US commercial brands of moist snuff, 1994. I. Assessment of nicotine, moisture, and pH

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Abstract

Objective **– To determine moisture content, pH, total nicotine, and unprotonated nicotine for each of the 17 moist snuff brands available in Westchester County, New York in 1994. Because batches of the same snuff brand can differ to some extent in chemical composition, and because duration and conditions of storage can cause further changes in composition, we also analysed samples of the five moist snuff brands that top the sales list, bought in six areas of the US, to gain meaningful values for these products, which together account for most of the sales.**

Design **– Initially, the 17 moist snuff brands were bought in several stores in Westchester County, New York. They were analysed in duplicate with standardised laboratory methods for moisture, pH, and nicotine. To obtain representative analytical values for the leading five brands nationwide, the snuff products were purchased in six areas of the US and were analysed to give the average values for the parameters of interest. Nicotine availability for each sample was calculated using the Henderson-Hasselbalch equation.**

Results **– In the 17 brands of moist snuff that were analysed, the moisture content varied between 27.5 and 59.0%, the pH between 5.39 and 7.99, and nicotine on a dry weight basis between 0.47 and 3.43%. For the five moist snuff brands that top the sales list, we found the following average values: for Skoal Bandits (2% of the market), packed in individual sachets, pH 5.37 (SD 0.12), nicotine 2.29% (SD 0.46), 0.23% (SD 0.05) of the nicotine was unprotonated; Skoal Bandits as well as Hawken (1% of the market, pH 5.71 (SD 0.10), nicotine 0.46% (SD 0.02), unprotonated nicotine 0.5% (SD 0.11) are considered to be low nicotine products; Skoal Original, Fine Cut (pH 7.46 (SD 0.14), 2.81% (SD 0.34) nicotine, 22.0% (SD 5.73) unprotonated nicotine) is regarded as a snuff brand with moderate delivery of nicotine (Skoal Original, Fine Cut and other Skoal brands account for 39% of the market); the leading moist snuff brands Copenhagen (42% of the market) and Kodiak (11% of the market) have pH values of 8.0% (SD 0.31) and 8.19 (SD 0.12), contain 2.91% (SD 0.18) and 2.50% (SD 0.22) nicotine, of which 49.0% (SD 16.7) and 59.7% (SD 6.01), respectively, are unprotonated. These are considered strong nicotine delivery systems.**

Conclusions **– These findings indicate that manufacturers of moist snuff may have a strategy of marketing starter brands (Skoal Bandits and Hawken) that establish the initial nicotine dependence of young people. With time, the dependence increases and, eventually, the young snuff user may switch to products with medium (Skoal, Fine Cut) and eventually high (Copenhagen, Kodiak) nicotine delivery, becoming thereby strongly dependent on nicotine.**

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Introduction

In 1984 the International Agency for Research on Cancer reviewed the scientific literature on the tumorigenicity of oral snuff, concluding that "there is sufficient evidence that the oral use of snuff of the types commonly used in North America and Western Europe is carcinogenic to humans".[1] A similar evaluation led the US Surgeon General to warn in 1986 that snuff dipping induces gingival recession and oral lesions, and that it causes cancer in the oral cavity.[2] In 1988 the Surgeon General concluded that "cigarettes and other forms of tobacco are addicting" and that "nicotine is the drug in tobacco that causes addiction".[3] When inserted twice daily into surgically created canals in the lower lips of rats, snuff induced benign and malignant tumours of the oral cavity, including tumours in the tongue.[4,5] Among several carcinogenic agents that have been detected in snuff are certain volatile aldehydes, benzo(a)pyrene, polonium-210, volatile N-nitrosamines (VNA), N-nitrosamino acids (NAA), and – as a major group of carcinogens – tobacco-specific N-nitrosamines (TSNA). The latter are formed from nicotine and minor tobacco alkaloids during the processing, manufacture, and storage of moist snuff.[6,7]

