HIGH-PRESSURE PHASE BEHAVIOUR OF NICOTINE / CARBON DIOXIDE SYSTEM

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Tobacco products are composed of a great variety of constituents. Nicotine, 1-methyl-2(3-pyridyl) pyrrolidine, is a highly toxic major alkaloid found in tobacco plants and plays an important etiological role in the development of human carcinogenesis. Nicotine is also accused of the addictive potential of smoking, being classified by the Drug Abuse Advisory Committee as an addictive substance. Carbon dioxide has been extensively used for the removal of nicotine from tobacco leaves in the production of new cigarettes with reduced nicotine content. Although detailed knowledge of phase behaviour is most important for the design of any separation process, solubility of nicotine in sub/supercritical CO_2 seems to have been scarcely studied. Reported measurements are restricted to the temperatures of 313 and 343 K, and covering a range of pressures of 0.9 – 8 MPa and 0.9 – 16 MPa, respectively.

In this work we present a phase behaviour study of the CO_2-nicotine binary system at 313.1 K, in a pressure range of 6 to 9 MPa. The phase equilibrium measurements were performed using an apparatus that employs a high-pressure sapphire cell and allows sampling of both vapour and liquid phases. From the experimental work, it could be concluded that, according to the Scott and Van Konynenburg classification of fluid phase equilibria, the system nicotine + CO_2 most likely shows type-V fluid phase behaviour. The characteristic of this type of phase behaviour is a three-phase (VLL) equilibrium, with a discontinuous critical curve. As expected, the mutual miscibility increases with increasing pressure and the mixture will be homogeneous above the upper critical pressures. These data may help in further studies on sub/supercritical CO_2 extraction of nicotine from nicotine-containing products.

INTRODUCTION

Tobacco products are composed of a great variety of constituents. Nicotine, 1-methyl-2(3-pyridyl)pyrrolidine, is a highly toxic major alkaloid which only exists in tobacco plants accounting for ~ 95% of its total alkaloid content [1, 2]. Nicotine is formed in the roots of the plant and transported to the leaves, where it is stated to be both a constitutive and induced defense in cultivated (*Nicotiana tabacum*) and wild (e.g., *Nicotiana sylvestris* and *Nicotiana attenuata*) tobacco, playing an important role as insecticide in the plant´s anti-herbivore defence [3, 4]. In humans, however, nicotine and nicotine derivatives have been implicated in causing various detrimental health effects including the increased risk for certain cancers [5 – 7]. Nicotine is also accused of the addictive potential of smoking, being classified by the Drug Abuse Advisory Committee as an addictive substance [8]. Nicotine chemical structure is shown in **Figure 1**.
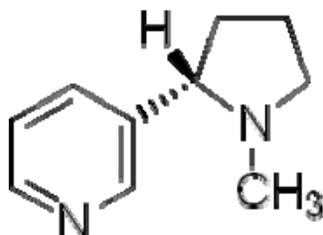
Figure 1. Chemical structure of Nicotine.

Carbon dioxide has been extensively used as liquid or supercritical fluid in the extraction of nicotine from tobacco products [9 - 11]. Moreover, supercritical extraction processes for the removal of nicotine from tobacco leaves have been patented as methods to produce new cigarettes with reduced nicotine content [12, 13]. Nevertheless, phase equilibrium of nicotine in sub/supercritical CO_2 has been scarcely studied [14], and focused on solubilities in the gas phase, restricted to temperatures of 313 and 343 K, and covering a range of pressures of 0.9–8.0 MPa and 0.9–15.9 MPa, respectively [15].

In this work we present a phase behaviour study of the CO_2-nicotine binary system, in the pressure range 6 to 9 MPa.
These data can provide helpful information for further studies on sub/supercritical CO_2 extraction of nicotine from nicotine natural contained products.

MATERIALS AND METHODS

Sample and Reagents

Nicotine (99% purity) was obtained from Fluka (Seelze, Germany). CO_2 N48 (99.9998 % CO_2 purity) was supplied by Air Liquide (Algés, Portugal).

Vapour-liquid equilibrium (VLE) apparatus and collection of the samples

An apparatus that employs a high-pressure sapphire tube as equilibrium cell and allows sampling of both vapour and liquid phases was used. The apparatus and the methodology were described in detail elsewhere [16]. Only a brief description is provided here. The cell, with a usable internal volume of approximately 30 cm^3, was a thick-walled sapphire tube placed inside an air bath. Both, the top and the bottom of the sapphire cell were connected to HPLC valves having sample loops. These loops were connected, through cold traps, to the expansion zone – calibrated large volumes. Cold traps were kept at a temperature of about -10 ^{o}C, ensuring precipitation of all components except CO_2, while the expansion zone allows an expansion of the CO_2 loop contents into calibrated large volumes. Measurement of pressure in those volumes before and after the expansion allowed the calculation of the CO_2 quantity in the sample, using an equation of state for CO_2 presented in literature [17]. The content of nicotine in cold traps was analyzed by GC as described below. The measurement uncertainties are: temperature ± 0.1 K, pressure ± 0.07 bar, mass ± 0.001 g and lines volumes ± 0.1 mL. The reproducibility was ± 0.002 mole fraction for the vapour phase and ± 0.012 for the liquid phase. A few data points related to the binary nicotine + CO_2 system were obtained visually by cloud-point method using the same apparatus. With the naked eye, disappearance of phase boundary was observed by slow CO_2 pressure increase. This pressure increase was obtained by using volume calibrated manually driven screw-injector connected to the bottom of the cell.

