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Cigarette Smoking Prevalence and Nicotine Risk Assessment Amongst Student Smokers in Yaoundé Cameroon

Wilfred A. Abia[1,2,3], Golwa Dinza[2]

[1]Department of Biochemistry, Laboratory of Pharmacology and Toxicology, Faculty of Science, University of Yaoundé 1, Cameroon
[2]Institute for Management and Professional Training (IMPT), Yaoundé, Cameroon
[3]Agri-Food Safety and One Health Agency (AFS1HA), Yaounde, Cameroon, CA, Africa

ABSTRACT

Cigarette smoking incidence among youths in Cameroon is on the rise and cigarette smoking is a major risk factor for many preventable disorders. Cigarette smoke is a complex mixture of over 5000 toxic substances with diversified toxicities including carcinogenicity and addiction. Nicotine, the harmful component of cigarettes, plays a central role in addiction and contributes to the onset or worsening of cardiovascular disorders. This paper provides preliminary data on cigarette smoking incidence and cigarettes-associated nicotine exposure amongst student smokers in higher institutes of learning in Yaoundé. A survey on cigarette smoking attitudes was conducted among students of higher institutions of learning in Yaoundé using structured questionnaires. Based on the data from the survey, nicotine exposure was calculated, and the potential associated risk was characterized. Seventeen percent of studied students (N=185) were cigarette smokers smoking on average 5.96 (range: 1-15; majority smoking 1-10) sticks of cigarettes per day each, with an average nicotine concentration of 4.77 mg/day, resulting in an estimated nicotine exposure incidence of 0.068 (range: 0.009-0.043) mg/Kg body weight/day. The average (maximum) nicotine exposure rate is 85 (53.8) times higher than the reference dose (0.0008 mg/Kg body weight/day). This places these students at an unacceptable risk. An enlarged survey may be required as well as educational intervention approaches such as awareness and sensitization campaigns against cigarette smoking among youths.

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1. INTRODUCTION

Cigarettes are the most widely sold form of manufactured tobacco products in the world (WHO, 2010). Cigarette smoking harms almost all organs of the body (US Department of Health and Human Services, 2004). Cigarette smoking is the main cause of preventable death, which kills more than 8 million people worldwide every year (WHO Tobacco Fact Sheet, 2021). It causes serious medical conditions including cardiovascular and respiratory diseases, e.g. coronary heart disease and lung cancer (WHO, 2016). Cigarette smoke is a complex mixture with over 5000 toxic substances (IARC, 2012; Rodgman, 2011; Talhout et al. 2011; Cunningham et al., 2011; Fowles and Dybing, 2003) which may generally be classified as, but are not limited to, neutral gases, carbon and nitrogen oxides, amides, imides, lactames, carboxylic acids, lactones, esters, aldehydes, ketones, alcohols, phenols, amines, *N*-nitrosamines, *N*-heterocyclics, aliphatic hydrocarbons, monocyclic and polycyclic aromatic hydrocarbons, nitriles, anhydrides, carbohydrates, ethers, nitro compounds and metals (IARC, 2012; Rodgman, 2011). Over 40 are known to be carcinogenic (West et al., 2003) e.g. benzene, formaldehyde, and vinyl chloride (National Cancer Institute, 2017). In addition to carcinogens in cigarettes are toxic metals such as arsenic and cadmium (Jaishankar et al., 2014) as well as radioactive toxic heavy metals like lead-210 and polonium-210 (Seiler and Wiemels, 2012), and

poisons such as ammonia, carbon monoxide, and nicotine (CDC, 2010).

