Pulse radiolysis study on aqueous solution of nicotine

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Abstract Nicotine has been studied for the first time by pulse radiolysis techniques. It has been found that hydrated electrons, hydrogen radicals and hydroxyl radicals can react with nicotine to produce anion radicals and neutral radicals, respectively, and the related rate constants have been determined.

Keywords Nicotine, Pulse radiolysis, Reaction kinetic

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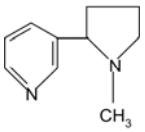
1 Introduction

Nicotine is an important alkaloid in Nicotiana. As a low-molecular weight substance with good lipid and water solubility, nicotine can easily be absorbed by skin, and transdermal nicotine as a replacement therapy is currently being used as an aid in smoking cessation.[1-3] Nicotine has peripherally stimulating effects, and its administration has been shown to enhance psychomotor performance and to increase blood pressure, heart rate, and cardiac output.[4-7] Nicotine is metabolized mainly by C-oxidation. Cotinine is the principal product, which is further oxidized to trans-3'-hydroxycotinine.[8,9] Other pathways of the nicotine metabolism include N-oxidation, N-demethylation and glucuronidation.[10] Several enzymes of the CYP-450 complex are purported to take part in nicotine metabolism: CYP2A6, 2B6, 2C9, 2D6, and 2E1. Since there has been no study about the chemical activity of nicotine up to now, this work will be the base to study other activities of nicotine deeply. By using the pulse radiolysis technology we have found that nicotine can react with hydrated electron, hydrogen radical and hydroxyl radical, and know the oxydoreduction reaction of nicotine, and further conclude the same reaction of nicotine with DNA, for there are a lot of groups like hydrated electron, hydrogen radical and hydroxyl radical in DNA. In experiments we have found there are four active groups in nicotine, which can react with hydrated electron, hydrogen radical and hydroxyl radical, respectively.

2 Experimental

The pulse radiolysis experiments were carried out on 10 MeV linear accelerator that delivered electron pulses with a duration of 8 ns. The average dose of a single electron pulse was 5~10 Gy determined by thiocyanate dosimetry. The analyzing light source was a 500 W xenon lamp, which could be intensified 100 times during the detecting period. The details were described elsewhere.[11]

The structure of nicotine can be expressed by



High purity nicotine, without impurities as detected by HPLC, was obtained from Germany, and t-BuOH was purified by distillation. All solutions were prepared with triply distilled water and deaerated with high purity nitrogen or nitrous oxide by bubbling for 20 min before used. Potassium hydroxide (AR), perchloric acid (AR) and some buffers were used to adjust the pH of the solution. All the experiments were carried out at room temperature.

3 Results and discussion

3.1 Reactions of hydroxyl radical with nicotine

In the pulse radiolysis of the aqueous solution containing 5×10^{-4} mol·L^{-1} nicotine at pH=7 saturated

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with nitrous oxide, the transient absorption spectra with two peaks at 320 nm and 460 nm were recorded at 5 μs and 50 μs as shown in Fig.1. In this solution, the yield of hydrogen atoms was very small at pH=7 and the hydrated electron was converted to OH radical by nitrous oxide. The transient spectra reflected the reaction of nicotine with hydroxyl radical.

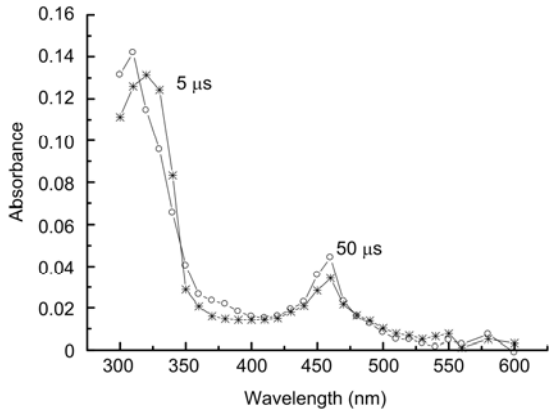

Fig.1 The transient absorption spectra of 5×10^{-4} mol·L^{-1} of nicotine with hydroxyl radical at pH=7 saturated with nitrous oxide.

By analyzing the kinetic at 320 nm and 460 nm, it is found that the transient species with maximum absorption at 320 nm and 460 nm are the same, as they follow the same decay rate constants of pseudo first-order kinetics. If we changed the concentration of nicotine under 10^{-3} mol·L^{-1} and analyzed the growth trace at 460 nm, a series of apparent growth rate constants were obtained. The absolute rate constants for the reactions of hydroxide radical with nicotine could be calculated from the slope by plotting the concentration of nicotine vs the apparent growth rate constants as listed in Table 1.

