RESEARCH PAPER

# Nicotine delivery capabilities of smokeless tobacco products and implications for control of tobacco dependence in South Africa

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**Objectives:** Smokeless tobacco (SLT) use is popular among black South African women and children. The study sought to determine the nicotine delivery capability of popular industrialised and traditional SLT brands in South Africa, and to provide information for policy action by regulatory authorities.
**Design:** Laboratory chemical analysis of four industrialised and one traditional SLT products commercially available, using previously published analytical methods. Potential for dependence was inferred from nicotine delivery capabilities determined by the percentage free base nicotine.
**Measurements:** Moisture, pH, total nicotine, and percentage free base nicotine.
**Results:** Total nicotine content was between 6–16 mg/g. The pH varied between 7–10 and this correlated with percentage free base nicotine, which ranged between 10–99%. The nicotine delivery capability of the traditional product was lower than that of the industrialised products except for the recently introduced portion bag snus, which had comparable total nicotine but the lowest pH and percentage free base nicotine. The most popular SLT brands showed the highest percentage free base nicotine ever reported for any industrialised SLT or cigarette brands. Small cans contained higher nicotine than the large cans of the same brand tested. Findings from the study support a potential for limited ''product graduation'' by users.
**Conclusions:** South African SLT users are mostly exposed to potentially very highly addictive levels of nicotine that may favour tobacco dependence and its consequent health risks. The increasing use of SLT by women of childbearing age support the need for intensified policy action to control its use.

South Africa is a tobacco producing country. Both cigarette smoking and smokeless tobacco (SLT) use are common with an estimated national prevalence of 24.6% and 6%, respectively.[1] Between 1992 and 1995 the consumption of snuff in South Africa increased by about 30% from 1.1 million kg to 1.5 million kg,[2 3] which is in contrast to the consistent decline in cigarette tobacco consumption since the introduction of the first tobacco legislation in 1993.[1] SLT is commonly used through the nose and less commonly used orally. SLT use is particularly popular among South African black women with a prevalence of 13.2%, as compared to smoking prevalence of 5.4% in the same population group during 1998.[1] Of particular concern is a recent report that suggests a prevalence, in 1999, of 18.6% among South African black children,[4] and a local study that reported that 10% of pregnant black/African women use SLT.[5] Long term use of oral SLT has been associated with development of oropharyngeal and upper respiratory tract cancers[6–9] and is a risk factor for cardiovascular disease[10–13] and adverse reproductive outcome.[14 15]

Nicotine is the addicting agent in tobacco that prevents cessation and sustains long term use. The pH of SLT strongly influences nicotine absorption through the nose and mouth, especially the free base (unionised) nicotine, which is the form most readily absorbed.[16 17] Therefore, unlike cigarettes where nicotine delivery depends upon the smoking pattern of the user, the nicotine dose obtained from a unit (''dip'' or ''sniff'') of SLT is primarily determined by characteristics of the product itself and to a lesser extent by the amount of snuff used, and behavioural and physiological factors unique to each user.[16] This has been confirmed in a within-subject laboratory study of four US brands of SLT.[18] The brands studied had nicotine content that ranged from 7.5–11.4 mg/g; the pH varied between 6–9; plasma concentrations of nicotine rose by 20 ng/ml after using the high pH product, but by 4 ng/ml after use of the lower pH product. The differences in nicotine absorption, and subjective and physiologic effects were found to be primarily dependent on their pH and not on the nicotine content.

In the developed countries, most consumers of SLT use industrially manufactured products. However, in developing countries such as South Africa, many SLT users regularly use traditional products[19] and others are having to choose from a limited range of industrialised products. Because of the lack of consistent associations between SLT and major diseases (particularly in the developed nations), SLT is considered to be less harmful than cigarettes and thus promoted as a reduced harm product.[20 21] SLT use is similarly perceived by two thirds of South African children as safe alternative to cigarette.[22]

Unlike cigarette products, manufacturers of SLT products in South Africa are not mandated to disclose the nicotine content of their products.[23] Therefore, there is no information available on the nicotine content or nicotine delivery capabilities of SLT products in South Africa. In order to begin to understand better the role of SLT use in total tobacco dependence, its disease burden in South Africa, and the control of SLT marketing, it is important that its nicotine delivery capability is determined. Information of this kind will not only be useful to regulatory authorities, but will also help professionals in determining adequate dosages of nicotine replacement medications used to aid cessation.