Despite the well-established facts that oral snuff is a human carcinogen, that it induces tumours in the oral cavity of laboratory animals, and that it contains carcinogens, standardised methods for the analysis of snuff

have not been developed for the major known carcinogenic VNA, TSNA, and NAA, nor have comprehensive reports been published on the concentration of nicotine and other toxic agents in the brands of oral snuff on the European or North American market. To inform the public about toxic and addictive agents in snuff is especially important for consumers both in Scandinavian countries and in the US, where moist snuff is heavily consumed. In both regions, moist snuff is the only tobacco product with increasing sales.[8,9] Between 1982 and 1994, the consumption of moist snuff in the US increased by 59%, in contrast with sales of all other types of smokeless tobacco products, and pipe tobaccos, cigars, and cigarettes (−24.3%) which have strongly declined.[8] In Sweden, moist snuff sales increased by 92% between 1970 and 1993.[9] The increase in the consumption of moist snuff is mainly due to the popularity of this type of smokeless tobacco among teenagers and adolescents, who are important targets for the snuff market.[10–12]

To provide information on the chemical composition of snuff, we report here on moisture content, pH, nicotine, and unprotonated nicotine in all of the available moist snuff brands on the US market in 1994. These include 17 moist snuff brands bought in retail stores in Westchester County, New York, as well as the five moist snuff brands that top the sales list, bought in: Boston, Massachusetts; Lexington, Kentucky; Denver, Colorado; Alameda, California; and Lansing, Michigan. The last five products cover about 95% of the moist snuff brands sold in the US in 1993.[13] We chose products from different locations so as to obtain average values for pH, moisture, and nicotine that would be more representative of the composition of the leading five brands across the entire US market than might be the case for values from products obtained in one region alone. This is especially important because storage at ambient and elevated temperatures affects the concentrations of certain moist snuff components, including the carcinogenic TSNA, VNA, and NNA, as well as the pH of moist snuff. It was reported that, after eight weeks of storage, the levels of carcinogenic TSNA rose from 6.24 to 18.7 ppm, NNA increased from 3.13 to 16.3 ppm, and VNA from 0.02 to 0.2 ppm in the leading moist snuff brand.[14]

Materials and methods

MOIST SNUFF

Seventeen US moist snuff brands, manufactured by four US tobacco companies, were bought from retailers (three cans of each brand with the same lot number) in six towns in Westchester County, New York, in July 1994. Without exception, the boxes containing sachets of moist snuff or loose moist snuff of different cuts had been stored on shelves in the stores; all stores but one were air-conditioned. The leading moist snuff brands (three cans of each brand with the same lot number) were also purchased in July 1994 in five other areas, namely, in the Northeast (Boston, Massachusetts), South (Lexington, Kentucky), Midwest (Lansing, Michigan), Central (Denver, Colorado), and West (Alameda, California). All cans of each snuff brand purchased at any given location carried the same number; of course, these lot numbers differed from place to place. Upon receipt of the products in the laboratory, they were immediately stored in a cold room (4 °C) and kept there until the time of analysis. Moisture content, pH, and nicotine were determined in the snuff immediately after opening three cans of each brand from each location and after homogenising their contents.

REAGENTS AND STANDARDS

All chemicals and solvents were analytical reagents of the highest purity from JT Baker Chemical Co., Phillipsburg, New Jersey, and Fisher Scientific Co., Fair Lawn, New Jersey. Nicotine and quinoline, an internal standard for the alkaloid analysis, were purchased from Aldrich Chemical Co. Inc., Milwaukee, Wisconsin. The purity of the reference compounds (> 99.5%) was verified by capillary gas chromatography with flame ionisation detector.

APPARATUS

Nicotine analyses were performed on a Hewlett Packard Model 5890 gas chromatograph equipped with a nitrogen–phosphorous detector and interfaced with a Hewlett Packard Model 3393A integrator (Hewlett Packard, Paramus, New Jersey). The gas chromatographic separation of alkaloids was performed on a DB-5 fused silica capillary column (60 m × 0.25 mm id, 0.25 μm film thickness) bought from J & W Scientific, Folson, California.

