be used as the active sites of crosslinking reaction with various crosslinking agents. The crosslinking reactions form new covalent bonds between the bacterial cellulose and the crosslinking agents, so that the assembly structure can be further regulated.

Citric acid (CA), as an environmentally friendly material, which is nontoxic, harmless, and relatively inexpensive, has been used to react with bacterial cellulose to prepare cellulose nanofiber foams with good sound absorption properties (17). The aerogels constructed by citric acid crosslinked bacterial cellulose (CA-BC) promote a 3D structure, reduce the collapse of the porous structure, and enhance water retention and mechanical strength (18). Since CA and BC are both generally recognized as safe (GRAS) by regulatory authorities and have been used in food products, CA-BC prepared from these two materials can be considered as food-grade materials for human oral consumption.

Herein, we present the first case of sustained nicotine release of CA-BC aerogel via crosslinking of bacterial cellulose obtained by biological fermentation and nicotine backfill by tobacco extract. The nicotine release behavior from the CA-BC aerogel was evaluated for their sustained release capabilities at various nicotine concentrations using the Weibull function and Gallagher-Corrigan model. Fourier transform infrared spectroscopy (FTIR), titration experiments, and scanning electron microscopy (SEM) were utilized to analyse the chemical composition and

microstructure of the materials. Moreover, the thermal stability and water absorption properties were investigated through thermogravimetric analysis and water absorption tests, respectively.

MATERIALS AND METHODS

Materials

Tobacco residue (flue-cured tobacco dust) was collected from the dust removal workshop of the cigarette factory of China Tobacco Henan Industrial Co., Ltd. (Zhengzhou, China). The fermentation strain used was *Acetobacter xylinum*, which was preserved in the laboratory under standard conditions: stored at $-80\text{ }^{\circ}\text{C}$ in a 20% glycerol solution to maintain viability and stability. NaOH (Analytical Reagent grade (AR), 98%), citric acid (AR, 99.5%), NaH_2PO_4 (AR, 99.99%), NaHCO_3 (AR, 99.8%), and phenolphthalein indicator (1%) were all produced by Aladdin Reagents Co., Ltd. (Riverside, CA, USA). Deionized (DI) water was obtained via purification on one ultra-pure water machine (CS-5, Wuhan Jibari Technology Co., Ltd., Wuhan, China). Commercial oral tobacco products were moist snuff (Timber Wolf Natural Fine Cut) and snus (loose product, Swedish Match AB, The Lab 13).

Synthesis and purification of BC

After optimizing the laboratory's preliminary research methods (16) for producing bacterial cellulose, *Acetobacter xylinum* was inoculated into the seed medium and fermented for 24 h to produce the seed mixture. The seed mixture was then inoculated into the tobacco fermentation medium at a 10% (v/v) inoculation rate. After being statically cultured in a constant-temperature incubator at $30\text{ }^{\circ}\text{C}$ (Thermo Fisher Scientific, Waltham, MA, USA) for 7 days, tobacco-coloured bacterial cellulose (BC) was obtained. The tobacco-coloured BC was soaked in a 0.1 mol/L NaOH solution and heated in a $70\text{ }^{\circ}\text{C}$ water bath (JULABO Tech, Seelbach, Germany) for 1 h to eliminate residual tobacco extract from the material, preventing potential interference in subsequent crosslinking reactions. This mixture was subsequently repeatedly washed with deionized water until the solution was neutral, obtaining grey-white BC, which was then sterilized at $120\text{ }^{\circ}\text{C}$ for 60 min and refrigerated for later use.

Preparation of tobacco fermentation medium: tobacco residue (100 g/L) was extracted at $70\text{ }^{\circ}\text{C}$ for 100 min, followed by filtration to obtain the filtrate. The tobacco residue, derived from flue-cured tobacco, consisted of 25.4% cellulose, 22.3% hemicellulose, 3.1% lignin, 6.2% pectin, 38.5% soluble substances, and 5.1% ash. Among the soluble substances, the sugar content was 25.1%, protein content was 9.2%, and nicotine content was 2.2%. The obtained filtrate was sterilized at $120\text{ }^{\circ}\text{C}$ for 10 min to obtain the tobacco extract 1#. This extract 1# was diluted with deionized water to obtain dilutions of 1:0.25 (extract 2#, extract/deionized water, v/v), 1:1 (extract 3#), 1:4 (extract 4#) and 1:9 (extract 5#) to prepare tobacco extract solutions with graded concentrations, which were then refrigerated for later use.

BC and CA crosslinking reaction

In accordance with methods described in the literature with slight improvements (19), sodium dihydrogen phosphate (NaH_2PO_4) and sodium bicarbonate (NaHCO_3) were mixed at a 1:1 molar ratio to serve as activators and were dissolved in 500 mL of deionized water. After the purified bacterial cellulose (BC) was disrupted by stirring, citric acid (CA) and BC were added to the activation solution at specific mass ratios ($\text{CA/BC} = 0.01, 0.02, 0.05, 0.1, 0.2, 0.5$, and 1). The mass ratio of CA to the activator was 1:1. The mixture was then fully activated by shaking in a $40\text{ }^{\circ}\text{C}$ orbital shaker for 24 h. After activation, the mixture was poured into a reflux condensation apparatus (HWCL-5 model, Zhengzhou Greatwall Scientific Industrial, Shangjie District, Zhengzhou, China) and refluxed at $150\text{ }^{\circ}\text{C}$ for 150 min to carry out the crosslinking reaction. After the crosslinking reaction was complete, the mixture was filtered, and the solid was washed three times with deionized water to remove any residual activator and unreacted CA. The solid content of the control sample (uncrosslinked BC) and the crosslinked CA-BC materials were adjusted to the same level and then refrigerated for later use.

Preparation of CA-BC aerogel

Tobacco extract (2 mL) with different concentrations (one of extract 1–5#) was added to 5 g of CA-BC to achieve varying nicotine contents in the material. The mixture was homogenized by shaking, and any air bubbles were removed. After three freeze-thaw cycles in liquid nitrogen, the material was freeze-dried for 12 h using a vacuum freeze-dryer (Lyovapor™ L-200, BUCHI, Flawil, Switzerland) to obtain CA-BC aerogel materials with different nicotine contents. The entire material preparation process and dissolution model are shown in Figure 1.

Chemical composition analysis

Infrared spectroscopy scanning tests (VERTEX70, Bruker Optics, Ettlingen, Germany) were conducted on the BC and CA-BC aerogel materials. The conditions for the infrared spectroscopy were as follows: characterization was performed using the potassium bromide (KBr) pellet method with a resolution set at 4 cm^{-1} and a scanning range of 400 to 4000 cm^{-1} . Titration experiments were carried out on the CA-BC aerogel materials with the following steps: 500 mg of the sample was placed in a conical flask, and a mixture of 50 mL of ethanol and deionized water (ethanol/water ratio of 4:1) was added to ensure that the sample was fully saturated. The mixture was stirred for 30 min to expose the ester bonds in the sample within the reaction mixture. 50 mL of NaOH solution (0.1 M) was then added to the flask, and the solution was left to stand for 2 h to ensure complete hydrolysis. After 2 h, a few drops of phenolphthalein indicator were added, and owing to the excess sodium hydroxide, the solution turned pale red (alkaline). The excess NaOH was titrated with an HCl solution (0.1 M) until the colour disappeared (the phenolphthalein indicator turned colourless), indicating the endpoint of the titration. The volume of HCl consumed at the endpoint was recorded.

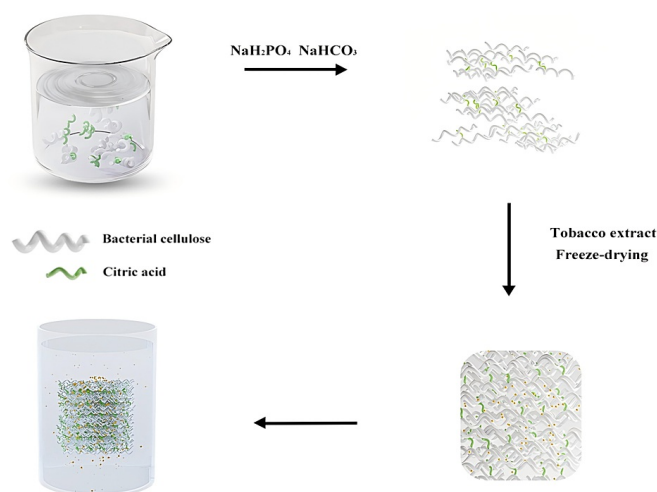


Figure 1. Schematic representation of material preparation and presentation of nicotinic dissolution intention.

The actual amount of CA bound was calculated as follows:

$$m = \frac{(V_{\text{NaOH}} - V_{\text{HCl}}) \times c_{\text{NaOH}}}{3} \times M_{\text{CA}}$$

where V_{NaOH} is the volume of NaOH added; c_{NaOH} is the concentration of the added NaOH, V_{HCl} is the volume of HCl consumed at the titration endpoint, and M_{CA} is the molar mass of CA.

Thermogravimetric analysis (TGA)

TGA tests (TGA 2(LF), Mettler-Toledo International Inc, Greifensee, Switzerland) were conducted on the BC and CA-BC aerogel materials. The temperature was initially maintained at 35 °C for 1 min. The temperature was then increased from 35 °C to 500 °C at a rate of 20 °C per min. The balance was protected with a helium flow of 60 mL/min, and the purge gas flow rate for the sample was set at 30 mL/min.

Water absorption test

Contact angle tests (Theta Flex, Biolin Scientific, Gothenburg, Sweden) and water absorption tests were performed on the BC and CA-BC aerogel materials. Contact angle test method: static contact angle measurement; medium: deionized water; volume: 2 μL . For the water absorption test method, consistent volume samples of BC and CA-BC aerogel materials were cut, and their dry weights were recorded. The samples were placed in beakers of the same size containing 50 mL of deionized water. After 0.5 h, 1 h, and 24 h, the samples were removed, the surface moisture was wiped off with filter paper, and the samples were then weighed to calculate the water absorption capability at different times. The formula for the water absorption calculation is as follows:

$$\text{Water absorption} = \frac{m_{\text{wet}} - m_{\text{dry}}}{m_{\text{dry}}} \times 100\%$$

where m_{dry} is the sample mass under the dry condition and m_{wet} is the sample mass after water absorption.

Nicotine release experiment

The nicotine dissolution test of the BC, CA-BC aerogels and commercial oral tobacco products was carried out via a previously described laboratory research method with slight improvements (20–22). A real-time alkaloid dissolution detector (Fucosi FODT-101, Shanghai, China) was used in the nicotine dissolution experiment. 150 mg of the loose test sample (unportioned) was placed in a 10 cm^3 dissolution cell, with a receiving pool containing 100 mL of ultrapure water. Since components (e.g., impurities) may generate interference in the detection accuracy of conventional single-wavelength method, this detection module was replaced with a three-wavelength synchronous detection system. This improvement enabled multi-wavelength signal correction to effectively eliminate interference, thereby significantly enhancing measurement reliability. The test conditions were as follows: the dissolution flow rate was 2 mL/min, the constant temperature bath was maintained at 37 °C, and the optical fibre probe was equipped with a width of 1 mm. The detection wavelength was 260 nm, the reference wavelength was 550 nm, and the second reference wavelength was 320 nm. The detection frequency was once every 5 seconds. The described nicotine quantification method was applied to test both the total nicotine content in the aerogel matrix and the released nicotine during dissolution process.

Method establishment and verification

To establish a standard working curve for nicotine according to the method mentioned above, standard nicotine solutions with concentrations of 9.1, 18.2, 36.4, 45.5, 91, and 182 $\mu\text{g/mL}$ were prepared. Standard sample testing was conducted, and the lowest concentration standard solution was measured ten times consecutively. The standard deviation (SD) of these ten results was used to determine

Table 1. Operating curve regression equation, LODs, and LOQs of nicotine.

Target	Linear range ($\mu\text{g} \times \text{L}^{-1}$)	Linear regression equation	R^2	LODs ($\text{ng} \times \text{mL}^{-1}$)	LOQs ($\text{ng} \times \text{mL}^{-1}$)
Nicotine	9.1–182	$y = 0.002826x - 0.0017$	0.9999	95	316

the method's limit of detection (LOD) and limit of quantitation (LOQ), which were 3 SD and 10 SD, respectively. The resulting working curve is presented in Table 1.

The regression equation for nicotine showed good linearity and is suitable for quantitative analysis. The low LOD and LOQ of this method indicate that it has high sensitivity, making it effective for detecting and quantifying the nicotine content even at a relatively low level.

BC aerogels with known nicotine contents were selected and spiked with nicotine at three different concentrations: low, medium, and high. Six replicates were tested for each level. After spiking, nicotine dissolution tests were performed on the samples according to the method mentioned above, and tests were conducted continuously for six days. The method precision was calculated via the relative standard deviation (RSD), and recovery rates were calculated based on the original content, added amount, and measured amount. The results are presented in Table 2.