Nicotine is a risk factor for cancer due to its damaging effects on DNA (National Cancer Institute, 2014). It plays a central role in addiction to cigarettes and causes, in addition, the relaxation of skeletal muscles with consequences, cardiovascular effects including hypertension (Isabelle, 2010). Nicotine (pK_a 7.9), when consumed via smoking cigarettes is mainly absorbed into the body via the lungs (Holloway, 2014). It is particularly metabolized in the liver and is excreted via urine through the kidneys (Holloway, 2014; Benowitz, Hukkanen and Jacob, 2009). These depend on many factors, including age, weight, type of cigarette, frequency of use, hydration, and physical activity levels (*Grunberg and Starosciak 2010;* Benowitz, Hukkanen, and Jacob, 2009). The average half-life of nicotine in humans is 2 (range: 2-4) hours (*Grunberg and Starosciak, 2010*). The pharmacology (including nicotine-induced addiction and smoking diseases) (Benowitz, 2010) and toxicology (Fagerström, 2014) of nicotine have been reviewed in detail. Generally, nicotine is known to bind to nicotinic cholinergic receptors, facilitates the release of neurotransmitters (i.e., dopamine), and thus mediates the complex addictive actions of nicotine in cigarette smokers (Benowitz, 2010). Therapeutically, nicotine is a stimulant in low doses, while in very high doses it is a depressant of nervous activity. Nicotine is well known to be very toxic in large doses, with the main symptoms of poisoning including mental confusion, sweating, vomiting, diminished pulse rate, and breathing difficulty (WHO, 2009; Griesbach, Amos and Currie, 2003; Fleming et al., 2002; Benowitz et al., 2007). In general, cigarette smokers have more chronic and co-occurring illnesses, including bronchitis, cardiovascular disease, cancer, and bronchopulmonary disease (WHO, 2009; Benowitz et al., 2007). Exposure to dose levels as high as 500 mg may lead to generalized blockage of body processes such as respiration and consequential death (Meyer, 2013). Notwithstanding, there is inadequate data on nicotine exposure from smoking cigarettes (Baumung et al., 2016), however, nicotine exposure via combustible cigarettes during smoking is considered to increase health risks amongst smokers (Action on Smoking Health, 2007) when compared to the smokeless tobacco products (Fiore, Schroeder and Baker, 2014). The lethal dose of nicotine depends on factors such as nicotine tolerance, speed of nicotine delivery, and route of administration. Generally, nicotine poisoning is rare, except otherwise via suicide (Kloosterman, 2013). Notwithstanding, several risk assessments are based on the carcinogenic compounds in cigarettes, but with inadequate focus on nicotine (Baumung et al., 2016) despite its adverse effects on body tissues such as the heart, reproductive system, lung, and kidney, as well its consistently demonstrated carcinogenic potential (National Cancer Institute, 2014; Mishra et al., 2015).

Cigarette smoking incidence among youths in Cameroon is on the rise and cigarette smoking is a major risk factor for many preventable disorders (MINSANTE, 2013; WHO, 2017, 2019). According to the 2013 Global Adult Tobacco Survey (GATS), 5.7% of adults (age 15 years and above) in Cameroon were cigarette smokers (MINSANTE, 2013). Between the years 2012 and 2018, cigarette smoking prevalence was 17.5%, of which 45% were young people (MINSANTE, 2013). Based on the World Health Organisation (WHO) Trend Reports, the trend of cigarette smoking in Cameroon is on a sharp rise from 2000 with prevalence of 6% to prevalence of 21% in 2015, a scenario projected to double from 2015 to 2025 (estimated at 43%) (WHO, 2017, 2019). As of 2016, the prevalence of adults (in the capital city of Cameroon, Yaoundé), smoking cigarettes was 8.4% (Pefura-Yone, 2016). Given the health implications of nicotine, a component of cigarettes, it is essential to carry out a risk assessment of cigarette-induced nicotine to better assess its role in the deterioration of the health of combustible cigarette smokers. The objective of the study was to evaluate the prevalence of cigarette smoking amongst students and perform a combustible cigarette-associated nicotine risk assessment amongst university students in Yaoundé Cameroon.

2. Materials and Methods

2.1. Study site and target population

The survey was carried out in Bonamoussadi, Yaoundé Cameroon, which is domicile to several students of higher institutions of learning especially the University of Yaoundé 1. Study population students of higher institutions of learning, living independently from their parents. Their parents provide their allowances and they decide how to use it, thus, easier for those who smoke to use part of the money to buy cigarettes.

2.2. Survey on Cigarette Smoking Practices

Several briefing sessions in this study were done with small groups of 3-5 students who were either on their way to or from learning institutions, as well as briefing sessions in public spaces (such as roadside) in Bonamoussadi. After understanding the purpose of this study, some students voluntarily provided data on the consumption or smoking of cigarettes using a structured questionnaire. The questionnaires were mainly adapted from the Global Adult Tobacco Survey sheet (GATS, 2nd edition 2011). The

questionnaires were administered face-to-face (one-to-one) using a questionnaire form (paper) and pen.

Only students who were willing to participate voluntarily were recruited in the survey. This was expressed by a student's self-request for the questionnaire or to respond to a briefing session. Each participant was confirmed as a student by both school writing materials on him/her and by friends' i.e. classmates who were either returning from or going to their higher institution of learning.

2.3. Nicotine Risk Assessment

Nicotine risk assessment was done according to the general procedure for chemical risk assessment (Wittwehr et al., 2020). The procedure had four steps including hazard identification (step 1); dose-response or toxicity assessment (step 2); exposure assessment (step 3); and risk characterization (step 4). Steps 1 and 2 were done through a literature search and data was compiled accordingly. Step 3 was carried out via a survey (described above in 2.2) for students who smoke using a questionnaire adapted from the GATS (GATS 2nd edition 2011). Step 4 consisted of a comparison of the reference dose of nicotine from manufactured cigarettes (from Step 2) and the estimated average nicotine exposure dose (from Step 3).

2.4. Data Analysis

Analysis of our survey data was done following the Global Adult Tobacco Survey guide (GATS 2nd edition 2011). The incidence of smoking cigarettes by students and the number of cigarettes smoked per day by daily smokers were determined using the Statistical Package for Social Scientists (SPSS).

3. Results and Discussion

Cigarette-associated nicotine risk assessment was done according to the general procedure for chemical risk assessment (Fisk, 2014; Little Pro, 2016). The hazard was identified (step 1) as nicotine in cigarettes and for which students become exposed when they smoke cigarettes. Dose-response or toxicity assessment (step 2) following exposure to nicotine in cigarettes was done via literature search, and subsequently, the reference dose was calculated based on the data set obtained. Later, exposure of students to nicotine following smoking of cigarettes was assessed (step 3) via a survey using questionnaires (described above). Lastly, the nicotine exposure associated risk was characterized (step 4) by comparing the exposed dose to the reference dose.

Step 1. Hazard Identification

The hazard considered in this study is nicotine (3 - [(2S) -1-methylpyrrolidin-2-yl] pyridine) (Figure 1). Nicotine is a toxic alkaloid found in the tobacco plant, *Nicotiana tabacum*. Nicotine (empirical formula: $C_{10}H_{14}N_2$; molecular weight: 162.23 mole is soluble in water; density: 1,010; melting point: -79 ° C; boiling point: 247 ° C) is considered a mixture under Classification Labelling and Packaging (CLP) regulation n° 1272/2008 (European Commissions, 2008) as toxic of category 1: H310 "Fatal in skin contact" and toxic of category 3: H301 "toxic if swallowed".

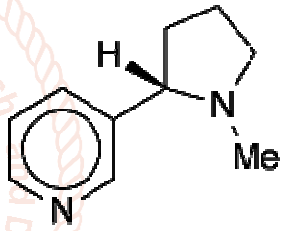


Figure 1. The structure of nicotine (source: https://www.acs.org/content/acs/en/molecule-of-the-week/archive/n/nicotine.html)

Considering that nicotine is used as a psychotropic during the inhalation of cigarette smoke, it is partly responsible for tobacco dependence. In tobacco, nicotine may be found in two main forms, namely, in the form of salt in the particulate phase, and the free forms in both particulate and gas phases. The most active form of nicotine is the free form. The physicochemical properties of nicotine are summarized in Table 1.

Table 1: Physicochemical properties of nicotine

Properties	Value	Reference
State of substance (20 °C, 101.3 kPa)	Colourless to pale yellow, oily liquid	O'Neil, 2006
Melting / freezing point	- 79 °C	Lide, 2007
Relative density (20 °C)	1,00925	O'Neil, 2006
Vapor pressure (25 °C)	0,038 mmHg	Boublik, 1984
Surface tension (20 °C)	38,61 Dynes.cm-1= 0,03861 N.m-1	US Coast Guard, 1984-1985
Solubility in water (25 °C)	1.106 mg/L	Seidell, 1941
Flash point	95°C	CDC, 2014
Flammability	Liquid combustible	CDC, 2014
Auto-inflammation point	244°C	CSST, 2014
Dissociation constant	pK_{b1} = 6,16 à 15°C; pK_{b2} = 10,96	Tomlin, 1994
Viscosity	Becomes viscous on exposure to air	Worthing, 1987

Step 2. Nicotine dose-response (toxicity) assessment

Evaluation of the acute toxicity of nicotine has been carried out by several authors. Two of these studies comply with the OECD guidelines (OECD, 2008, 1987). These are the work of Van den Heuvel et al. (1990) and Yam et al. (1991) which both result in the same LD_{50} value of 70 mg/Kg, thus placing nicotine in category 3 (European Commissions, 2008). But the French company Agence Nationale de Sécurité Sanitaire de l'alimentation, de l'Environnement et du travail (ANSES, 2015) in its appraisal work, as a precaution retained the LD_{50} value of 3.34 mg/Kg (value from the study by Lazutka et al., 1969) for the oral route and has classified nicotine in category 1 (European Commissions, 2008). Several publications report cases of fatal nicotine poisoning (Mayer, 2014; Solarino et al., 2010). These are usually accidents or intentional poisoning. The value of the amount of nicotine during autopsies after death from intoxication cases varies from 0.6 mg/L (blood test from the femoral vein) (Solarino et al., 2010) to 52 mg/L (blood test) (Tiess and Nagel, 1966).

The value of the Non-Observed Adverse Effects Level (NOAEL) and the Low Observable Adverse Effect Level (LOAEL) has been deduced based on nicotine toxicity evaluation studies. A 10-day study in rats, based on the observation of pathological changes in the liver, established a NOAEL value equal to 1.25 mg/kg of body weight (US EPA, 2008 study based on data from Yuen et al., 1995). One of the LOAEL values based on observing the acceleration of the heart rate by intravenous administration of nicotine from an acute human toxicity study is estimated at 0.008 mg/Kg of body weight (EFSA, 2009, based on data from Lindgren et al., 1999). Another child study based on the observation of symptoms of poisoning varied by dermal administration of nicotine found a LOAEL value of 0.01 mg/Kg of body weight, higher than the previous one (EFSA, 2009 based on data from Woolf et al., 1997).

The European Food Safety Authority (EFSA, 2009) has fixed an acute reference dose (ARfD), as well as, an acceptable daily intake (ADI) for nicotine to be 0.0008 mg/Kg body weight. In brief, EFSA's ARfD is based on a LOAEL of 0.0035 mg/Kg body weight for pharmacological effects following intravenous application of nicotine in humans.

Step 3. Nicotine exposure assessment

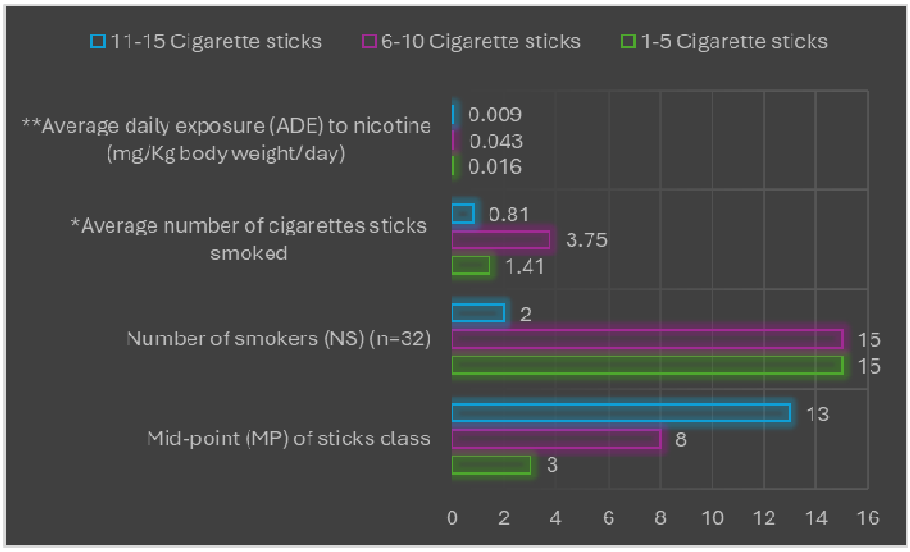
To assess students' exposures to cigarette-induced nicotine, a survey on cigarette intake frequency/attitudes was performed among students of higher institutions of learning living in Yaoundé, with questionnaires administered in Bonamoussadi. The findings (Table 2) revealed that 17% (32/185) of the studied student population were current smokers of cigarettes. Contrarily, 83% (153/185) students were not currently smoking cigarettes, amongst whom were 17/153 (11%) male students who were formerly smoking cigarettes and 136/153 (89%) including all the 27 female students, who had never smoked cigarettes before.