It was the aim of this study to determine nicotine delivery capabilities of SLT products on the South African market. Potential for nicotine dependence was inferred from measures of nicotine delivery capability, namely percentage free base nicotine and pH of the commercially available industrialised and traditional products.

## MATERIALS AND METHODS

Four industrially manufactured SLT brands and one popular traditional homemade brand were each tested. The industrialised products tested were Ntsu, Taxi Red, Singleton Menthol, and Tobacco-rette original (pre-packed in pouches). The Taxi and Ntsu brands tested included the small and the large can samples. None of the SLT containers were dated, but all were purchased during January 2003. Similarly, none of the SLT products, except for Tobacco-rette, carried a batch number. In order to account for potential sample variability, a representative sample can of each brand, except for portion bag Tobacco-rette, was tested. Representative cans were made from a mixture of four different cans—two bought at different times (four weeks apart) from two separate vendors. Mixture was done under sterile laboratory condition and repackaged products were shipped immediately (on ice packs) to the laboratory in the USA for independent analysis. Only one can sample of Tobacco-rette was tested because the separate purchases from the two different sources were observed to have the same batch numbers despite a one month separation in sourcing date. As there were no other known retail stores stocking this recently introduced brand, only one can of this product was analysed. Upon receipt of the products in the laboratory, they were stored in the cold room (4℃) until the analysis commenced. Moisture content, pH, and nicotine were determined in the SLT products immediately after opening a can of each brand.

The moisture content was determined in about 10 g of raw tobacco using a Denver Model IR-200 Moisture Analyzer. Samples were heated with an infrared heat source to liberate water and other volatile components while continuously weighing the sample with an electronic balance until an end point was reached where weight no longer changed. Using a calibrated pH meter, the pH was determined for a suspension of 2 g of raw tobacco in 10 ml of distilled water one hour after mixture.[16] Nicotine analysis was performed using sample preparation protocol and gas chromatography as described by Malson and colleagues.[24]

Nicotine analysis of each representative product sample was done five times and the average values recorded. The percentages of free base nicotine were calculated according to the Henderson-Hasselbalch equation by using a pKa value of 8.02 for nicotine.[16] The nicotine delivery capabilities of the products influenced by the pH levels were then categorised as proposed by Henningfield and colleagues.[16]

## RESULTS

Table 1 presents the data for moisture content, pH, and nicotine content and dosing capability of the four industrialised and one popular traditional homemade SLT mixture on South African market. The values for nicotine content were reproducible within a standard deviation of 7% of the mean (coefficient of variation). The moisture content of the tested products varied between 14.7–48.8%, except for Singleton Menthol—a dry snuff, with a moisture content of 1.8%. On the basis of wet weight, the total nicotine concentration varied between 0.6% (6 mg/g) for Singleton and 1.6% (16 mg/g) for both the Tobacco-rette and the traditional homemade mixture. However, the fraction of the rapidly absorbed free base nicotine ranged from about 10.1% for Tobacco-rette to 99.1% for Singleton, and indeed increased as pH levels rose. A striking observation was that the total nicotine content of small cans of Taxi and Ntsu brands were 38% and 66% higher than their respective large cans, despite comparable pH levels and moisture contents.