Table 2 indicates that the method's spike recovery rate ranges between 93.5% and 105%. The intraday precision ranged from 0.6% to 1.5%, and the interday precision ranged from 0.9% to 2.1%. These results demonstrate that the method is sufficiently precise and accurate to meet the quantitative requirements of this study.

Microscopic morphology observation

The BC and CA-BC aerogels were characterized via scanning electron microscope (SEM) (EVO10, Zeiss, Jena, Germany). After freeze-drying, the sample was glued to conductive tape. The sample was placed in a vacuum sputtering device, and gold was applied to the surface for 1 min. The sample was then inserted into a SEM at an observation voltage of 5 kV for observation and photography.

RESULTS AND DISCUSSION

Material preparation

The appearance of the prepared material is shown in the Figure S1 of the [supplementary information](#). Figure S1a shows the CA-BC aerogel material without tobacco extract, and the overall appearance of the material is white. Figure S1b shows the appearance of CA-BC after tobacco extract is added, and the material shows a light-yellow

colour caused by tobacco components. During the preparation process, the yield of BC obtained by fermentation was approximately 2 g/L, and the solid content of CA-BC obtained by crosslinking was approximately 2.07%. BC materials and CA-BC materials with different nicotine contents (2.0%, 1.6%, 1.0%, 0.4%, 0.2%) were prepared by adding different quantity of the tobacco extract.

Chemical composition analysis

Figure 2a shows the crosslinking reaction route of BC and CA. As shown in Figure 2b and Table 3, the peak near at 3400 cm^{-1} was generated by the stretching vibration of $-\text{OH}$. The hydrogen-bonding effect in the BC aerogel was almost the strongest, so that a peak appears at a lower wavenumber of 3381 cm^{-1} . After crosslinking with CA, some hydrogen bonds in BC were broken, the peaks moved towards the high wavenumber of 3417 cm^{-1} , and the spectral band half-peak width turned narrower. The peaks at approximately 2923 cm^{-1} and 2848 cm^{-1} were attributed to the stretching vibrations of the aliphatic alkane $\text{C}-\text{H}$ bonds and were observed in all of the materials. The locally amplified peak (Figure 2c) at 1704 cm^{-1} was generated by the stretching vibration of carbonyl $\text{C}=\text{O}$ in the ester bond structure, which confirmed the formation of the ester structure after crosslinked with CA, but the peak was not easy to observe because of its low intensity and was covered by the peak at 1645 cm^{-1} . The peak at 1645 cm^{-1} corresponded to the stretching vibration of carboxycarbonyl $\text{C}=\text{O}$. Several peaks between 1000 cm^{-1} and 1200 cm^{-1} might be attributed to the cellulose structure, where peaks at 1058 cm^{-1} and 1110 cm^{-1} were generated by the stretching and bending vibrations of the $\text{C}-\text{O}$ bond in the $\text{C}-\text{O}-\text{C}$ group. The peaks at 1031 cm^{-1} and 1163 cm^{-1} were related to the stretching vibration of the $\text{C}-\text{O}$ bond in the $\text{C}-\text{OH}$ group. The BC and CA-BC aerogels were titrated to obtain the actual CA content of the material, and the titration results are shown in Figure 2d, where the crosslinking efficiency was the actual CA content/CA input and the actual CA/BC ratio was the actual CA content/BC content. The results showed that the actual CA content of 1% CA-BC $\sim$ 20% CA-BC was close to the theoretical CA content, the crosslinking efficiency was greater than 92%, and the actual crosslinking ratio was similar to the theoretical crosslinking ratio. The actual CA contents of the 50% CA-BC and 100% CA-BC materials were significantly

Table 2. Test for precision, repeatability, and stability of the method.

Target	Primary content (μg)	Additive quantity (μg)	Detection value (μg)	Average recovery (%)	Intraday RSD (%)	Interday RSD (%)
Nicotine	3152	1500	4349.6	93.5	1.4	2.1
		3000	6459.6	105	1.5	1.9
		6000	9518.0	104	0.6	0.9

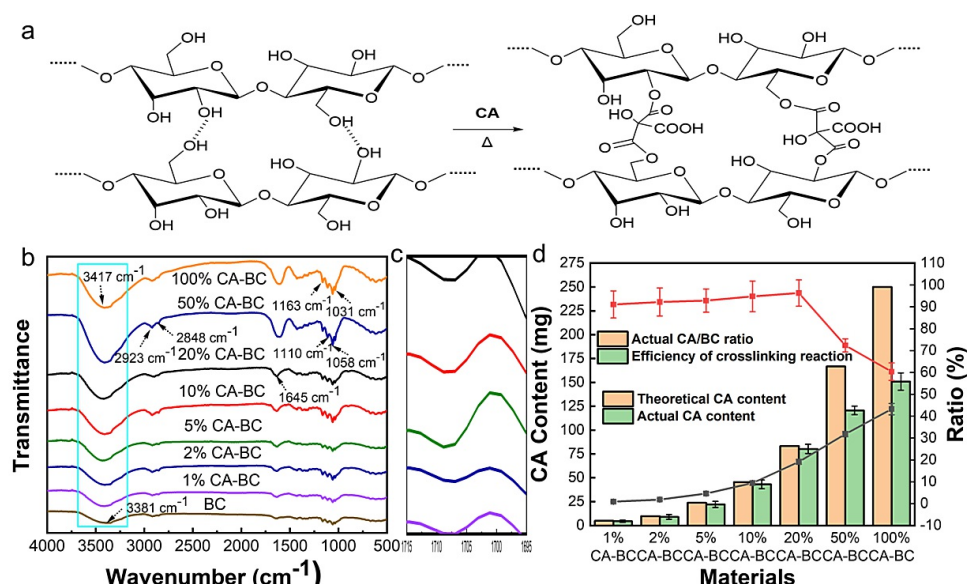


Figure 2. Synthesis route of BC and CA crosslinking (a). FTIR spectra of aerogels (b) and partially enlarged image (c). The theoretically calculated and experimentally measured CA contents of the materials (d).

lower than the theoretical CA content, indicating that there was a limit to the CA binding of BC through crosslinking reactions and that the theoretical 100% crosslinking ratio was only 42% of the actual crosslinking ratio using this specific method.

