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Review

Sugars as tobacco ingredient: Effects on mainstream smoke composition

Reinskje Talhout *, Antoon Opperhuizen, Jan G.C. van Amsterdam

Laboratory for Toxicology, Pathology and Genetics, National Institute for Public Health and the Environment (RIVM), P.O. Box 1, 3720 BA Bilthoven, The Netherlands

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Abstract

Sugars are natural tobacco components, and are also frequently added to tobacco during the manufacturing process. This review describes the fate of sugars during tobacco smoking, in particular the effect of tobacco sugars on mainstream smoke composition. In natural tobacco, sugars can be present in levels up to 20 wt%. In addition, various sugars are added in tobacco manufacturing in amounts up to 4 wt% per sugar. The added sugars are usually reported to serve as flavour/casing and humectant. However, sugars also promote tobacco smoking, because they generate acids that neutralize the harsh taste and throat impact of tobacco smoke. Moreover, the sweet taste and the agreeable smell of caramelized sugar flavors are appreciated in particular by starting adolescent smokers. Finally, sugars generate acetaldehyde, which has addictive properties and acts synergistically with nicotine in rodents. Apart from these consumption-enhancing pyrolysis products, many toxic (including carcinogenic) smoke compounds are generated from sugars. In particular, sugars increase the level of formaldehyde, acetaldehyde, acetone, acrolein, and 2-furfural in tobacco smoke. It is concluded that sugars in tobacco significantly contribute to the adverse health effects of tobacco smoking.
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Keywords: Tobacco; Additives; Sugar; Pyrolysis; Smoke; Addiction

Contents

* Corresponding author. Tel.: +31 30 274 4505; fax: +31 30 274 4446.
E-mail address: Reinskje.Talhout@rivm.nl (R. Talhout).

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1. Introduction

Tobacco smoke constitutes the most significant cause of morbidity and mortality in the world (WHO, 2000). In 2000, an estimated 4.8 million premature deaths in the world were attributable to tobacco smoking due to cardiovascular diseases (~35%), chronic obstructive pulmonary disease (~20%), and various types of cancer, in particular lung cancer (~18%) (Hoffmann and Hoffmann, 1997; Hoffmann et al., 2001; Ezzati and Lopez, 2003; Byrd, 2004). Upper limits for the most harmful components in tobacco smoke are expected to be set in the near future in an attempt to decrease the negative impact of smoking (Bates et al., 1999b; IARC, 2004; Henningfield et al., 2004).

The composition of tobacco smoke depends on the chemical nature of natural tobacco, the various ingredients added to tobacco, and the design characteristics of the product. Since consumer acceptance of tobacco smoke is, amongst others, proportional to the sugar level in tobacco (Shelar et al., 1992; Rodgman, 2002), manufacturers select natural high-sugar tobaccos or add sugars during tobacco manufacturing.

Sugars are generally recognized as being safe (GRAS) when used in food products, but this recognition does not imply their safety as tobacco additive. In burning tobacco, sugars are pyrolyzed, which results in a large number of highly toxic or even carcinogenic degradation products (Vleeming et al., 2005). In addition, compounds are generally more toxic via the inhalatory route as compared to their toxicity following ingestion, because the respiratory system largely lacks the detoxifying metabolic pathways of the digestive system (Bates et al., 1999a; Fowles, 2001; Vleeming et al., 2005).

This paper reviews the generation of heating/combustion products from sugars in tobacco (naturally present and/or intentionally added), which serve to mask the adverse taste of tobacco smoke and enhance its addictiveness.

2. Sugars in tobacco products

2.1. Amounts and identity of sugars in tobacco products

Sugars like glucose, fructose and sucrose, are natural components of tobacco (Fox, 1993; Leffingwell, 1999). Sugars in tobacco are formed via enzymatic hydrolysis of starch during the period after priming (harvesting) and the early stages of the curing process (Leffingwell, 1999). The sugar content of tobacco types is highly variable, but primarily depends on the method of curing (Leffingwell, 1999). For instance, sugars are largely metabolized during air-curing (Burley, Maryland and cigars) (Elson et al., 1972; Fox, 1993; Leffingwell, 1999; Seeman et al., 2003). By contrast, flue- and sun-cured tobaccos contain higher sugar levels because the metabolizing enzymes are rapidly inactivated at the relatively high temperatures employed during this curing process (Elson et al., 1972). The latter curing process results in sugar levels of over 20 (flue-cured, like Virginia) and 10 (sun-cured, like Oriental) weight percent of dried tobacco, respectively (Elson et al., 1972; Fox, 1993; Leffingwell, 1999; Seeman et al., 2003). A typical American blended product contains approximately 25–35% of both flue-cured and air-cured tobaccos, and 3–15% of Oriental tobacco, together with smaller amounts of other tobaccos (Fisher, 1999). Its sugar content is about 12%, of which 8% is of natural origin (Fox, 1993).

During the manufacturing process of a tobacco product, up to 13% w/w of sugars and sweeteners are intentionally added to tobacco (Leffingwell, 1999; Fowles and Bates, 2000; Rodgman, 2002; Seeman et al., 2003). Sugars used as cigarette additive include glucose, fructose, invert sugar (glucose/fructose mixture), and sucrose (Leffingwell, 1999; Seeman et al., 2003). In addition, many tobacco additives contain high amounts of sugars, e.g. fruit juices, honeys, molasses extracts, corn and maple syrups, and caramel (Fox, 1993; Rustemeier et al., 2002; Seeman et al., 2003).

Table 1 lists the amounts and functions of several carbohydrate additives as reported by five major tobacco manufacturers on their websites. These manufacturers do not report the amount of added sugar per brand, but give the so-called quantities not exceeded (QNEs). The QNE is the highest level of an ingredient that a manufacturer adds to any single brand, and is expressed as the percentage by weight (% w/w) of the additive in the tobacco blend (including moisture). