

Nicotine Reduction in Tobacco and Tobacco Smoke

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IN addition to the selection of low-nicotine varieties of tobacco, several approaches have been used, or suggested for use to reduce the nicotine in tobacco smoke by alteration of the alkaloid content of leaf. In a general way, these approaches can be divided into three categories: physical methods, such as heat, steam, or solvent extraction; chemical techniques utilizing oxidants or other reactive chemical agents; and biological methods, such as fermentation.

PHYSICAL METHODS

The basic dissociation constants for nicotine (1) are 7.94×10^{-12} and 4.90×10^{-7} (for the pyridyl and *N*-methylpyrrolidinyl moieties, respectively), and the *pH* values of domestic cigar and cigarette tobaccos are within the range of 4.90–7.25 (2). Thus, nicotine in most tobaccos exists primarily in the salt form, although the presence of this alkaloid and related bases bound in high-molecular weight pigments with unknown linkages has been reported recently (3). Therefore, physical methods for reducing nicotine in leaf usually require alkalization before treatment to release the free bases. The latter may then be removed by water, organic solvents, or passage of moist air through the tobacco with or without heat (4). This general approach suffers from several economic and technical disadvantages, including undesirable alteration of the flavor, aroma, and combustibility of the treated tobacco. However, several brands of domestic cigarettes marketed over 30 years ago contained tobacco denicotinized by such processes (5). At present, one brand of U.S. cigarettes employs a physical method to reduce the nicotine; since commercial practices are confidential, details of the process are unavailable.

Another physical method involves the quick heating of tobacco to 100°C with concurrent passage of air through the tobacco and is believed to act by thermal dissociation of the nicotine salts (4). Although this method was employed in Austria in the past, the costs involved in the process apparently mitigated against its widespread use. A method for nicotine reduction involving electrolysis has also been reported (4).

CHEMICAL APPROACHES

In the chemical approach, several agents have been used experimentally to reduce nicotine levels in leaf. Among these are compounds which oxidize nicotine to derivatives having lower toxicity than the parent alkaloid, *e.g.*, oxynicotine. Hydrogen peroxide and ozone have been employed in this manner. However, as expected, other leaf constituents also react with these oxidants, and the aroma and certain physical properties of the tobacco are affected deleteriously (4). Treatment of experimental tobaccos with nitrous oxide, carbon monoxide, and sulfur dioxide has given variable results with relatively small reductions of nicotine (about 5 to 20%) in some cases (6).

Of the various chemical agents suggested for use in nicotine reduction, ethylene and propylene oxides have created the most interest. Of the two, ethylene oxide has been studied more extensively and has been employed commercially as a fumigant and fermentation accelerator in some European countries. This oxide is an alkylating agent which acts by ring fission, forming a 2-hydroxyethyl radical that alkylates nucleophiles. In the case of nicotine, the major reaction product is *N*-(2-hydroxyethyl)-3-(2'-*N'*-methylpyrrolidiny)pyridine, which occurs in leaf as the salt (7). The same product is obtained from the dihydrochloride and monoacetate of nicotine, but a second monoalkylated compound formed by reaction with the pyrrolidine nitrogen of nicotine is also produced from the monoacetate (8). In addition, *N*-methylaminoethanol may be formed from reactions between the oxide and methylamine or other aliphatic amines in tobacco when extremely high concentrations of ethylene oxide are employed (9). In treating tobacco with ethylene oxide, concentration of gas, proportion of gas to tobacco, reaction time, reaction temperature, and moisture content of tobacco are some important variables (10, 11). The oxide also reacts with other tobacco constituents and may influence flavor deleteriously when some conditions of treatment are employed (10). In one study (10), about 40-50% of the leaf nicotine was alkylated in this reaction without altering the flavor of the smoke, but higher levels of bound nicotine were accompanied by the development of undesirable organoleptic properties.

Data on the thermal stability of leaf nicotine bound in this way are sparse. Pyrolytic experiments on the alkylated reaction products indicate that cleavage occurs easily, yielding nicotine, pyridine, and other basic compounds (8). In the case of ethylene oxide-treated cigarettes, reductions

of 25% of the nicotine in smoke have been claimed (11) and only traces of nicotine in smoke have been reported when all the leaf nicotine reacted with the oxide (7). Other data indicate that about 30% of the alkylated nicotine in leaf is cleaved, releasing the alkaloid and related products into the smoke (8). The thermolability of the alkylated nicotine may not be unexpected, since a thermal cleavage superficially similar to the classical Hofmann degradation can be visualized easily.

More recent work in Austria has shown that treatment of tobacco with ethylene oxide under conditions used in commercial practice has little effect on tobacco aroma and flavor and results in only small reductions (usually less than 5% in nicotine, dry smoke condensate, and benzo[*a*]pyrene contents of smoke and nicotine levels of leaf for most tobacco types (12).

It is believed that the use of ethylene oxide in U.S. commercial practices is very limited, if not nil. Fumigants are probably not used to any large extent for tobaccos grown domestically and intended for domestic use, but when such agents are required, methyl bromide may be employed. Although this halide is also an alkylating agent, there is apparently no significant binding of leaf nicotine into methyl derivatives of high thermal stability.