Thermogravimetric analysis

Figure 3 shows the thermogravimetric (TG) and derivative thermogravimetric (DTG) curves of different materials. Figure 3 shows that different materials exhibited similar thermogravimetric processes, and the TG curves were composed of three stages. The first stage was the drying stage, and the temperature range was 35–100 °C. In this stage, the mass of all the materials decreased slightly, and the weight loss rate was almost unchanged, mainly because of the evaporation of physically adsorbed water in the material. The weight loss observed between 100–250 °C was caused by the volatilization of small-molecule compounds adsorbed on the material. Since the mass loss was negligible, this temperature range was not considered as part of the material's main decomposition stages. The second stage was the rapid pyrolysis stage of the material. The temperature range was 250–460 °C, which was mainly the breakage of the glucoside bonds in the cellulose structure, as well as some C–O bonds and C–C bonds,

resulting in new compounds and volatile compounds with low molecular weights. In this stage, the maximum weight loss temperature of the CA-BC material shifted to the high-temperature region, and the shift increased with CA content increasing.

The DTG curve (Figure 3b) shows that the CA-BC material had a lower weight loss rate than that of the BC material, which indicated that the CA-BC material had better thermal stability because of more ester bonds. The third stage was the post cracking stage. When the temperature reached 460 °C, the thermal cracking of most substances in this stage ended, the carbonization of residual materials mainly began to occur, and the pyrolysis rate did not change much.

Water absorption analysis

The water absorbency and surface wettability of the material may influence its nicotine release behavior. Higher water absorbency could accelerate nicotine dissolution and release by facilitating water uptake, at the same time, higher surface wettability reflects stronger hydrophilicity, which might similarly promote water absorption and subsequent nicotine release.

Characterization of these two properties helps to elucidate the differences in nicotine dissolution behavior among materials. The water absorbency and surface wettability for

Table 3. FTIR peak wavenumbers, assignments, and interpretations.

Wavenumber (cm^{-1})	Assignment	Interpretation
3381–3417	–OH stretch vibration	Hydrogen bond reduction after crosslinking
2923, 2848	C–H stretch vibration	Aliphatic groups present in all materials
1704	C=O stretch vibration	Ester bond formation after crosslinking
1645	C=O stretch vibration	Carboxycarbonyl group
1058, 1110	C–O–C stretch and bend vibration	Cellulose backbone structure
1031, 1163	C–OH stretch vibration	Hydroxyl groups in cellulose

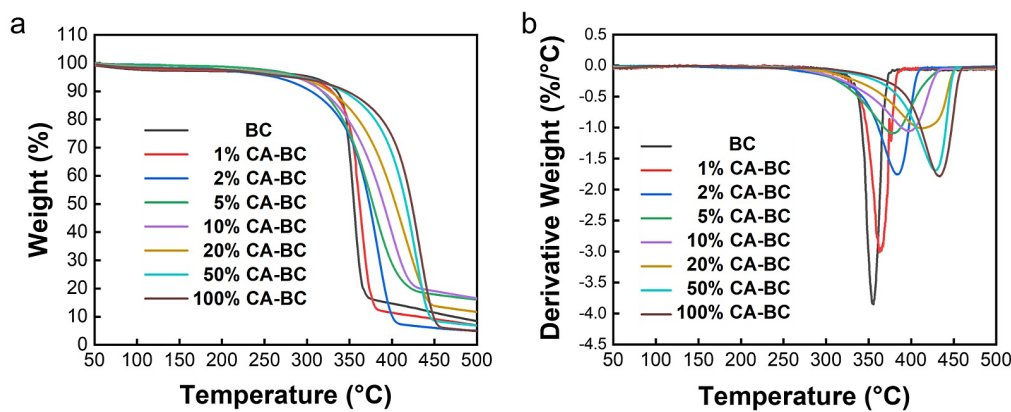


Figure 3. TG curves of BC aerogel material and CA-BC aerogel materials (a). DTG curves of BC aerogel material and CA-BC aerogel materials (b).

the BC and CA-BC aerogels are shown in Figure 4. The water absorption capability of all the samples was greater than 1800%, indicating excellent water absorption ability (Figure 4a). The sample basically reached equilibrium for water absorption at 0.5 h and then absorbed little water. The water absorption capability of the CA-BC material was lower than that of the BC material, and the water absorption ability decreased with increasing CA content, as the material changed from 1% CA-BC to 100% CA-BC, its water absorption decreased from 3381% to 2220%.

On the one hand, the material's reduced hydrophilicity perhaps caused by cyclic hydrogen-bonded structures formed among hydroxyl, carboxyl and carbonyl groups, which restricted their ability to form hydrogen bonds with water molecules. On the other hand, the free movement of the polymer molecular chain was hindered by an increase in the number of covalent bonds between CA and BC after

crosslinking. This resulted in the reduced diffusion of water in CA-BC (23). The results and photos of the contact angle experiment are shown in Figure 4b–4f. The contact angle of all the materials was less than 90°, indicating that the material was hydrophilic. With increasing CA content in the material, the contact angle increased from 46.6° to 66.1°, which was mainly caused by the decrease in the number of hydrophilic hydroxyl groups.

Nicotine dissolution test

In accordance with the methods mentioned above, nicotine dissolution tests were conducted on the BC and CA-BC aerogels, and the results are shown in Figure 5. Figure 5a presents the nicotine dissolution curves of the BC and CA-BC materials. The dissolution curves indicated that the dissolution process of all the materials included two stages: the rapid nicotine dissolution and a subsequent deceleration