METHODS

The analytical methods for the determination of water, alkaloids, and pH in snuff were previously reported: the water content was determined in 10 g of raw tobacco by distillation with benzene;[15] pH was determined for a suspension of 2 g of raw tobacco in 20 ml distilled water after 15 minutes of shaking the vial on a wrist-action shaker; nicotine content in raw tobacco was determined by a procedure slightly modified from that described by Madsen *et al*,[16] that is, 75 mg of snuff were suspended in 3 ml of 1% (w/v) potassium hydroxide in methanol; quinoline (64.5 ppm) was added as an internal standard. After shaking on a wrist-action shaker for six hours, a 50-μl aliquot of the tobacco extract was placed in a 2-ml vial and diluted with 100 μl 1% potassium hydroxide solution in methanol that contained the internal standard for gas chromatography-N–P detector analysis. Gas chromatographic analyses of nicotine were performed as described earlier.[17] All analyses were done in duplicate. The data for pH, moisture content, and nicotine were reproducible within a standard deviation of 5% of the mean.

The percentage of unprotonated nicotine, depending on the pH, was calculated according to the Henderson-Hasselbalch equation.[19] The pKa of 8.02 for nicotine, which was used in the equation, was adopted from the *CRC handbook of chemistry and physics*.[20]

Results

Table 1 presents the data for moisture content, pH, and nicotine of the 17 moist snuff brands that were purchased in Westchester County, New York. On the basis of dry weight, the nicotine concentrations in the snuff brands varied between 0.47% for Hawken Wintergreen and 3.43% for Skoal Long Cut Mint. Nicotine in the three leading brands (Copenhagen (42% of the US market in 1993,[13] Skoal (39%), and Kodiak (11%), representing 92% of all moist snuff brands sold) shows a spread of between 2.42% and 3.43%. The moisture content of 15 of the moist snuff brands varied between 46.3% and 59.0%; Gold River Long Cut, with a moisture content of 27.5%, and Hawken Wintergreen with 28.3% were the two exceptions.

It is well established that free, unbuffered nicotine is the form of this major tobacco alkaloid that is absorbed the fastest.[3,18] At pH 5.2 practically all of the nicotine is monoprotonated; as the pH level rises, the percentage of unprotonated nicotine increases; at pH 7.0 one finds about 9% and at pH 8.0 about 50% unprotonated nicotine.[3,19] Whereas Skoal Bandits Classic (pH 5.39), Hawken Wintergreen (pH 5.65), and Gold River Long Cut (pH 5.70) contain 0.5% or less of the nicotine in unprotonated form, the other 14 moist snuff brands contain various amounts of free nicotine; for example, Kodiak Wintergreen (11% of the US moist snuff market, pH 7.99) generates about 48.3% of free nicotine (table 1). The leading brand, Copenhagen (pH 7.69) generates about 31.9% free nicotine and Skoal, Original Fine Cut, Wintergreen (pH 7.27) approximately 15.1%.

Table 2 lists the data for the five leading commercial moist snuff brands[13] that were bought in six different regions of the US. The cans of each moist snuff brand bought at different locations carried different lot numbers. As was expected, we recorded differences. For example, in Copenhagen (42% of the US market in 1993) pH ranges from 7.60 to 8.37 (average 8.0 (SD 0.31)); moisture content between 57.0% and 61.6% (58.8% (SD 1.78)), and nicotine content between 2.71% and 3.16% (2.91% (SD 0.18)). These variations are primarily due to differences between batches of the same product and are also influenced by duration and conditions of storage.[14,21,22] A recent study has shown that storage conditions of moist snuff can significantly affect the pH and thus the amount of unprotonated nicotine in the product.[14,21] During prolonged storage of moist snuff, the pH increases significantly. Based on this observation, and because there are quantitative differences in the chemical composition between batches of the same snuff brand, it is not surprising that we observed remarkable spreads in nicotine and pH values and concomitant variations in unprotonated nicotine in a given snuff brand when the product was purchased at six different locations in the US. Specifically, the pH values for the six samples of Copenhagen varied between 7.60 and 8.37 (8.0 (SD 0.31)), and the fraction of unprotonated nicotine ranged from 27.5 to 69.1% (49.0% (SD 16.7)).