BIOLOGICAL APPROACHES

Perhaps the most practical processing approach for reducing nicotine in tobacco leaf is biological. Generally, cigarette tobaccos in the United States are subjected to a period of prolonged storage (1.5–3.0 years) before being manufactured into cigarettes. This “aging” process involves the packing of leaf strips with relatively low moisture contents (10–13% for flue-cured) into large hogsheads and storage in unheated warehouses at ambient temperatures (2, 13) resulting in subtle chemical changes that are reflected in improved flavor and aroma (14). The available information on these chemical changes (13–15) indicates that small losses (1–15%) of nicotine usually occur during aging, but reduction as high as 34% has been reported for Burley tobacco (15). Also, a decrease in *p*H (from about 5.25–4.80) may occur during aging. Cigar tobaccos and snuff are subjected to a more vigorous process (“fermentation”) involving a series of steps in which high levels of leaf moisture (up to 50%), high humidity, and high temperature (up to 50°C) are employed for shorter periods than aging. Fermentation extensively alters cellular constituents, including nicotine, and increases *p*H. As much as 90% of the nicotine may be transformed during fermentation (13), but lower values (50% or less) are frequently obtained. Some of the loss is due to mechanical leaching with the added water, but most of it is a result of enzymatic and/or microbial transformation of nicotine into volatile or nonvolatile products, with the latter predominating. The major nonvolatile products are oxynicotine, cotinine, nicotinic acid, nicotinamide, *N*-methylnicotinamide, alkyl pyridyl ketones, and polymeric pyridine compounds (16) which may be related to the com-

plex brown leaf pigments (3). About 75% of the nicotine transformed during fermentation is found in these products (4), most of which are pharmacologically less active than nicotine (17). To date, cigarette tobaccos have not been fermented industrially in the United States, but some European commercial practices include a mild fermentation of sun-cured and other tobacco types.

NICOTINE ABSORPTION FROM SMOKE

Although a correlation exists between the total nicotine levels of leaf and smoke, a similar relationship is not found between the nicotine level absorbed by the smoker and the total nicotine concentration in smoke. This effect is probably due in part to the influence of pH on the partitioning of nicotine between the particulate and vapor phases of smoke. High pH favors release of the more volatile free bases from the particulate phase and a displacement of the particulate-vapor equilibrium of nicotine toward the vapor phase. Flue-cured, air-cured, and cigar tobaccos show progressively higher pH in the smoke produced therefrom, and progressively larger proportions of nicotine in the vapor phase would be expected in this series. Laboratory studies have shown that a direct relationship does exist between the pH of smoke and the degree of nicotine absorption in simulated saliva (18). Approximately fivefold increases in absorption are apparent in tobacco smoke varying in pH from 5.0–8.0. Clinical data confirming this pattern have also been obtained (19). Of course, other factors may affect the nicotine levels of smokers, such as degree of inhalation and puff volume, which in turn may also be influenced by pH through effects on the irritative properties of the smoke.

CURRENT AND FUTURE INVESTIGATIONS

From the above, it is apparent that one may theoretically reduce the free nicotine absorbed by the smoker by increasing the acidity of the smoke. One way to do this would be through increasing the acidity of the leaf. In studies conducted almost 40 years ago, acidification of tobacco by the addition of citric acid, oxalic acid, and sulfuric acids was claimed to increase the bound nicotine in leaf (5), but these findings require confirmation. The use of citric acid in this manner is known to increase the mildness of cigarette smoke (20) and is claimed to inhibit in part the ciliostatic activity of smoke (21). The effect of such acidification on the partitioning of nicotine between particulate and vapor phases of smoke has not been determined. However, since essentially all the nicotine in smoke from domestic cigarettes is believed to be in the particulate matter, it is doubtful whether further acidification of the tobacco would affect the vapor-particulate equilibrium significantly.

Another possible avenue of exploiting the *pH* effect may involve filtration. There are indications that selective filtration of nicotine (presumably from the vapor phase) may be achieved (22). If the *pH* of the smoke were raised to increase the nicotine in the vapor phase and a selective filter used to remove the alkaloid, the free nicotine available for absorption might be reduced. The total quantity of nicotine that would have to be removed from smoke under such conditions would be substantial. Presently used filters have limited capacities and may not be capable of removing all the nicotine, phenol, and gaseous components that would be potentially filterable from smoke having large proportions of nicotine in the vapor phase.

Although there are many domestic patents for special filters that claim to remove nicotine from smoke (23), including ion exchange resins, none of these has apparently been employed commercially.

The use of additives in cigarettes to alter combustion patterns and chemical composition of smoke is another possible route to nicotine reduction. The use of sodium nitrate in this way has produced some slight selective reduction of nicotine in addition to a decrease in benzo[*a*]pyrene (24).

A potential complicating factor in the entire problem has been the recent finding that nicotine and related alkaloids and bases occur in smoke as moieties in high-molecular weight pigments (25, 26). These pigments comprise at least 3-5% of smoke condensate and must be considered major constituents. Although studied incompletely, available data indicate that the alkaloids are firmly linked within the pigment molecule and are not hydrolyzed by conventional acidic hydrolysis but are released during experimental pyrolysis (27). Although it has not been possible to obtain analytical values for the total nicotine contents of the pigments thus far, it appears that their contribution to the total alkaloid content of smoke may be relatively small. The *in vivo* fate of these pigments is obviously unknown.

SUMMARY

At present, the most practical commercial approach for reduction of nicotine in smoke is that used most widely in the United States: selection of low-nicotine tobacco varieties and leaves. Almost all the available physical and chemical methods to reduce the nicotine in leaf have economic or technical shortcomings that mitigate against their commercial adoption. However, promising avenues for further research are available, including the use of ethylene oxide to bind leaf nicotine and the possibility of fermentation of cigarette tobaccos. Also, alteration of nicotine levels in smoke by the use of tobacco additives or a combination of selective filtration and *pH* modification should be investigated more extensively.

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