Table 2: Incidence of cigarette smoking amongst studied student population in Bonamoussadi, Yaoundé Cameroon

Cigarettes smoking practice	Total (N=185)	Male	Female
Currently smoking	32	32	0
Currently not smoking	153	126	27
Former smoker	*17*	*17*	*0*
Never smoked	*136*	*109*	*27*

Figure 2 below provides information on the estimated number of cigarettes smoked by students daily. There were as many students who smoked 6-10 sticks of cigarettes per day (n=15) as those who smoked 1-5 sticks daily. Most students smoked 1-10 sticks of cigarettes while 6.25% (2/32) of the students smoked 11-15 sticks of cigarettes daily.

Equations 1 and 2 below were used to calculate the total number of sticks of cigarettes smoked per day and the average daily exposure (ADE) levels to nicotine from cigarettes respectively. To estimate the average daily exposure to nicotine, two assumptions were further made as follows: (a) Each cigarette stick contains an average of 0.8 mg of nicotine (Calafat et al., 2004); and (b) The average adult body weight is 70 Kg (EFSA, European Food Safety Agency, 2012). Therefore, the total average number of cigarettes sticks smoked was estimated at 5.96 sticks per day. Additionally, the estimated average concentration of nicotine present in the 5.96 sticks of cigarettes is 4.77 mg/day. As a result, the ADE to nicotine by the studied students who smoke cigarettes is 0.068 mg/Kg body weight/day. In terms of the three sub-range of cigarettes smoked, the students who smoke 6-10 sticks of cigarettes per day on average are relatively the most exposed to nicotine with an ADE level of 0.043 mg/Kg body weight/day) when compared with those who smoke 1-5 (ADE: 0.016 mg/Kg body weight/day) and 11-15 sticks (ADE: 0.009 mg/Kg body weight/day).



**The average number of cigarette sticks smoked per day was calculated using the formula:*

Equation 1:

$$\text{Average Daily Number of Sticks of Cigarettes Smoked per Day} = \frac{\sum \left[\text{Mid-point of each class of cigarettes sticks smoked per day}\right] x \left[\text{Number of smokers per class}\right]}{\text{Total number of smokers}}$$

***The average daily exposure (ADE) to nicotine was calculated using the formula:*

Equation 2:

$$\text{Average Daily Exposure (ADE)} = \frac{\text{Average number of cigarettes sticks smoked per day} \; x \; \text{Average nicotine content per cigarette stick}}{\text{Average Body Weight}}$$

Figure 2: Estimated number of cigarette sticks smoked per day by the 32 students who were current cigarette smokers.

Therefore, the class of student smokers who smoke 6-10 sticks of cigarettes per day on average are relatively the most exposed to nicotine when compared with those who smoke 1-5 and 11-15 sticks. Notwithstanding, on an individual basis, the number of cigarettes smoked daily is directly proportional to cigarette-associated nicotine exposure levels. Furthermore, the nicotine exposure-associated health complications for smokers may vary according to their health status.

Step 4. Nicotine risk characterization

Nicotine risk characterization was assessed by comparing the value of the ADE (0.068 mg/Kg body weight/day) to nicotine with the maximum tolerable limit or reference dose of nicotine (0.0008 mg/Kg body weight/day). The ADE amount was over eighty-five times (relative to the 1-5, 6-10, and 11-15 sticks cigarettes with ADE of 20, 53, and 11 times respectively) higher than the reference dose, and thus unacceptable. Such exposure places the students who smoke at risk, as nicotine may serve as a risk factor for many diseases, including cardiovascular diseases mainly hypertension (Omvik et al., 1996; Trap-Jensen et al., 1988). Additionally, the studied smokers may become addicted to cigarette smoking – a situation that may increase the risk of suffering from other cigarette-induced diseases such as cancers.

Appraisal of the risk assessment of cigarettes-derived nicotine amongst student smokers

This cigarettes-induced nicotine exposure and risk assessment study mainly targeted students of higher institutions of learning in the Bounamoussadi area in Yaoundé. The hazard, nicotine, was indirectly estimated from the number of sticks of cigarettes smoked daily. The dose-response assessment was based on existing literature, while the nicotine exposure assessment was indirectly estimated through a survey, wherein 185 (158 male and 27 female) students responded. In total, this study revealed 17.3% smoking incidence amongst the 185 studied students, all being male students. This is in line with the 17.5% prevalence of smoking in Cameroon (MINSANTE, 2013). Furthermore, this current study revealed the average number of cigarettes consumed

per day by students to be 5.96. This figure is lower than the national average of 8.7 sticks of cigarettes per day (MINSANTE, 2013). Relatively, the estimated nicotine exposure dose (0.068 mg/Kg body weight/day) in this study is lower when compared with the 0.229 mg nicotine exposure per Kg body weight/day for adult/student smokers who consume 20 sticks of cigarettes per day (Cunningham et al., 2011). Notwithstanding, smokers in this current study are at risk.

Limitations of the Risk Assessment Study

The use of certain additives such as ammonia may conceal the amount of nicotine taken by the cigarette smoker (RJR, 1973; Lorillard, 1976), which suggests that the dose of nicotine exposure would be higher than that calculated if this assumption is considered. In addition, people who smoke cigarettes and other types of tobacco will likely experience increased levels of nicotine exposure and therefore have a nicotine exposure level higher than 0.068 mg/kg body weight per day when considering multiple sources of exposure.

Specifically, this current study has focused on nicotine risk assessment involving only active cigarette users (n=32). Passive smokers and consumers of other forms of tobacco were not included in this risk assessment. Furthermore, the risk assessment of nicotine alone is not sufficient to understand and assess the harmful effect of the other substances that are present in cigarettes on the health of consumers. In this context, all other sources of nicotine exposure as well as certain co-exposures (toxic substances from tobacco) must be considered. Furthermore, this study considered smokers generally, irrespective of the brand of cigarettes they smoke. Knowing that nicotine contents may vary from one cigarette to another and may even be smaller or larger than the 0.8 mg value used in the study, the risk value stated in this study is general irrespective of the type/brand of cigarette.

Finally, because some 45-65% of students were exposed to second-hand cigarette smoke in public places (WHO Regional Office for Africa: 2003-2011 Global Youth Tobacco Survey Factsheets, 2012, https://www.afro.who.int/sites/default/files/2017-06/facts-on-tobacco-use-in-the-african-region.pdf), it is clear that there is additional second-hand exposure which has not been evaluated in this study.

4. Conclusion and Prospects

Cigarette smoking is a major health hazard, with youths as major propagators and victims. 17% (32/185) studied students were cigarette smokers smoking on average 5.96 sticks of cigarettes (average nicotine concentration: 4.77 mg/day; estimated nicotine exposure incidence: 0.068 mg/Kg body weight/day) per day each. The average nicotine exposure level is 85 times higher than the reference dose (0.0008 mg/Kg body weight/day). This places these students at an unacceptable risk. Considering the small sample size, an enlarged survey may be required. Meanwhile, given the risk factors and or harmful health effects associated with cigarette smoking, and specifically the addictive effects of nicotine, a preventive/educational intervention approach requiring awareness and sensitization campaigns against cigarette intake amongst youths, cannot be emphasized (Mbatchou, Atangana and Kuaban, 2015; Pefura-Yone, 2016). To this end, the WHO framework convention that offers a control program called MPOWER addressing six evidence-based tobacco control measures that are most effective in reducing tobacco use is ideal, with creative tailor-made amendment (WHO, 2008). Similarly, the Mental Health and Integrated Risk Assessment Team of the Integrated Health for All Foundation (IHAF) Cameroon, has begun taking steps in this direction, raising awareness against substance and drug abuse including cigarettes and alcohol amongst students (*Jato, Abia, and IHAF, 2020 Report: Addressing Substance Abuse among Secondary School Students*) and which needs to be encouraged and passed-over to other action groups.

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