The differences in composition of the other four leading moist snuff brands were similar to those measured in Copenhagen. One exception stands out. The pH of Skoal Bandits Straight bought at five locations measured 5.37 (SD 0.12). The pH level for the same brand bought in Westchester County, New York was 7.42, and that of a second sample bought at another store in Westchester was 7.30. This major difference between the Westchester samples and the other five samples of the same brand could reflect a significant change in the

*Table 1 Nicotine, moisture, and pH levels of 17 moist snuff brands bought in Westchester County, New York**

	Brand	Moisture (%)	pH of snuff suspension	Nicotine (% dry weight)	Nicotine (mg/g)	Unprotonated nicotine (%)
1	Copenhagen	57.0	7.69	2.71	11.7	31.9
2	Skoal, Original Fine Cut, Wintergreen	59.0	7.27	2.78	11.4	15.1
3	Skoal, Long Cut, Straight	58.2	7.51	3.11	13.0	23.6
4	Skoal, Long Cut, Classic	56.5	6.82	2.65	11.5	5.93
5	Skoal, Long Cut, Wintergreen	56.5	7.22	3.27	14.2	13.6
6	Skoal, Long Cut, Spearmint	56.7	7.26	3.34	14.5	14.8
7	Skoal, Long Cut, Mint	57.8	7.51†	3.43	14.5	23.6
8	Skoal, Long Cut, Cherry	55.9	7.44	2.42	10.7	20.8
9	Skoal Bandits, Straight	52.9	7.42‡	2.11	10.0	20.1
10	Skoal Bandits, Classic	53.0	5.39	2.57	12.1	0.23
11	Skoal Bandits, Wintergreen	50.1	6.82	1.82	9.1	5.93
12	Skoal Bandits, Mint	49.2	7.37	1.71	8.7	18.3
13	Kodiak, Wintergreen	56.8	7.99	2.61	11.5	48.3
14	Hawken, Wintergreen	28.3	5.65	0.47	3.4	0.43
15	Silver Creek, Wintergreen	51.9	6.29	1.71	8.2	1.83
16	Gold River, Long Cut	27.5	5.70	0.81	5.9	0.48
17	Red Man, Fine Cut, Straight	46.3	6.74	2.45	13.2	4.98

Brands 1–12 are manufactured by the US Tobacco Company, brands 13 and 14 by the Conwood Company, brands 15 and 16 by the Helme Tobacco Company, and brand 17 by the Pinkerton Tobacco Company.
* All brands were bought between 6 July and 30 July 1994 (details of lot numbers, place of purchase, and storage conditions of the snuff boxes in each store are available.)
† A sample bought in July 1994 gave a pH value of 5.56. Purchase of the same moist snuff – Skoal, Long Cut, Mint, in September 1994 (in a different store) gave a pH value of 7.51.
‡ A second time we bought samples of the same brand in Westchester, NY, 22 August 1994. The pH value was now 7.30.

Table 2 Nicotine, moisture, and pH levels of the leading five moist snuff brands bought at six different locations in the US

Brand	*US market share, 1993 (%)*	*Place of purchase*	*Moisture (%)*	*pH of suspension*	*Nicotine (% dry weight)*	*Nicotine (mg/g)*	*Unprotonated nicotine (%)*
Copenhagen	42	Westchester, NY	57.0	7.69	2.71	11.7	31.9
		Boston, MA	58.0	8.32	3.16	13.3	66.6
		Lexington, KY	57.9	7.83	2.75	11.6	39.2
		Denver, CO	57.9	7.60	2.87	12.1	27.5
		Alameda, CA	61.6	8.37	3.09	11.9	69.1
		Lansing, MI	60.4	8.19	2.88	11.4	59.7
			58.8±1.78	8.0±0.31	2.91±0.18	12.0±0.7	49.0±16.7
Skoal, Original, Fine Cut, Wintergreen	39*	Westchester, NY	59.0	7.27	2.78	11.4	15.1
		Boston, MA	57.3	7.70	2.69	11.5	32.3
		Lexington, KY	57.0	7.35	2.32	10.0	17.6
		Denver, CO	57.3	7.39	2.74	11.7	19.0
		Alameda, CA	59.0	7.56	3.31	13.6	25.7
		Lansing, MI	57.6	7.47	3.04	12.9	22.0
			57.9±0.90	7.46±0.14	2.81±0.34	11.9±1.3	22.0±5.73
Kodiak, Wintergreen	11	Westchester, NY	56.8	7.99	2.61	11.3	48.3
		Boston, MA	54.7	8.25	2.24	10.1	62.9
		Lexington, KY	59.0	8.17	2.40	10.4	58.5
		Denver, CO	56.5	8.15	2.37	10.3	57.4
		Alameda, CA	54.1	8.30	2.49	11.4	65.6
		Lansing, MI	58.5	8.30	2.88	12.0	65.6
			56.5±2.0	8.19±0.11	2.50±0.22	10.9±0.8	59.7±6.01
Hawken, Wintergreen	1	Westchester, NY	28.3	5.65	0.47	3.4	0.42
		Boston, MA	24.6	5.77	0.46	3.5	0.56
		Lexington, KY	30.1	5.80	0.45	3.1	0.60
		Denver, CO	31.2	5.53	0.48	3.3	0.32
		Alameda, CA	NA	NA	NA	NA	NA
		Lansing, MI	29.9	5.78	0.42	2.9	0.57
			28.8±2.6	5.71±0.10	0.46±0.02	3.2±0.2	0.50±0.11
Skoal Bandits Straight	2	Westchester, NY	52.9	(7.42)†	2.11	9.9	(20.06)†
		Boston, MA	49.4	5.15	2.24	11.3	0.13
		Lexington, KY	54.1	5.42	2.02	9.2	0.25
		Denver, CO	68.4	5.44	3.16	10.0	0.26
		Alameda, CA	50.1	5.48	1.84	9.2	0.29
		Lansing, MI	54.0	5.36	2.34	10.8	0.22
			54.8±6.3	5.37±0.12	2.29±0.46	10.1±0.8	0.23±0.05