Analysis of nicotine content in the samples

Analyses were carried out on a Shimadzu GCMS-QP2010 (Shimadzu Corporation, Kyoto, Japan) gas chromatograph quadrupole mass spectrometer. The column used was a DB-5MS (J & W Scientific) capillary column, 30 m x 0.32 mm I.D. and 0.25μm phase thickness. The column temperature program started at 50 ^{o}C until 200 ^{o}C at 5 ^{o}C/min. The temperature was kept at 200 ºC for 5 min. One μL of sample was injected in split injection mode (1:20). The carrier gas, helium, was set at 1.5 mL/min and the injector temperature was 300 ^{o}C. Mass spectrometry detection was performed at 1.25 kV and samples were scanned from 30 to 700 amu. Nicotine was identified by comparison with standard mass spectra obtained in the same conditions and compared with the mass spectra from library Wiley 229 and NIST 147. GCMS Solutions software was used for data acquisition. Standard solutions of nicotine covered the range of 25.8-129.2 ppm.

RESULTS

Exploration of the phase behaviour for nicotine / CO_2 system was carried out in the view cell, in order to visually detect the existence of three-phase regions. According to the phase rule, for a binary system in three-phase region, degree of freedom is 1 meaning that at a selected temperature there is only one pressure that satisfies the equilibrium conditions. In other words,

whatever the initial volume of nicotine is used, at that pressure the compositions of each of the three phases is fixed.

Various quantities of nicotine were introduced to the cell, and CO_2 was added slowly while the pressure was gradually increased. Schematic presentation of phase development in binary nicotine / CO_2 system, as CO_2 pressure is continuously increased by adding CO_2, at 313.15 K, is shown in Figure 2.
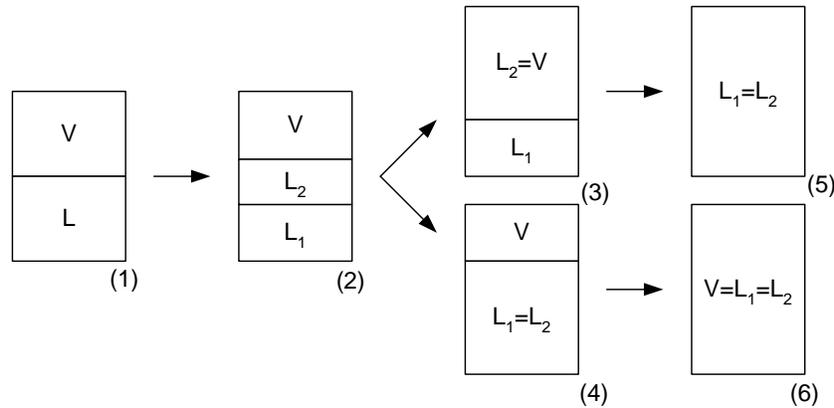
Figure 2. Phase development in binary nicotine / CO_2 system as CO_2 pressure is continuously increased by adding CO_2, at 313.15 K

Fig. 2(1) shows the cell filled with nicotine and CO_2 at a relatively low pressure as biphasic system. At a unique pressure of 8.37 MPa, a third phase formed between the liquid and gas phases (Fig.2(2)). Further, a small addition of CO_2 led to either the middle liquid phase completely merged with the vapour phase forming $L_2=V$ (Fig. 2(3)), or the two bottom phases merged into a single liquid phase $L_1=L_2$ (Fig. 2(4)). Finally, as pressure increased, the system passed through bubble or dew point.

The experimental VLE data for the CO2 + nicotine system at 313.2 K are reported in Table 1.

Table 1 Phase equilibruim data of the CO_2 + nicotine system at 313.2 K. All compositions are given as a mole fraction of CO_2

p / MPa	$x_{L, CO2}$	$x_{V, CO2}$	
	Tie-lines		
5.95	0.65213	0.99936	
7.10	0.74351	0.99913	
7.49	0.77127	0.99890	
8.09	0.85123	0.99833	
8.24	0.87104	0.99829	
	Cloud points		
p / MPa	x_{CO2}		
8.60	0.97920		
8.49	0.99513		
8.54	0.92404		
8.55	0.95168		
	Three-phase equilibrium		
p / MPa	$x_{L1, CO2}$	$x_{L2,CO2}$	$x_{V, CO2}$
8.37	0.88629	0.97004	0.99776

Figure 3 illustrates the phase diagram in terms of CO_2 mole fraction. To the best of our knowledge, there are only two data points at 313.1 K at the vapour side of the diagram available in literature [15]. For comparison purposes, these literature values are included in Figure 2 in magnified insert. The literature values overestimate the mole fraction of CO_2 in the vapour phase: (a) 0.99974 versus our value of 0.99913 at 7.09 MPa, and (b) 0.99891 versus our value of 0.99833 at 8.09 MPa.
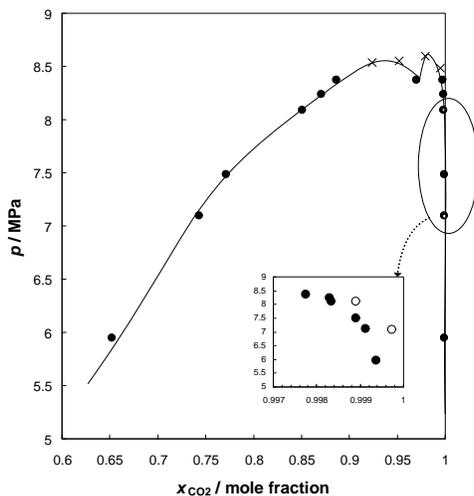
Figure 3. Pressure-composition phase-equilibrium diagram for CO2 + nicotine system at 313.2 K. The insert shows the magnification of the selected part of phase diagram including two data points from the literature [15]. The line is drawn as guide to the data.

The mutual miscibility increases with increasing pressure and the mixture is homogeneous above the upper critical pressures. The two-phase region is located inside the envelopes (binodal curve) from which, parallel to the x-axis, tie lines linking concentrations in equilibrium can be directly identified. The system exhibits three phases (L_1L_2V) at 8.37 MPa. At pressures above 8.37 MPa, there are two two-phase reagions (L_1L_2 and L_2V) forming two critical points. It could be concluded that, according to the Scott and Van Konynenburg classification of fluid phase equilibria, the system nicotine + CO_2 most likely shows type-V fluid phase behaviour. The characteristic of this type of phase behaviour is three-phase equilibrium (VLL) and a discontinuous critical curve.

CONCLUSION

Isothermal vapour liquid equilibria were determined experimentally for nicotine + CO_2 system at temperature 313.1 K. It corresponds to an upper critical solution pressure type phase separation where the two-phase region is located inside the binodal curve. Three phases (L_1L_2V) are present at 8.37 MPa. There are two pressure maxima of the binodal curves which indicate the two critical pressure–composition coordinates. The first one corresponds to liquid-liquid, while the second one corresponds to vapour-liquid two-phase region.

REFERENCES

[1] Baldwin, I.T., Journal of Chemical Ecology, Vol. 15, **1989**, p. 1661

[2] Hashimoto, T., Yamada, Y., Annual Reviews in Plant Physiology and Plant Molecular Biology, Vol. 45, **1994**, p. 257

[3] Steppuhn, A., Gase, K., Krock, B., Halitschke, R., Baldwin,I.T., PLoS Biology, Vol. 2, **2004**, p. 1074.

[4] Preisser, E.L., Gibson, S.E., Adler, L.S., Lewis, E.E., Acta Oecologica, Vol. 31, **2007**, p. 210

[5] Wong, H.P.S., Yu, L., Lam, E.K.Y., Tai, E.K.K., Wu, W.K.K., Cho, C.H., Toxicological Sciences, Vol. 97(2), **2007**, p. 279

[6] Kleinsasser, N.H., Sassen, A.W., Semmler, M.P., Harreus, U.A., Licht, A.K., Richter, E., Toxicological Sciences, Vol. 86, **2005**, p. 309

[7] Hecht, S.S., Nature Reviews Cancer, Vol. 3(10), **2003**, p. 733

[8] Kleiner, K., New Scientist, Vol. 143, **1994**, p. 10

[9] Fischer, M., Jefferies, T., Journal of Agricultural and Food Chemistry, vol. 44, **1996**, p. 1258

[10] Rincón, J., De Lucas, A., Garcia, M.A., Garcia, A., Alvarez, A., Carnicer, A., Separation Science and Technology, Vol. 33(3), **1998**, p. 411

[11] Yonei, Y., Kobari, M., Yokoyama, C., Arai, K., Kagaku Kogaku Ronbunshu, Vol. 21(4), **1995**, p. 674

[12] Burasado, R., Guratsubusu, H.J., Japanese Patent JP1196285, **1989**

[13] Xie, Z.W., Chinese Patent CN1899142, **2007**

[14] Gahrs, H.J., Berichte Der Bunsen-Gesellschaft-Physical Chemistry Chemical Physics, Vol. 88(9), **1984**, p. 894

[15] Suzuki, J., Yonei, Y., Yokoyama, C., Kagaku Kogaku Ronbunshu, Vol. 21(3), **1995**, p. 608

[16] Lopes, J.A., Nunes da Ponte, M., Journal of Supercritical Fluids, Vol. 34, **2005**, p. 189

[17] Span, R., Wagner, W., Journal of Physical and Chemical Reference Data, Vol. 25(6), **1996**, p. 1509

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