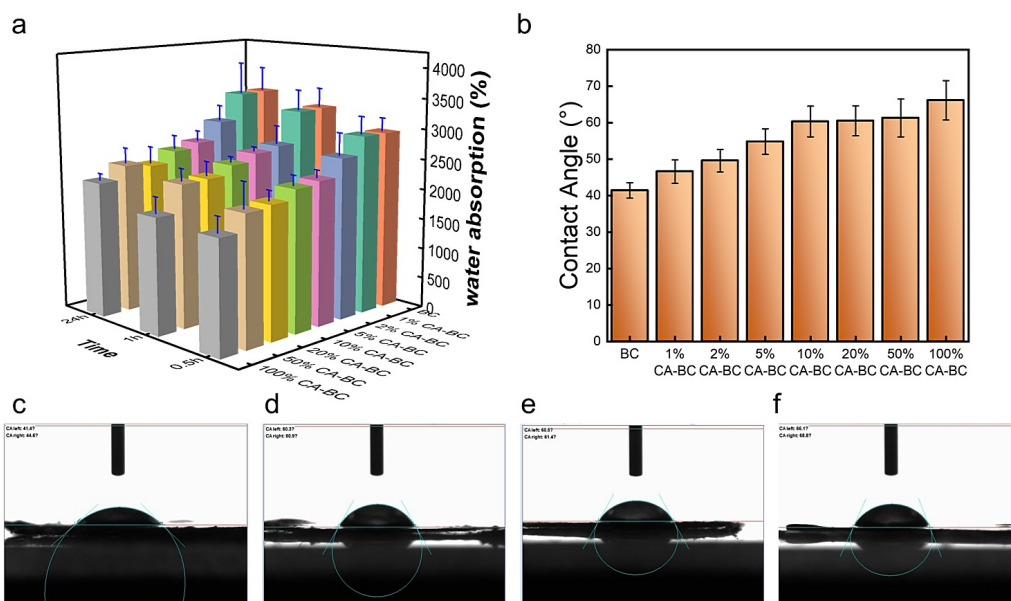
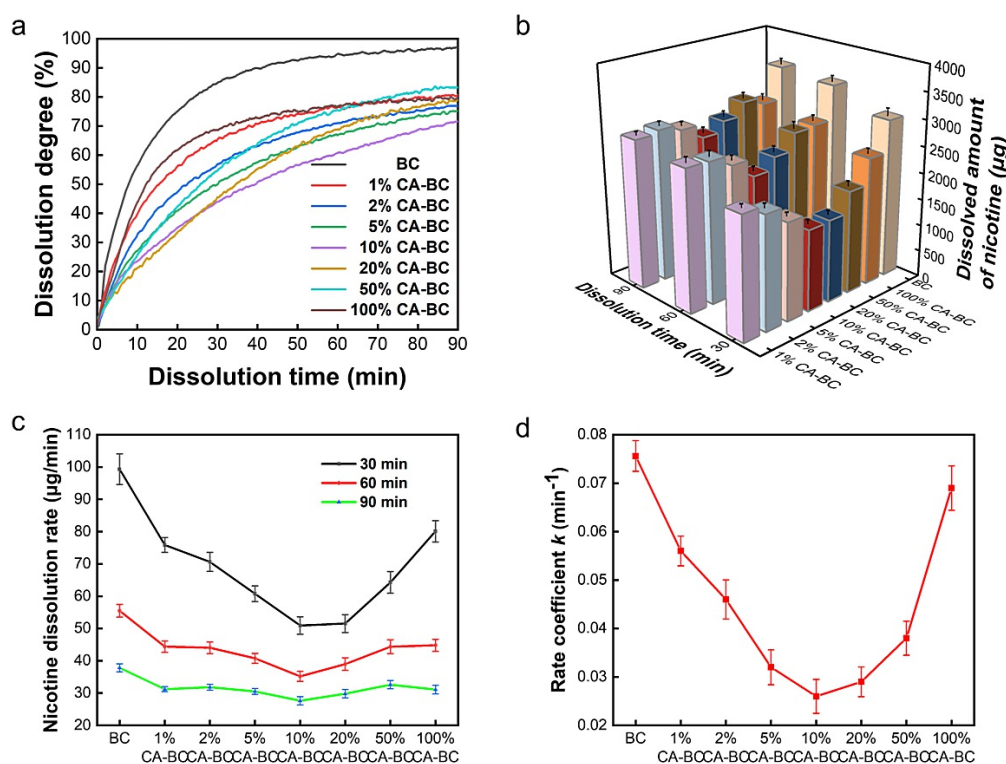


Figure 4. Contact angle of water (a) and water absorption (b) for BC and CA-BC aerogels, and photos acquired after stable droplet deposition of BC (c), 10% CA-BC (d), 20% CA-BC (e) and 100% CA-BC (f).



phase. The rapid dissolution phase of nicotine concluded within the first 30 min, during which the materials were infiltrated by the dissolution medium, and nicotine quickly diffused from the materials into the medium. At this stage, all the materials exhibited rapid nicotine dissolution, but the nicotine dissolution rate of the crosslinked materials was significantly slower than that of the uncrosslinked materials. Differences existed in the nicotine dissolution curves of materials with varying crosslinking ratios, with an increasing proportion of CA in the materials resulting in the dissolution curve first flattening and then steepening. The steepest dissolution profile observed in 100% CA-BC could be attributed to its highly crosslinked matrix, in which pore structure seemed to be too large to sustain nicotine release. The large porous architecture failed to provide sufficient diffusion path restriction for nicotine molecules, resulting in their rapid initial burst release (24). The slowing phase of BC material dissolution was relatively short, quickly reaching a plateau, whereas the deceleration phase for CA-BC materials was more pronounced, with 10% CA-BC material demonstrating sustained dissolution capability. Figure 5b and Figure 5c show the cumulative nicotine dissolution amount and the average nicotine dissolution rates of the materials at different dissolution times. The nicotine release from BC material was 3405 μg , whereas for CA-BC materials, it ranged from 2487 μg to 2935 μg , significantly lower than that of BC material. The results indicated that the cumulative nicotine dissolution amount of CA-BC materials was lower than that of BC materials at the same time point, particularly during the first 30 min, where the majority of nicotine was dissolved, demonstrating a significant