*37% includes Skoal Original and various Skoal Long Cuts.
†For confirmation we purchased another sample of Skoal Bandits, Straight, on 22 August 1994. The pH was now 7.30, thus we assume the Westchester samples originated from another manufacturing method than the samples from the other five cities. The value for the Westchester sample is not included in the calculation of the average value.
NA = not analysed.

manufacture of this brand of moist snuff, such as the addition of ammonium, sodium, and/or potassium salts during the fermentation, for the products bought in Westchester County.[23] In Sweden, sodium carbonate is added during the snuff production, most of which changes to sodium bicarbonate during processing.[24]

Discussion

This study reports major differences in pH levels (5.15–8.37), nicotine content (0.42–3.43% based on dry weight), and the percentage of unprotonated nicotine (0.13–69.1) of the moist snuff brands that are marketed in the US. More importantly, this investigation documents significant variances in the level of unprotonated nicotine within the 17 moist snuff brands. This observation is of major consequence as nicotine is the addicting agent in snuff.[3] The measurement of the pH values for individual snuff brands suspended in saliva could not be carried out for logistic reasons. However, attempts should be encouraged to measure the pH values accordingly.

Disregarding the dippers' intensity of oral manipulation, primarily three factors govern the delivery of nicotine from a snuff product into the bloodstream of the snuff dipper. These are the (long or fine) cut of the tobacco, the type of packaging, and the concentration of nicotine and the proportion unprotonated. Skoal Bandits (table 2, brand 5) comes in sachets, which are placed in the mouth and release nicotine slowly so that the oral cavity is only minimally irritated.[25] This brand contains relatively low levels of nicotine (2.29% (SD 0.46)) and has a low pH (5.37 (SD 0.12)) and, therefore, a low percentage of unprotonated nicotine (0.23% (SD 0.05)). Thus, Skoal Bandits and also Hawken (table 2, brand 4; nicotine 0.46% (SD 0.02), pH 5.71 (SD 0.10), unprotonated nicotine 0.5% (SD 0.11)) can be regarded as brands with relatively low nicotine delivery. Skoal Original, Fine Cut (table 2, brand 2) contains relatively high levels of nicotine (2.81% (SD 0.34)), has a pH near neutral (7.46 (SD 0.14)), and a medium content of unprotonated nicotine (22.0% (SD 5.73)); thus, it may be regarded as a snuff brand with moderate nicotine delivery. Copenhagen (table 2, brand 1), a fine-cut snuff of high nicotine content (2.91% (SD 0.18)), a high pH (8.0 (SD 0.31)) and a high percentage of unprotonated nicotine (49.0% (SD 16.7)), as well as Kodiak (2.50% (SD 0.22); 8.19 (SD 0.11); 59.7% (SD 6.01)) must be regarded as high nicotine delivery systems.

