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Contamination of Plant Foods with Nicotine: An Overview

Hassan El-Ramady [(1)*], Neama Abdalla [(2)], Tarek Alshaal [(1)], Ahmed Elhenawy [(1)], Megahed Amer [(3)], Ahmed S. Shehata [(4)], Jana Paulsen [(5)], Maik Kleinwächter [(5)], Dirk Selmar [(5)], Hussein Taha [(2)]

[(1)] Soil and Water Dept., Faculty of Agri., Kafrelsheikh Uni., Kafr El-Sheikh, Egypt
[(2)] Plant Biotechnology Dept., Genetic Engineering Div., National Research Center, Giza, Egypt
[(3)] SWERI, Agricultural Research Center, Egypt
[(4)] Vegetable Crops dept., Faculty of Agriculture, Cairo Uni., Giza, Egypt
[(5)] Applied Plant Science Dept., Institute for Plant Biology, TU Braunschweig, Braunschweig, Germany
* Corresponding author: (ramady2000@gmail.com)

Abstract

It is well known that, the explorer "Christopher Columbus" encountered tobacco in the 1400s during his earliest journey to the New World. Tobacco plant is native to North America and other parts of the Western Hemisphere. Furthermore, plant of tobacco contains nicotine and its use has a history that dates back to the earliest records of settlers arriving in America. Moreover, American Indians introduced these settlers to the tobacco plant. In various recent publications elevated nicotine concentrations have been reported to occur in many different foods and plant derived commodities (such as fungi, tea, fruit teas, spices and medicinal plants). Whereas, it is recorded that, high nicotine contaminations are also present in many plant derived products. Up till now, the causes of these contaminations are unknown and they are found in both conventional and in organic products. Thus, field and *in vitro* experiments are required to elucidate the origin for these nicotine contaminations. Therefore, this work aims to highlight on the nicotine contamination in some different food plants.

Key words: Tobacco, Nicotine, Contaminant, Food Plants, *In Vitro* Study

1. Introduction

It is well known that, a cigarette is more than a thin roll of finely chopped tobacco wrapped tightly in paper. This cigarette provides a way to deliver a drug (nicotine) into the body. Furthermore, tobacco played a vital role in the earliest days of the New World and the development of tobacco as an industry mirrors the civilization and, ultimately, industrialization of much of the Americas. Before a single European explorer set foot on the soil of the famed New World, tobacco was there. The plant flourished across much of the Americas, and tobacco crops could be found from Brazil to the St. Lawrence River (**Wagner 2003)**. The tobacco plant's leaves can be dried and then crumbled. In northern climates, tobacco was chewed or smoked in pipes; for Native Americans in North America, the so-called "peace pipe" was a sacred object. Whereas, in tropical climates, tobacco leaves were more commonly wrapped together or wrapped around corn husks and smoked as a kind of cigar. This nicotine ($C_{10}H_{14}N_2$, a pyridine ring and a pyrrolidine ring) is a highly toxic alkaloid. It is actually a colorless liquid and doesn't turn brown until it is burned (**Shoji et al. 2010)**. By the middle of the 20th century, doctors began to establish the link between smoking and an increased risk of developing cancer. The National Cancer Institute confirmed that, a person who smokes 20 cigarettes per day is 10 times more likely to develop lung cancer than a nonsmoker (**Wagner 2003)**. There are several reports, books and papers concerning nicotine and its effects (e.g., **Mayer 2014; Balfour and Munafò 2015**). It is reported that, nicotine accounted for many psychopharmacological effects and this was elegantly described in 1931 by **Lewin** as follows: "The decisive factor in the effects of tobacco, desired or undesired, is nicotine" (**Henningfield et al. 2009**). Therefore, the United States Food and Drug Administration (FDA), the World Health Organization (WHO) and the European Commission (EC) have taken a strong science-based approach to tobacco disease control and product regulation (**EC 2004, 2007**). Furthermore, there are many other national and regional efforts to illustrate the global public health and regulatory importance of nicotine and tobacco science that has included psychopharmacological research (**Henningfield et al. 2009**). Therefore, the aim of this work is to elucidate the reasons for these contaminations in order to establish strategies for the sustainable prevention of these contaminations.

2. Historical background of nicotine

It is well documented that Christopher Columbus was the first encounters tobacco (*Nicotiana tabacum*) during his voyage to the New World in 1492. Tobacco spread around the world within 125 years and carried back by explorers. Tobacco traveled to Spain, Italy, and Portugal, whereas Dutch

and Portuguese sailors carried it with them to China, Japan, and the East Indies. In the mid 1500s, tobacco spread to France by a man named Jean Nicot (**Wagner 2003)**. Nicot swiftly sent some seeds of the plant back to France, accompanied by his own letters proclaiming the wonder of this new drug (nicotine). In 1612, John Rolfe produced the first successful commercial tobacco crop in Jamestown. In 1987, Congress banned smoking on flights of less than two hours whereas, the Food and Drug Administration (FDA) announced plans to regulate nicotine as a drug in 1994 (**Wagner 2003)**.

Tobacco is a word bombarding people daily in cigarette advertisements and from rows of tobacco products in stores. The word *tobacco* was in fact a name applied in error to the plant that European explorers witnessed smoked by Native Americans. The name originally referred instead to the cane pipe, called a *tabaco* or *tavaco,* used to sniff smoke (**Charlton 2004**). It is indicated that, tobacco use by not only South and Central American indigenous populations but also Egyptian, Persian, Chinese and African populations (**Hammond 2009**). Pipe smoking made its way to Egypt in 1601–1603 and to Turkey in 1605 (**Robinson 1985**). By 1600, the plant had spread through Europe to Italy, Spain, France, England, Belgium, and Switzerland and had begun its move beyond Europe to Japan, China, Indian, Java, Africa, and the Philippines (**Mancall 2004**).

3. What is nicotine?

Nicotine is the main alkaloid in tobacco and other tobacco species where it occurs at concentrations ranging from 2% to 8% (**EFSA 2011**). Nicotine is a stimulant, and just like cocaine, amphetamines, or methamphetamines, nicotine works by speeding up the processing rate of the central nervous system. Nicotine is highly addictive, and smokers can quickly become dependent on cigarettes and suffer serious symptoms of withdrawal when they try to quit. Nicotine is really a poisonous alkaloid (a compound that contains carbon and nitrogen and is found in some plants; some are poisonous, others can be used for medicinal purposes). Nicotine travels through the body, affecting the brain and central nervous system, the hypothalamus, and pituitary gland (meaning that it affects the hormone system), and then accumulates in the brain. When you smoke a cigarette, nicotine races through your body, reaching your brain within 10 seconds from the time you inhale **(Wagner 2003)**.

Nicotine is the principal substance responsible for tobacco addiction (**Silagy et al. 2004**), but it also enhances attention and cognitive performance (**Pons et al. 2008**). **Connolly et al. (2007)** confirmed that a statistically significant trend in increased nicotine yield, of 0.019 (1.1%) mg cig^{-1} $year^{-1}$ over the period 1997–2005 and 0.029 (1.6%) mg cig^{-1} $year^{-1}$ over the period 1998–2005. The increasing trend was observed in all major market categories (mentholated vs. non-mentholated, and full flavor vs. light, medium (mild) or ultra light). Nicotine yield in smoke was positively associated with nicotine concentration in the tobacco and number of puffs per cigarette, both of which showed increasing trends during the study period **(Connolly et al. 2007)**.

4. How much nicotine can kill a human?

The human toxicity of nicotine has become increasingly relevant in the past couple of years through marketing of new nicotine-containing products. These products include smokeless tobacco and liquids for electronic nicotine delivery systems (electronic cigarettes) that are freely available in most countries. It is reported that the lethal dose of nicotine for adults is 60 mg or less (30–60 mg), leading to safety warnings that ingestion of five cigarettes or 10 ml of a dilute nicotine-containing solution could kill an adult. This 60-mg dose would correspond to an oral LD_{50} of around 0.8 mg kg^{-1} (**Mayer 2014**). Based on 20 % oral bioavailability of nicotine (**Hukkanen et al. 2005**) and assuming linear kinetics, an oral dose of 60 mg would give rise to a plasma concentration of about 0.18 mg L^{-1}. The fatal nicotine intoxications suggest that the lower limit of lethal nicotine blood concentrations is about 2 mg L^{-1}, corresponding to 4 mg L^{-1} plasma, a concentration that is around 20-fold higher than that caused by intake of 60 mg nicotine. Thus, a careful estimate suggests that the lower limit causing fatal outcomes is 0.5–1 g of ingested nicotine, corresponding to an oral LD_{50} of 6.5–13 mg kg^{-1}. This dose agrees well with nicotine toxicity in dogs,

which exhibit responses to nicotine similar to humans (**Mayer 2014**). Therefore, nicotine is a toxic compound that should be handled with care, but the frequent warnings of potential fatalities caused by ingestion of small amounts of tobacco products or diluted nicotine-containing solutions are unjustified and need to be revised in light of overwhelming data indicating that more than 0.5 g of oral nicotine is required to kill an adult (**Mayer 2014**).

5. Is nicotine a contaminant for plant foods?

To face the changing environments, plants have evolved the ability to synthesize a tremendous repertoire of structurally diverse secondary metabolites, (**Shoji et al. 2010**). Among these secondary metabolites, nitrogen containing low molecular weight compounds, collectively called alkaloids are known to function in the chemical defense of plants against herbivores, pathogens and abiotic stress. Nicotine is arguably the most popular alkaloid due to the prevalence and long history of smoking. Smoking of nicotine-containing tobacco leaf products can be traced back to as early as 5000 BC, as a component of religious rituals (**Shoji et al. 2010**). It is found that, nicotine was in low concentrations in other crops belonging to the family of *Solanaceae*, such as tomatoes, aubergines, peppers and potatoes. Nicotine binds stereo-selectively to the nicotinic acetylcholine receptors of autonomic nervous systems, the adrenal cortex, the neuromuscular synapses and in the brain. Because of this activity as agonist of nicotine acetylcholine receptors, nicotine exhibits also insecticidal activities and the compound was used as active substance in plant protection products. Thus, at European level it falls under the legislation for pesticides (**EFSA 2011**).

Thus, it could be concluded that, there are generally three nicotine sources for contamination of plant: the first source belongs the plants, which synthesize the endogenous nicotine under certain conditions (e.g. stress), the second source represents nicotine results form contaminations by smokers (smoke of cigarettes / nicotine residues at the fingers of harvesters) and finally nicotine, which is taken up from the soil (e.g. resulting from butts of cigarettes thrown away). These previous sources for contamination of plants with nicotine did not include the illegal usage of nicotine in insecticides.

6. Can plant synthesize nicotine?

As mentioned before, some plants can synthesize nicotine (endogenous nicotine) under certain conditions (e.g., stress; **Selmar et al. 2015a, b**), whereas, in tobacco plants, nicotine could be synthesized in roots, based on nicotinic acid and the amino acid L-ornithine and systematically distributed in the whole plant (**EFSA 2011**). Therefore, roots can synthesize a large amount of nicotine and then transport to the shoot after wounding of tobacco plants. Under these conditions, plant jasmonic acid can act as a long-distance signal between the wounding stimulus and response in tobacco plants. Furthermore, auxin can serve as a negative signal to regulate nicotine synthesis in roots of tobacco plants, even when plants are not wounded (**Li et al. 2007**). Moreover, removing the shoot apex after girdling the stem base still stimulates nicotine synthesis in roots. Due to girdling prevented the involvement of signals transported in the phloem, this wound likely induced a response of nicotine synthesis in roots regulated by a signal transported *via* an alternative pathway (**Li et al. 2007**). As drought stress and pathogen attack are known to induce efficiently the synthesis of various secondary plant products, corresponding trials have to be performed. Moreover, methyl jasmonate and salicylic acid as most important signalling compounds in plant defence metabolism should be applied to induce putative nicotine biosynthesis.

7. Further research and conclusion

Due to a regulation of EU-commission (No. 396/2005) the maximum concentration for foods was defined as 0.01 mg kg^{-1} (**EC 2005**). Surprisingly, recent analyses revealed that elevated nicotine concentrations occur in many different foods and plant derived commodities, such as fungi, tea, fruit teas, spices and medicinal plants (**EFSA 2009**). For example, it is found that high nicotine contaminations are presented in many plant derived products from Egypt (**EFSA 2011**). Whereas, lots of dried camomile flowers produced in Egypt

revealed nicotine concentrations up to 0.5 mg kg^{-1}, exceeding the limit value 50-times. As temporary arrangement, the European Food Safety Agency (EFSA) raised – only for a limited time – the maximum nicotine concentration allowed in foods. After that, the contaminations must be excluded. Thus, there is a strong and prompt research requirement. Apart from any EU regulation, the cause of nicotine contaminations must be elucidated in order to remedy any potential hazard and to avoid any health impairment by toxic nicotine (**Fig. 1**).

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Fig. 1: Tobacco plant under the investigation with nano-selenium (100 mg kg^{-1}), it could be observed rooting of this plant resulting from nano-Se effect (photos by El-Ramady). Contamination of food plants with nicotine needs to be carried out *in vitro*.

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