$$F(t) = F_{\max}(1 - e^{-kt}^\beta)$$

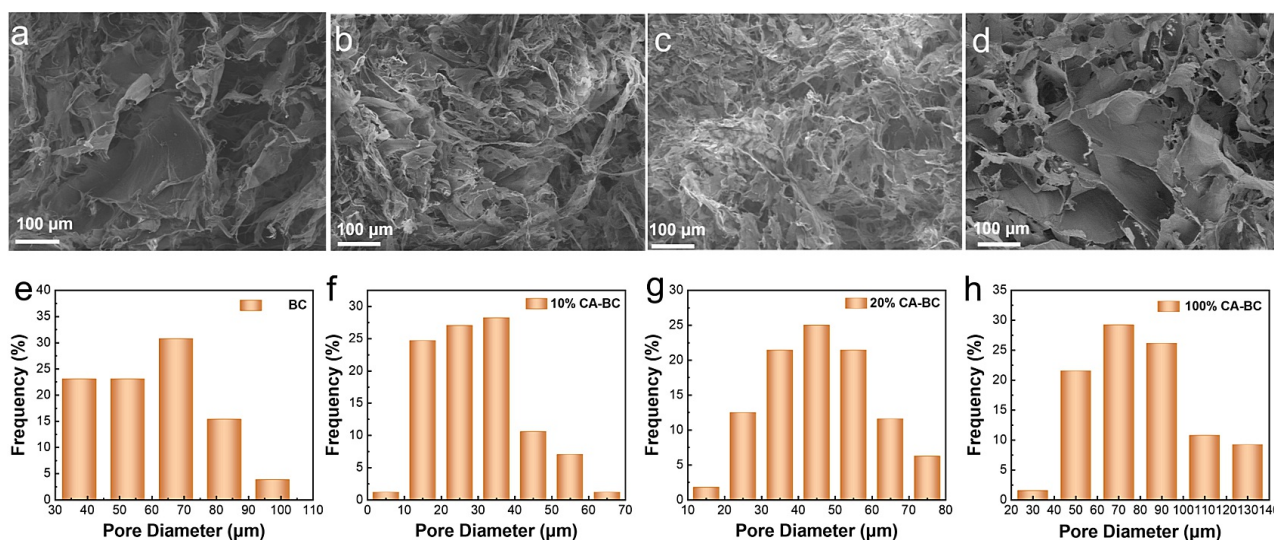


Figure 6. SEM images of BC (a), 10% CA-BC (b), 20% CA-BC (c), and 100% CA-BC (d) aerogels; the pore size distributions of BC (e), 10% CA-BC (f), 20% CA-BC (g), and 100% CA-BC aerogels (h).

strated a decrease in the coefficient, with the minimum k value of 0.0260 observed at 10% CA-BC, representing a 66% reduction from the BC material. For the CA-BC materials, the k value initially decreased and then increased as the CA proportion rose. This finding was consistent with the previous discussion, indicating that the 10% CA-BC material had the optimal nicotine sustained-release effect. The observed dissolution rate differences among materials may be caused by their distinct structural architectures. Compared to pristine BC, crosslinked CA-BC appeared to form a more complex micro-network structure, potentially explaining the 50% reduction in nicotine release rates. The crosslinking reaction between CA and BC generated ester bonds, thereby altering the original fiber network structure. The stable ester bonds connected cellulose chains, forming a mesh-like structure. These networks were proposed to simultaneously restrict nicotine diffusion through tortuous pathways while maintaining sufficient interconnected channels for constant release.

Micromorphology analysis

To further investigate the relationship between the internal structure of different materials and their nicotine release rates, scanning electron microscopy (SEM) was used to characterize the morphology of the materials. Figure 6a–6d show the difference in the microscopic structures between the BC aerogel and CA-BC aerogel (Figure 6 shows the SEM images of four materials, and the SEM images of all eight materials are shown in the [supplementary Figure S2](#)). The BC aerogel exhibited a two-dimensional irregular sheet-like structure, where cellulose fibres were connected through high-density hydrogen bonds to form fibre sheets. However, the weak hydrogen bonding forces were insufficient to effectively connect these fibre sheets, resulting in large intersheet gaps in the BC aerogel material. This structure was ineffective at constraining nicotine, allowing nicotine to quickly dissolve through these gaps. In contrast, the SEM images of CA-BC show that after crosslinking

BC with citric acid (CA), the original sheet-like structure transformed into a clustered structure. This was attributed to the formation of ester bonds between CA and BC, which were stronger than the hydrogen bonds within BC itself. As a result, the sheet-like structure formed by hydrogen bonding in BC was disrupted and reformed into a clustered structure. This clustered structure reduced large pores within the structure, resembling a net that constrains nicotine release. This network structure was most prevalent in materials with 5% CA-BC, 10% CA-BC, and 20% CA-BC, which explains why these three materials exhibited the most significant sustained-release effect for nicotine. However, as the CA content further increased, excessive ester bond formation led to overly dense fibre clusters, reverting to a sheet-like structure. This typical structure of BC contained large intersheet gaps and pores, which failed to effectively constrain nicotine. Therefore, materials with high CA contents, particularly the 100% CA-BC material, exhibited a weaker sustained-release effect for nicotine. The analysis of the pore size distribution across different materials was conducted using ImageJ software following scanning electron microscopy imaging.

The results are shown in Figure 6e–h (Figure 6 shows the aperture statistics of four materials selected, and the aperture statistics of all eight materials are shown in the [supplementary Figure S3 and Figure S4](#)). In the range of ~ 40 – 100 μm , the pores of the BC material were mainly distributed at approximately 70 μm (the average pore diameter is 63 μm). Crosslinking BC with CA increased the connectivity between polymer chains, resulting in reduced pore sizes with a predominant distribution range of 10 – 80 μm for 1% CA-BC, 2% CA-BC, 5% CA-BC, 10% CA-BC, and 20% CA-BC (with average pore size of 52 μm , 42 μm , 40 μm , 30 μm , and 46 μm , respectively). The smaller pore sizes contributed to a slower dissolution rate of solutes, partially explaining the ability of the materials to modulate nicotine release. Higher crosslinking ratios (50% and 100%) increased the fibre density, leading to the formation of larger pores between 80 – 140 μm (the

Table 4. Dissolution results of BC and 10% CA-BC at different nicotine contents.

Material	Dissolution parameters	Nicotine content (%)				
		2.0	1.6	1	0.4	0.2
10% CA-BC	Dissolution degree (%)	72.19	74.47	87.03	96.77	98.62
	Rate coefficient k (min^{-1})	0.0345	0.0513	0.0536	0.0728	0.0905
	Nicotine dissolution amount (μg)	2165.7	1787.3	1305.5	580.6	295.9
BC	Dissolution degree (%)	97.59	99.93	98.45	98.21	98.60
	Rate coefficient k (min^{-1})	0.1546	0.1540	0.1236	0.1230	0.1467
	Nicotine dissolution amount (μg)	2927.7	2398.3	1476.8	589.3	295.8

average pore diameters were 68 μm and 81 μm , respectively), which facilitated faster solute release.

Validation experiments at different nicotine content levels

To further validate the sustained release effect of nicotine from the materials, BC with different nicotine contents were used as the control group, while 10% CA-BC aerogel materials with varying nicotine contents were used as the experimental group. Dissolution experiments were conducted on materials with five different nicotine contents, and the results were fitted using the Weibull model. The nicotine dissolution curves of the samples are shown in the [supplementary Figure S5](#), and the dissolution extent and dissolution rate coefficient k are presented in the Table 4. Figure S5 shows that at all five nicotine contents, the BC material always exhibited a steeper dissolution curve. Table 4 shows that at the same nicotine content, the rate coefficient k of 10% CA-BC was always lower than that of BC, indicating that the 10% CA-BC material demonstrated a slower release effect regardless of the nicotine content. The amount of nicotine dissolved in 10% CA-BC aerogel was found to be $2\text{--}15 \text{ mg} \times \text{g}^{-1} \times \text{h}^{-1}$ when it was dropped into the collection cup. It is worth noting that in the previous work, the released amount of nicotine during the first 60 min was $4\text{--}15 \text{ mg/g}$ for commercial oral tobacco products (20, 25). As such, the amount of nicotine released by this novel sustained-release CA-BC material can meet practical requirements. Additionally, as the nicotine content decreased, the k value of the 10% CA-BC material gradually increased, approaching that of the BC material. The k value decreased from 0.0905 to 0.0345 indicated that the slow-release effect of nicotine in the 10% CA-BC material was influenced by the nicotine content within the material, allowing for the modulation of the release rate by adjusting nicotine levels.