Table 1 The apparent rate constants for reaction of OH radical with nicotine determined at 460 nm. (K_{app} is the apparent rate constant and k is the rate constant)

C ($\times10^{-4}$ mol·L^{-1})	K_{app} ($\times10^{5}$ s^{-1})	k (L·mol^{-1}s^{-1}) ($\times10^{9}$
0.44	1.51	
0.66	1.86	
0.89	2.26	1.56
1.32	2.89	
1.78	3.24	

If the irradiated doses increased at the same concentration of nicotine, we found that the transient species observed at 460 nm decayed fast as shown in Fig.2. It could be suggested that the bimolecule decay of transient species play more important role at higher concentration . The reaction mechanism for OH radical with nicotine could be summarized as follows:

$$H_2O \xrightarrow{\text{ionizing}} e_{aq}, OH, H$$

$$e_{aq}^- + N_2O \rightarrow N_2 + OH + OH^-$$

$$\text{Nicotine} + OH \longrightarrow [\text{Nicotine}]^\bullet + H_2O$$

$$[\text{Nicotine}]^\bullet + [\text{Nicotine}]^\bullet \longrightarrow [\text{Nicotine}]_2$$

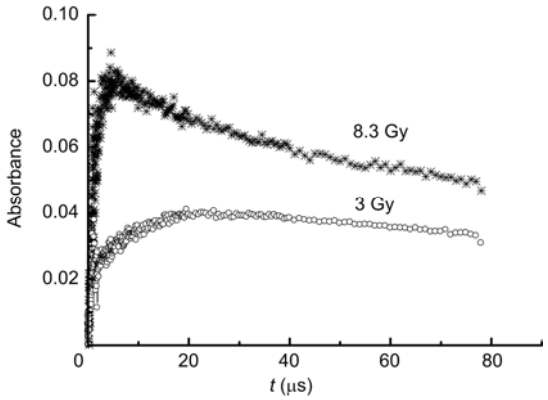

Fig.2 The growth and decay traces at different doses for 1×10^{-1} mol·L^{-1} nicotine solution at 460 nm saturated with nitrogen.

3.2 Reactions of hydrated electron with nicotine

In the pulse radiolysis of the aqueous solution containing 5×10^{-4} mol·L^{-1} of nicotine and 0.1 mol·L^{-1} of t-BuOH at pH=7 deaerated with purity nitrogen, transient absorption spectra with two peaks at 310 nm and 460 nm recorded at 5 μs and 50 μs shown in Fig.3 were observed. At 1 μs we saw another absorption peak after 600 nm. If the solution was saturated with nitrous oxide, these transient absorption spectra mentioned above disappeared completely. Since OH radicals produced in the irradiated water were scavenged by t-BuOH, the transient species observed at 310 nm and 460 nm should be assigned to anion radicals of nicotine due to the addition of hydrated electron, and the transient species after 600 nm should be hydrated electrons. Comparing the build-up and decay kinetic at 310 nm and 460 nm, we found that the growth and decay process were the same, so we concluded that both of them were the same transient species. The reaction mechanism could be written as below:

$$H_2O \xrightarrow{\text{ionizing}} e_{aq}^-, OH, H$$

$$OH + \text{t-BuOH} \longrightarrow \text{t-BuO}^\bullet + H_2O$$

$$e_{aq}^- + \text{Nicotine} \longrightarrow [\text{Nicotine}]^-$$

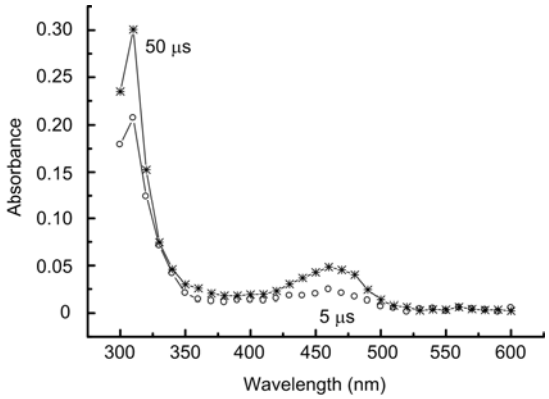

Fig.3 The transient absorption spectra of 5×10^{-4} mol·L^{-1} of nicotine solution with hydrated electron saturated with nitrogen.

With the change of dose (*D*), we found the apparent growth rate constant of the transient species not changed. So we concluded that the formation trace followed the pseudo first-order kinetics. We also changed the concentration of these samples under 1×10^{-3} mol·L^{-1}, obtaining a series of apparent decay rate constants of e^-_{aq} at 600 nm. Since the apparent formation rate constants of the transient species of nicotine are equal to the decay rate constants of e^-_{aq} at 600 nm, we can plot the concentration of nicotine vs the apparent growth rate constants of the transient species, and the slope value is the rate constant for the reaction of hydrated electrons with nicotine as listed in Table 2.

