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Commentary

It Ain't Necessarily So

by

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The following is a line-up of the allegations made by C. BATES, M. JARVIS and G. CONNOLLY in "Tobacco Additives – Cigarette Engineering and Nicotine Addiction" (1). These allegations are not in agreement with the facts reported in the scientific literature (2–18). [Beitr. Tabakforsch. Int. 19 (2000) 51–54]

AMMONIUM COMPOUNDS

Allegation:
Ammonium compounds are used by the cigarette industry (i) to increase nicotine uptake by the smoker (in terms of both amount and rate) and, thereby, enhance the addictive potential of nicotine as well as (ii) to cheat the determination of smoke nicotine by the FTC (Federal Trade Commission) method which is almost identical to the ISO (International Organization for Standardization) method, with the objective of reducing the amounts measured.
The increase of the *pH value* of cigarette smoke (i.e., a shift towards alkalinity), resulting from the addition of ammonium compounds to tobacco, is claimed to be the causal mechanism for both effects. Increasing the *pH value* is said to increase both the proportion of *free* nicotine in the smoke and the amount of *gas phase nicotine* which is not detected by the FTC/ISO method and which exerts intensified physiological effects on the smoker (1).

Use: Ammonium compounds are used for two reasons. On the one hand, they react during tobacco processing and smoking with certain substances (predominantly sugars) and form valuable flavor compounds (2, pp 274–275); on the other hand, diammonium phosphate in particular serves as a processing agent in the manufacturing of some types of tobacco sheet (2, p 270).

Content: The content of ammonium ions (NH_4^+) in tobacco of commercial American blend cigarettes is 0.1–0.4% (3, 4). Even with the addition of ammonium compounds, their concentration in the tobacco of cigarettes is within the range typical for raw tobacco (2, p 266).

Transfer: The transfer of ammonium ions into mainstream smoke in the form of free ammonia (NH_3) is rather ineffective (< 5%) (3, 4). Therefore, the addition of ammonium compounds to tobacco is a quite impractical way to control the concentration of ammonia in smoke. Whilst the addition of ammonium compounds to tobacco can increase the ammonia content of mainstream smoke (4), other tobacco blend components such as nitrates and amino acids have a larger influence on the ammonia content of mainstream smoke. During combustion, these nitrogen-containing tobacco constituents form and transfer ammonia into mainstream smoke (5). An evaluation of ten commercial U.S. cigarettes (3) revealed that mainstream smoke ammonia was strongly correlated with "tar" yields, and that cigarettes with comparable "tar" yields have approximately equal amounts of ammonia in mainstream smoke despite the fact that they differed in their ammonia content of tobacco by a factor of three.

Effects: Despite considerably varying ammonia contents in mainstream smoke (between 1.4 μg and 33 μg per cigarette) an investigation of commercial cigarettes showed only small differences in the *pH value* of smoke (6.00–6.35); within this small range of 0.35 pH units no correlation was apparent with the smoke ammonia levels (3). This is a clear indication of the fact that ammonia in smoke has no appreciable effect on *smoke pH*.
These findings were confirmed in a second study (4) which included experimental cigarettes with ammonia

contents in mainstream smoke of 7.5 to 12.5 μg per cigarette. The smoke *pH values* [using a different measuring method compared to (3)] were between 5.10 and 5.35. It should be pointed out, however, that pH is a measure of the activity of hydrogen ions in a dilute aqueous solution at equilibrium. Tobacco smoke is not a dilute aqueous solution at equilibrium. Thus *smoke pH* values, obtained by measuring an aqueous extract of smoke, cannot be directly extrapolated to the tobacco smoke itself but can provide an indication of the relative concentrations of water-extractable acids and bases in smoke.
The determination of smoke nicotine by the FTC/ISO method is not cheated by the ammonia content of mainstream smoke. In fact, using test cigarettes with different amounts of smoke ammonia (between 1.0 μg and 24 μg per cigarette), the trapping efficiency of the Cambridge filter for mainstream smoke nicotine in all cases was > 99% (4).

Conclusions:

- The addition of ammonium compounds to tobacco under commercial conditions
  - does not increase the *pH value* of cigarette mainstream smoke [a fact which eliminates the basis for the allegations raised in (1)];
  - does not increase the nicotine content of cigarette mainstream smoke;
  - has no influence on the determination of smoke nicotine when the FTC/ISO method is used.

SUGARS – ACETALDEHYDE

Allegation:
The addition of sugars results in an increase of acetaldehyde in cigarette smoke – a process which can be controlled by the manufacturer. Acetaldehyde and nicotine act synergistically, thereby increasing the addictive potential of nicotine (1).

Use: Sugars (i.e., monosaccharides such as glucose and fructose – these also in the form of corn syrup – and disaccharides like sucrose) are used in the casing of Burley-containing American blends. Sufficient sugar content in tobacco is necessary to avoid excessive harshness of taste and to neutralize irritating substances in the smoke. Certain tobaccos are easier to process following the addition of sugars.
Acetaldehyde is not added to tobacco (except possibly as a minimal constituent of a natural flavor).