Mechanism explanation

Given the above, the 10% CA-BC aerogel material exhibited different nicotine release rates at different nicotine contents. To further explore the relationship between nicotine content and release rate, as well as the underlying causes, a unified analysis was conducted on the dissolution curves of 10% CA-BC materials with nicotine contents of 2%, 1.6%, 1%, 0.4%, and 0.2%.

Figure 7a and Figure 7b show that as the nicotine content decreased, the degree of dissolution tended to increase, indicating that materials with lower nicotine contents were

more likely to release nicotine completely. Additionally, as the nicotine content decreased, the dissolution curves became steeper. The fitting results of the Weibull model (Figure 7c) show that as the nicotine content decreased, the dissolution rate coefficient of the material increased from 0.0345 to 0.0905. Since the materials were prepared using the same crosslinking ratio, explaining the differences caused by nicotine content on the basis solely of structural considerations was challenging. Therefore, an attempt was made to explain these differences based on the mechanism of nicotine release. During dissolution testing, distinct surface swelling deformation was observed, necessitating the application of the Gallagher-Corrigan model to analyze these dynamic morphological changes. The Gallagher-Corrigan model is particularly applicable to biphasic dissolution processes in swellable polymeric materials like CA-BC aerogel, as well as other complex systems undergoing swelling and/or degradation in release media. It accounts for an initial phase of rapid solute release followed by a second, slower release phase owing to polymer degradation mechanisms. The equation describing the Gallagher-Corrigan model is as follows:

$$F = F_{\max}(1 - e^{-k_1 t}) + (F_{\max} - F_B) \left(\frac{e^{k_2 t - k_2 t_{\max}}}{1 + e^{k_2 t - k_2 t_{\max}}} \right)$$

$F_{\max}$ represents the final nicotine dissolution extent over the entire duration, F_B represents the proportion of nicotine released in the first stage, $t_{\max}$ represents the time at which the maximum release rate occurs in the second stage, and k_1 and k_2 are the kinetic constants for the first and second stages, respectively. The Gallagher-Corrigan model fitting results are shown in Figure 7d. As the nicotine content decreased, the proportion of the first stage (F_B) in the dissolution process increased from 42.37% to 91.12%. This indicated that the lower the nicotine content in the material was, the greater the proportion of nicotine released by diffusion in the first stage, leaving less nicotine available for release during the polymer relaxation-controlled second stage. This explains why a lower nicotine content led to a higher release rate coefficient. The Gallagher-Corrigan model consists of a rapid solute release diffusion stage and a slower polymer relaxation stage. When the nicotine content in the material was low, most of the nicotine was released during the diffusion stage, resulting in an overall steeper dissolution curve. The kinetic constants of the two stages also support this view. As the nicotine content

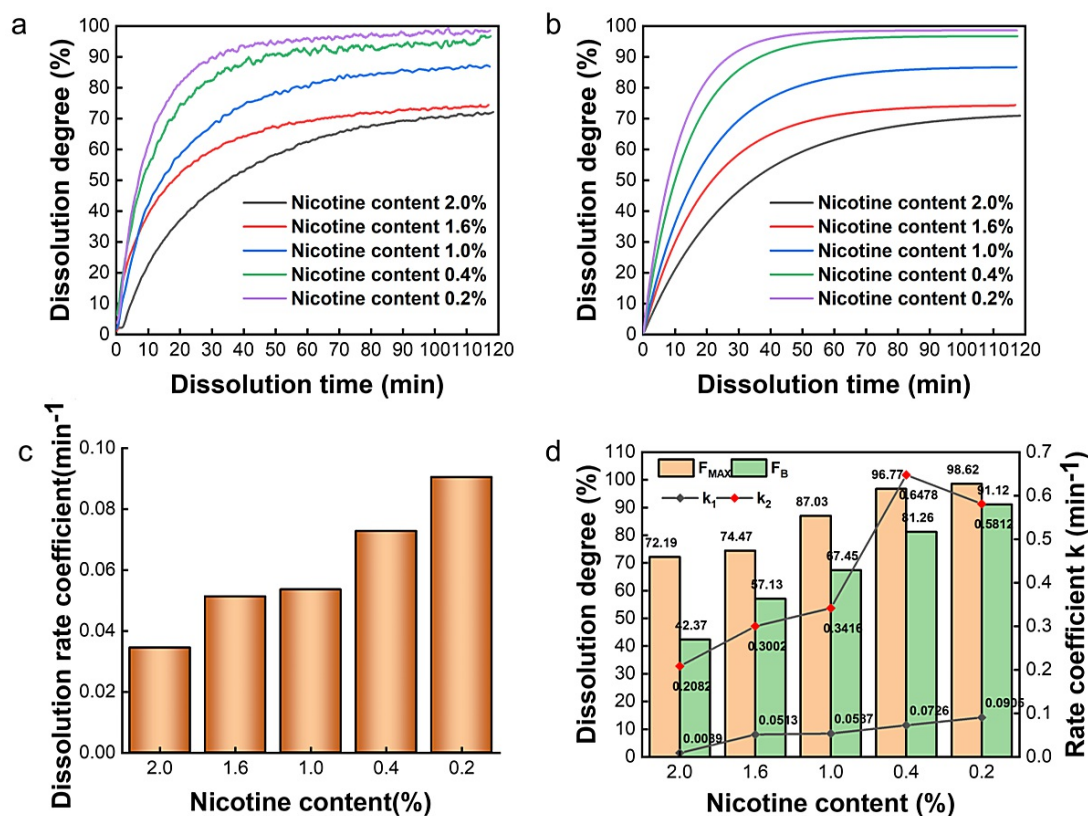


Figure 7. Dissolution curves of 10% CA-BC materials with 0.2%–2.0% nicotine contents (a), fitting curves of the Weibull model to the dissolution results (b), histogram of the dissolution rate coefficient k fitted by the Weibull model (c), and parameter statistics obtained by fitting the Gallagher-Corrigan model (d).

decreased, the dissolution rate coefficients k_1 and k_2 both increased, with k_1 rising from 0.0089 to 0.0905 and k_2 from 0.2082 to 0.5812. This indicated an acceleration in nicotine dissolution from the material.

The dissolution profiles of BC aerogel and CA-BC aerogels with the same nicotine content were fitted using the Gallagher-Corrigan model, and the fitting results are presented in Table 5. $F_B/F_{\max}$ represents the proportion of the initial rapid-release phase relative to the total release process. The results show that all CA-BC materials exhibited lower $F_B/F_{\max}$ values than BC, with the 5%–20% CA-BC group displaying the smallest initial release fraction and the lowest dissolution rate constants (k_1 and k_2), indicating optimal sustained-release performance under the Gallagher-Corrigan model. Combined with the earlier discussion on microstructure, the superior release kinetics of 5%–20% CA-BC aerogels could be attributed to their three-dimensional fiber networks, which effectively restricted nicotine diffusion (reducing k_1) while enabling controlled release through the swelling of aerogel (modulating

k_2). Insufficient crosslinking ($CA/BC < 5\%$) resulted in a discrete network, whereas excessive crosslinking ($CA/BC > 20\%$) led to inter-sheet gaps that facilitate rapid nicotine release. By precisely tuning the CA/BC ratio (5%–20%), the chemical crosslinking, porous structure, and swelling behavior of the material could be synergistically optimized, allowing precise regulation of nicotine release kinetics.

Comparative analysis with commercial products

As discussed previously, the CA-BC aerogel could modulate nicotine dissolution profiles to achieve sustained-release properties. To validate this improvement, dissolution testing was performed comparing the optimized 10% CA-BC aerogel with two commercial oral tobacco products. The dissolution profiles (Figure 8a) demonstrate that the 10% CA-BC aerogel exhibited the most gradual dissolution kinetics, releasing only 912.6 mg of nicotine after 10 min – significantly less than the commercial

Table 5. Model fitting results for dissolution profiles of BC and CA-BC aerogels.

Parameters	BC	1% CA-BC	2% CA-BC	5% CA-BC	10% CA-BC	20% CA-BC	50% CA-BC	100% CA-BC
$F_B/F_{\max}$	0.9987	0.9721	0.9253	0.9077	0.8444	0.8059	0.9281	0.9812
k_1 (min^{-1})	0.0849	0.0538	0.0352	0.0280	0.0201	0.0213	0.0304	0.0720
k_2 (min^{-1})	1.6163	0.8050	0.8014	0.7539	0.5947	0.5922	0.5858	0.8796

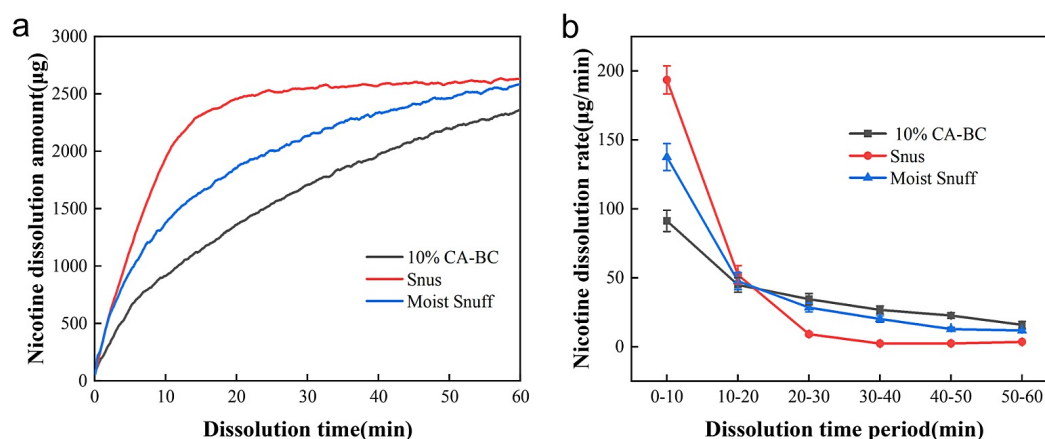


Figure 8. Nicotine dissolution amount profiles (a) and nicotine dissolution rates (b) of 10% CA-BC aerogel, snus, and moist snuff.

products (1935.9 mg and 1376.2 mg), confirming effective suppression of the initial burst dissolution. Furthermore, the aerogel showed relatively stable dissolution behavior from 10 to 60 minutes. Analysis of dissolution rates reveals that the 10% CA-BC aerogel not only showed a lower nicotine dissolution rate than that of both commercial products but also displayed more stable dissolution kinetics throughout the dissolution process (Figure 8b). During 30–60 min, the 10% CA-BC aerogel maintained stable dissolution rates which were higher than those of the commercial products. These results demonstrate that the 10% CA-BC aerogel successfully prevented initial nicotine burst dissolution while maintaining controlled, prolonged nicotine delivery.

CONCLUSIONS

To achieve controlled nicotine release for modern oral nicotine products, this study synthesized aerogels as the nicotine carrier based on bacterial cellulose (BC) using aqueous extracts of tobacco dust waste and citric acid as crosslinker. The aerogels with added nicotine were characterized for their morphology, structure, and thermal stability, together with nicotine dissolution rates.

The results indicated that the aerogel materials exhibited a more sustained nicotine release, and the degree of this effect could be adjusted by modifying the CA feed ratio during material preparation. Moreover, the nicotine release rate can be further controlled by adjusting the nicotine content in the 10% CA-BC aerogel material. Compared with the BC aerogel, the CA-BC aerogel materials demonstrated better thermal stability and slightly lower water absorption. At the microscopic level, the cross-linked materials exhibited adjustable pore structure, forming a clustered network structure that reduced interlayer gaps and pore collapse. Pore size analysis also showed that the crosslinked materials had a narrower pore size distribution.

The novel aerogels prepared in this work could be used as a substrate for sustained nicotine release by backfilling tobacco extract. The prepared aerogels were also environmentally friendly due to recycling tobacco waste. It thus has the potential to be a candidate material for oral pouched nicotine products.

ETHICAL APPROVAL

This study does not involve human or animal research; therefore, ethical approval is not applicable.

DECLARATION OF INTERESTS

The authors disclosed no conflicts of interest related to this article.

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SUPPLEMENTARY INFORMATION

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