Table 2 The rate constants for reaction of e^-_{aq} with nicotine at 460 nm

C ($\times10^{-4}$ mol·L^{-1})	K_{app} ($\times10^{6}$ s^{-1})	k ($\times10^{9}$ L·mol^{-1}s^{-1})
0.18	1.05	
0.35	1.32	
1.42	1.73	3.61
2.13	2.13	
3.55	2.45	

3.3 Reactions of hydrogen atom with nicotine

The aqueous solution containing 5×10^{-3} mol·L^{-1} nicotine and 0.1 mol·L^{-1} t-BuOH was saturated with nitrogen at pH=1. Since hydrated electrons and OH radicals were scavenged by H^+ and t-BuOH respectively and only hydrogen atoms could remain in the solution after the pulse radiolysis, the transient species with maximum absorption at 340 nm and 420 nm as shown in Fig.4 can be assigned to the H adduct radicals of nicotine. The reaction process in this case can be described in the following:

$$H_2O \xrightarrow{\text{ionizing, pH = 1}} H, OH$$

$$OH^{\bullet} + \text{t - BuOH} \rightarrow \text{t - BuO}^{\bullet} + H_2O$$

$$H^{\bullet} + \text{Nicotine} \rightarrow [\text{Nicotine - H}]^{\bullet} \longrightarrow P$$

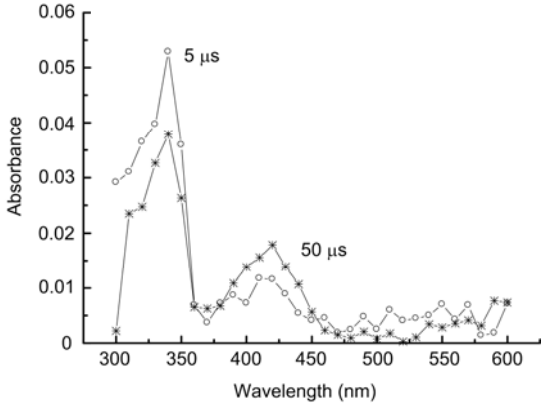

Fig.4 The transient absorption spectra of 5×10^{-3} mol·L^{-1} of nicotine solution with hydrogen radical saturated with nitrous oxide at pH=1.

The rate constant for the adduct reaction of hydrogen to nicotine can be obtained with the same method mentioned above. The transient species at 340 nm form and decay fast, while the species at 420 nm form slowly, which means that the transient species at 420 nm form with the decay of the species at 340 nm, with the reaction mechanism mentioned above. The results obtained are listed in Table 3.

Table 3 Rate constants for reactions of hydrogen atoms with nicotine at 340 nm and 420 nm

λ (nm)	C (mol·L^{-1})	K_{app} ($\times10^{5}$s^{-1})	k ($\times10^{7}$ L·mol^{-1}s^{-1})
340	0.002	1.36	
	0.01	2.35	
	0.025	4.11	1.01
	0.05	6.87	
	0.1	11.8	
420	0.002	0.418	
	0.01	0.51	
	0.025	0.613	0.0663
	0.05	0.75	
	0.1	1.09	

4 Conclusion

In the pulse radiolysis of the aqueous solution of nicotine, all of primary irradiated products of water, hydrated electron, hydroxide radical and hydrogen atom, can react with nicotine to produce anion radical, hydrogen abstraction radical and hydrogen adduct radical. Related rate constants for these reactions have been determined. The further reactions of these transient species of nicotine need to be explored to study its exact role in biological metabolism of human.

References

1 Florek E, Piekoszewski W, Wrzosek J. Pol J Pharmacol, 2003, **55**(1): 97-102

2 Svensson CK. Clin Pharmacokinet, 1987, **12**: 30-40

3 Palmer KJ, Buckley MM, Faulds D *et al*. Drugs, 1992, **44**: 498-529

4 Sherwood N, Kerr JS, Hindmarch I *et al*. Psychopharmacology, 1992, **108**: 432-436

5 Pritchard WS, Robinson JH, Debethizy JD *et al*. Psychophysiology, 1995, **32**: 19-27

6 Chen G Q, Lin B Z, Dawson MI *et al*. Int J Cancer, 2002, (2): 171-178

7 Parrott A. Human psychopharmacology: Clinical and experimental, 2001, **16**(4): 361-362

8 Neurath GB, Dunger M, Orth D *et al*. Int Arch Occup Environ Health, 1987, **59**: 199-201

9 Lambe EK, Picciotto MR, Aghajanian GK *et al*. Neuropsychopharmacol, 2003, **28**(2): 216-225

10 Takeda D, Nakatsuka T, Papke R *et al*. Pain, 2003, **101**(1-2): 13-23

11 Yao S D, Sheng S G, Cai J H *et al*. Radiat Phy Chem, 1995, **46**(1): 105