## DISCUSSION

The present study has for the first time documented that popular SLT or snuff brands on the South African market have high nicotine content and vary in percentage of free base nicotine and, thus, in nicotine delivery capability. Therefore, SLT use commonly initiated for cultural reasons and perceived medicinal properties[25] may quickly be subverted by the addicting effects of nicotine. SLT use is further encouraged because its use is a socially discrete habit and less expensive than cigarettes; a can of SLT typically costs 3 Rands (US$0.40) compared to 12 Rands (US$1.50) for a pack of cigarettes. The concentration of total nicotine in SLT products tested was comparable to that in commercial filtered cigarettes.[24 26] Local surveys have demonstrated that an average SLT user will ''dip'' or ''sniff'' about four times a day and for 30 minutes each time.[19 27] With an estimated 2 g bolus of loose snuff commonly dipped, daily total nicotine exposure averages between 50–130 mg. However, with up to 99% free base nicotine, the nicotine exposure of an SLT user may be equivalent to up to 20 cigarettes per day. Therefore a nicotine replacement medication regimen should be equivalent to that used for smokers who take 20 cigarettes a day.

South African SLT users, can also be categorised as ''heavy'' users, considering an estimated nicotine yield of up to 400 mg/week.[28] These users may therefore also be at a considerable health risks associated with long term use of these products. It is pertinent to note that a previous study suggested as many as 36% of women SLT users who reported to have once attempted to quit had no success and about 67% of surveyed users wish to quit,[29] thus confirming potential for these products to establish chemical dependence. While larger sampling is needed to confirm the higher levels of nicotine found in the small can packages of two of the popular SLT brands tested, the potential implication is that those who desire to quit by cutting down on the amount of SLT purchased may be unintentionally sustaining dependence by using higher nicotine content products. SLT products have indeed escaped the same scrutiny and regulation placed on cigarette products. Even though SLT nicotine delivery capabilities make them as addictive as cigarettes, many South Africans are unaware of the potential health hazards of SLT use.[20 26] This is despite the fact that industrialised SLT packages are mandated by legislation to carry a warning label—''causes cancer''.[30] In addition to the

**Table 1** Categorisation of smokeless tobacco products based on immediate nicotine delivery capabilities

| Brand/type | Moisture (%) | Nicotine (% wet weight) | Calculated % free base nicotine | pH | Nicotine delivery capability |
|---|---|---|---|---|---|
| Tobacco-rette | 14.7 | 1.6 | 10.1 | 7.1 | Low |
| Traditional | 43.1 | 1.6 | 60.2 | 8.2 | Medium high |
| Ntsu (small can) | 48.8 | 1.5 | 86.1 | 8.8 | Very high |
| Ntsu (large can) | 45.9 | 0.9 | 88.4 | 8.9 | Very high |
| Taxi (small can) | 44.1 | 1.1 | 99.1 | 10.0 | Very high |
| Taxi (large can) | 31.4 | 0.8 | 98.5 | 9.9 | Very high |
| Singleton | 1.8 | 0.6 | 99.2 | 10.1 | Very high |

type of information provided in this report, there is a need for data on concentration of nicotine derived N-nitrosamines, the major carcinogen in all SLT products. The traditional SLTs may also contain a considerable amount of toxic combustion products from the ash, which comes from burning of a commonly consumed vegetable plant—''Mukango''—used in the mixture.[18 25]

The present study also indicates that a graduated series of pH levels (7.1–10) exists across the five SLT products tested. This is comparable to findings from the USA, considering that we have used a similar method for pH determination.[16] The existence of SLT products with low, medium, high, and very high nicotine delivery capability on the South African market is consistent with the concept of ''product graduation''—that is, higher dosage products are available for users who develop the desire or crave for more nicotine.[16] Tobacco-rette, a Swedish snus recently introduced onto the South African market for oral use, is manufactured by a subsidiary of the parent company that manufactures Taxi. Although having a comparable or higher total nicotine content (mg/g), it showed the lowest pH and percentage of free base nicotine available for absorption. This product may fit in as a ''starter brand'' that may facilitate initiation of nicotine dependence among new users, especially young people.[31] However, in the absence of this brand which is indeed yet to gain significant market share, users are only able to graduate from the traditional product to any of the limited range of industrial products. It is therefore conceivable that users who develop tolerance to any one of the industrial products will more likely, in the absence of an alternative high nicotine delivery SLT product, switch to a more rapid nicotine delivery system such as the smoked tobacco. This gateway hypothesis is further supported by studies showing a higher proportion of children reporting initiation of use of SLT at an earlier age than reported for use of cigarettes.[4 21]

The nicotine content of brands tested in this study was less than that reported for the Sudanese traditional product (Toombak), higher than values reported for Swedish snus,[32] but within the range of values reported for the US brands.[16 33] However, except for Tobacco-rette, the percentage free base nicotine from the products tested in the present study is higher than that from most of the leading US or Swedish brands. The pH and percentage of free base nicotine reported for the Taxi and Singleton menthol brands in the present study is indeed the highest ever reported for any industrialised snuff brand.

The present study confirms that there may be a considerable variation in nicotine delivery capabilities of SLT products across nations and among products (even when manufactured by the same parent company). The very high pH and free base nicotine in the majority of the South African industrialised products compared to the US and Swedish brands may be part of an industry strategy to sustain addiction and keep the market, as the products traditionally used by the indigenous population already have high pH because of the addition of ash. The higher nicotine content in the Sudanese traditional SLT (Toombak), on the other hand, may be attributed to the differences in tobacco species used in preparation of the different products—*Nicotina rustica* is used in the Sudan,[32] while the South African SLT products are made from *Nicotina tabacum*.

The use of menthol in SLT may result in even higher nicotine exposure, as similar observations have been made with mentholated cigarettes.[34] It is also pertinent to note the significant ethnic variation in nicotine metabolism, which partially determines the nicotine exposure.[35 36] Kandel and Chen[36] also reported that for the same amount of nicotine exposure, nicotine dependence rates are higher among females than males and higher among adolescents than adults. Furthermore, there is evidence of elevated risk of tobacco dependence among offspring of mothers who were exposed during pregnancy to nicotine equivalent to the amount determined in this study for an average SLT user.[37] These findings emphasise the need for country specific analysis of health effects of tobacco products on population groups. Most of the existing literature on SLT is derived from western nations where most users are white male snuff dippers with access to a wide range of SLT products with varying nicotine delivery capabilities. Because most adult users of SLTs mostly consumed via nasal application in South Africa are women from low socioeconomic background, and that there is evidence to suggest that levels of smoking among women have not significantly decreased,[38] there is a rationale for comparative assessment of the role of SLT in harm reduction within different social and biological context.

### What this paper adds

Most of the existing literature on smokeless tobacco (SLT) is derived from developed nations where most users are white male moist snuff dippers with access to a wide range of SLT products. However, until now little has been known about SLT products or pattern of use in less developed nations; thus there is a lack of perspective of its implication for control of tobacco dependence and consequent health risks. This study confirms that there may be a considerable variation in nicotine delivery capabilities of SLT products across nations and among products, even when manufactured by the same parent company. This paper also provides a rationale for comparative assessment of the role of SLT in harm reduction within a biological and social context different from that obtained in the developed nations—namely, use of a limited range of industrialised SLT products with considerably higher nicotine delivery capabilities, and consumption by black/African women of childbearing age.

## Conclusions

Popular South African industrialised SLT brands have very high nicotine delivery capability and thus high potential for dependence and consequent health risks. The limited range of SLT products available along the progress of dose graduation may favour a potential gateway for cigarette use. The popularity of SLT, especially among black women of childbearing age, supports the need for intensified policy action to control its use.

In line with the recently adopted World Health Organization international health treaty—the Framework Convention for Tobacco Control—it is recommended that manufacturers of SLTs be mandated to report to the authorities, and visibly disclose on package labelling, the pH and free base nicotine levels so that consumers are better able to make informed health choices. Furthermore, future studies of the role of SLT as a gateway for cigarette use among black South African women should be encouraged.

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