Content: Depending on the type of the blend, total sugar content in finished tobacco may be as high as 20% (6). Acetaldehyde is found in cigarette tobacco only in exceedingly small amounts.

Transfer: During smoking, all carbohydrates (mono-, di-, oligo- and polysaccharides) are burned or decomposed by pyrolysis. There is no relationship between the content of simple sugars (i.e., mono- and disaccharides) in tobacco and the amount of acetaldehyde in the smoke (6, 7). The extraction of sugars from tobacco does not result in less acetaldehyde being formed during smoking (8). The ^{14}C-label in glucose or sucrose is only minimally (0.05% and 0.06%, respectively) recovered in smoke in the form of acetaldehyde (9).
The essential source materials in tobacco for the formation of acetaldehyde are the structural polysaccharides of the leaves and ribs (cellulose, hemicelluloses and pectin) as well as starch (5, p 421; 10).

Effects: Acetaldehyde when formed during smoking is found at > 98% in the gas phase of mainstream smoke (5, p 412). To a larger part (45–70%) it is absorbed in the mouth and the upper airways and rapidly metabolized; a smaller proportion is exhaled (11). Due to the very short half-life of acetaldehyde in a biological environment (a few seconds only) no increase of acetaldehyde levels in blood is observed in smokers (12).
On the other side, nicotine is absorbed in the lungs with very high efficiency (80–90%) (13).

Conclusions:

- Sugars (i.e., mono- and disaccharides) in tobacco (whether naturally present or added) do not contribute with any significance to the formation of acetaldehyde during smoking. Natural polysaccharide constituents of tobacco (such as cellulose) are the main source of acetaldehyde in mainstream smoke.
- In the body, acetaldehyde is very rapidly converted to acetic acid. Therefore, smoking does not cause an increase of the acetaldehyde concentration in the blood – let alone in the brain.
- The pharmacokinetic properties of acetaldehyde and nicotine are so different that synergistic effects – particularly in the brain – are practically impossible. Any acetaldehyde in the blood is metabolized so quickly that it cannot reach the brain.

COCOA – THEOBROMINE

Allegation:
Theobromine acts as a bronchodilator; it facilitates the inhalation of smoke and the uptake of nicotine (1).

Use: Theobromine is not used as an additive. It is a constituent of cocoa (2.6%) (14). Cocoa is used in casings for Burley-containing American blends and serves to enhance natural Burley taste. The addition of cocoa, however, does not result in a sweet or chocolate-like aroma in the tobacco smoke.

Content: Assuming a 5% concentration of cocoa in tobacco, the theobromine content of a cigarette would be approximately 1 mg. In reality, the cocoa concentration in tobacco is ≤ 2%.

Transfer: The transfer rate of theobromine to mainstream smoke is about 13% (15). Assuming 5% cocoa in tobacco and a consumption of 40 cigarettes per day, the maximum uptake by a smoker would be 5.2 mg theobromine per day.

Effects: The therapeutic principle of bronchodilation with theobromine calls for sustained plasma levels of 10–20 mg/L. In a clinical study, the administration of approximately 450 mg theobromine during the day resulted in a peak plasma concentration of 9.8 mg/L (16). Because of its relatively weak pharmacological effect theobromine is no longer used for therapeutic purposes. In a pharmacokinetic model (40 cigarettes with 5% cocoa smoked during the day, assuming 100% absorption from the lung), the peak plasma level of theobromine was estimated to be 0.08 mg/L (= 1/125 to 1/250 of the therapeutically effective concentration).

Conclusions:
- The plasma levels of theobromine which are achieved during smoking are far below the concentrations required for pharmacological effects.
- Consequently, no observations have been reported that cocoa or theobromine attenuate – or even eliminate – the transitory bronchoconstriction which is known to be caused by cigarette smoke.
- It can practically be ruled out that the addition of cocoa to cigarettes results in a bronchodilating effect during smoking.

LICORICE – GLYCYRRHIZIN

Allegation:
Glycyrrhizin (occasionally also called glycyrrhizinic acid) acts as a bronchodilator; it facilitates the inhalation of smoke and thereby the uptake of nicotine (1).

Use: Glycyrrhizin is not used as an additive. It is a constituent of licorice (6.8%) (17). Licorice is used in casings for Burley-containing American blends; it enhances natural Burley taste and gives the tobacco smoke a special aroma.

Content: In a study, the amount of glycyrrhizin in the tobacco of American cigarettes was determined to be as high as 311 μg (3).

Transfer: Because of its thermal instability glycyrrhizin is not transferred into mainstream smoke in undecomposed form and only marginally (~ 2%) as a degradation product (18).

Effects: There is no proof in the scientific literature for bronchodilating effects of glycyrrhizin in humans.

Conclusions:
- Glycyrrhizin is not transferred to mainstream smoke.
- Glycyrrhizin has no bronchodilating effects.
- It can be ruled out that the addition of licorice to cigarettes results in a bronchodilating effect during smoking.

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