The existence of snuff brands with low, medium, and high nicotine delivery supports the concept that the product design is aimed at creating and maintaining nicotine dependence.[26, 27] Brands with low nicotine availability may well be "starter brands" that initiate the nicotine dependence of young people. As indicated in the marketing plans of the dominant US company in this field, with time, the strategy calls for increased dependence on nicotine so that eventually the snuff dipper "graduates" *via* a snuff with moderate nicotine delivery to brands with higher degrees of nicotine delivery and potential bioavailability.[28] These latter brands can then satisfy the

increased craving of the snuff dipper for nicotine as tolerance to lower nicotine brands develops. Thus, it is not surprising that Copenhagen with its high nicotine delivery has dominated the US moist snuff market during the last 12 years with 40–47 % of the sales of all brands.

Moist snuff is the only tobacco product in its major sales territories with a marked increase in sales; in the US sales have risen by 53 % between 1982 and 1994[13], and in Sweden by 92 % between 1970 and 1993.[9] The consumers most responsible for this increase are teenagers and adolescents.[10,29,30] It is of concern that a novice may buy a product with a low bioavailability of nicotine that is geared to the non-tolerant individual, and that this person may then progress unknowingly via an intermediate product to one with high bioavailability of nicotine.

In addition to surveys of the type reported here, there is a need for data on the concentrations of the nicotine-derived N-nitrosamines, the major carcinogens in the various moist snuff brands. The content of ammonium and potassium salts in the snuff brands[23] should also be monitored regularly. Such additives not only influence the pH of the snuff and thus the potential bioavailability of nicotine, but they also increase the concentrations of the carcinogenic N-nitrosamines in snuff.[14,22,31] This study has documented that the moist snuff brands on the US market vary significantly in nicotine content (2.9–14.5 mg/g), the pH values (5.15–8.37), and percentage of unprotonated nicotine (0.13–69.1).

We hope that this finding will encourage regulatory agencies to take appropriate action to prevent oral snuff manufacturers from causing and maintaining nicotine dependence among young people. As a first step, overall nicotine level, pH levels, and free nicotine level should be disclosed in advertising, promotion, and labelling of snuff containers.

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1 International Agency for Research on Cancer. Tobacco habits other than smoking; betel quid and areca-nut chewing; and some related nitrosamines. *IARC monograph on the evaluation of the carcinogenic risk of chemicals to humans*. 1985; **17**: 37–136.
2 US Department of Health and Human Services. *The health consequences of using smokeless tobacco*. Bethesda, Maryland: National Cancer Institute, 1986. (NIH Publication No 86–2874.)
3 US Department of Health and Human Services. *The health consequences of smoking: nicotine addiction. A report of the Surgeon General, 1988*. Rockville, Maryland: Public Health Service, Centers for Disease Control, Office on Smoking and Health, 1988. (DHHS Publication No (CDC) 88–8406.)
4 Hecht SS, Rivenson A, Braley J, DiBello J, Adams JD, Hoffmann D. Induction of oral cavity tumors in F344 rats by tobacco-specific nitrosamines and snuff. *Cancer Res* 1986; **46**: 4162–6.
5 Johansson SL, Hirsch JM, Larson P-A, Saidi J, Österdahl B-G. Snuff-induced carcinogenesis: Effect of snuff in rats initiated with 4-nitroquinoline-N-oxide. *Cancer Res* 1989; **49**: 3063–9.
6 Brunnemann KD, Hoffmann D. Chemical composition of smokeless tobacco products. *Natl Cancer Inst Smoking Tobacco Control Monogr* 1993; **2**: 96–108.
7 Hoffmann D, Brunnemann KD, Prokopczyk B, Djordjevic MV. Tobacco-specific N-nitrosamines and areca-derived N-nitrosamines: chemistry, biochemistry, carcinogenicity and relevance to humans. *J Toxicol Environ Health* 1994; **41**: 1–52.
8 US Department of Agriculture Economic Research Service. *Tobacco Situation and Outlook Report. Tech Rep Ser* 1994; **228**: 4–9.
9 Glogan T. Swedish government wages war on tobacco industry. *Tobacco J Int* 1993; **3**: 20–24.
10 Orlandi MA, Boyd G. Smokeless tobacco use among adolescents: A theoretical overview. *Natl Cancer Inst Monogr* 1989; **8**: 5–12.
11 Ramström LM, Tibblin H. *Tobacco habits in Sweden. Natl Smoking Health Assoc.* Stockholm, Sweden: Tema Tabak, 1986.
12 D'Onofrio CN. Marketing smokeless tobacco: implications for preventive education. *Natl Cancer Inst Smoking Tobacco Control Monogr* 1993; **2**: 247–59.
13 US Department of Agriculture, Economic Research Service. Tobacco situation and outlook report. *Tech Rep Ser* 1994; **227**: 4–7.
14 Djordjevic MV, Fan J, Bush LP, Brunnemann KD, Hoffmann D. Effects of storage conditions on levels of tobacco-specific N-nitrosamines and N-nitrosamino acids in US moist snuff. *J Agric Food Chem* 1993; **41**: 1790–94.
15 VonBethmann SB, Lipp G, vanNooy H. Feuchtigkeitsbestimmung im Tabak. *Beitr Tabakforsch* 1961; **1**: 19–21.
16 Madsen JP, Bush LP, Gay SL. Effect of curing on polyamine content of leaves of *Nicotiana tabacum*. L. Genotypes with different alkaloid levels. *J Agric Food Chem* 1985; **33**: 1182–85.
17 Djordjevic MV, Brunnemann KD, Hoffmann D. Identification and analysis of a nicotine-derived N-nitrosamino acid and other nitrosamino acids in tobacco. *Carcinogenesis* 1989; **10**: 1725–31.
18 Brunnemann KD, Hoffmann D. The pH of tobacco smoke. *Food Cosmet Toxicol* 1974; **12**: 115–24.
19 Weast RC, Lide DR, eds. *CRC handbook of chemistry and physics*. 70th ed. Boca Raton, Florida: CRC Press, 1989, D-162.
20 Armitage AK, Turner DM. Absorption of nicotine in cigarette and cigar smoke through the oral mucosa. *Nature* 1970; **226**: 1231–2.
21 Anderson RA, Fleming PD, Burton HR, Hamilton-Kamp TR, Sutton TG. Nitrosated, acetylated and oxidized pyridine alkaloids during storage of smokeless tobacco; effects of moisture, temperature and their interactions. *J Agric Food Chem* 1991; **39**: 1280–87.
22 Andersen RA, Fleming FD, Hamilton-Kemp TR, Hildebrand DF. pH Changes in smokeless tobacco undergoing nitrosation during prolonged storage: effects of moisture, temperature, and duration. *J Agric Food Chem* 1993; **41**: 968–72.
23 Pape SM. *Smokeless tobacco ingredient list as of April 4, 1994*. Report to Subcommittee on Health and the Environment, Committee on Energy and Commerce, US House of Representatives. Washington DC: Patton, Boggs and Blow, May 3, 1994, 45.
24 Gothia Tobak. *Rökfri tobak fran Göteborg*. Göteborg, Sweden, 1994.
25 Andersson G, Axéll T, Lårsson A. Impact of consumption factors on soft tissue changes in Swedish moist snuff users. A histological study. *J Oral Pathol Med* 1990; **19**: 453–8.
26 Connolly G. *In the search for a perfect starter product. Manipulation of nicotine in oral snuff brands*. Boston, Massachusetts: Massachusetts Department of Public Health, May 1994; 7.
27 Henningfield JE, Radzius A, Cone EJ. Estimation of available nicotine content of six smokeless tobacco products. *Tobacco Control* 1995, **4**: 57–61.
28 Connolly GN. The marketing of nicotine addiction by one oral snuff manufacturer. *Tobacco Control* 1995; **4**: 73–9.
29 Modéer T, Lavstedt S, Ahlung C. Relation between tobacco-accumulation and oral health in Swedish school children. *Acta Odontol Scand* 1989; **38**: 223–227.
30 Bergström J. The use of smokeless tobacco in Sweden. *Natl Cancer Inst Smoking Tobacco Control Monogr* 1993; **2**: 74–7.
31 Hecht SS, Chen C-HB, Ornaf RM, Jacobs E, Adams JD, Hoffmann D. Reaction of nicotine and sodium nitrite: formation of nitrosamines and fragmentation of the pyrrolidine ring. *J Org Chem* 1978; **43**: 72–6.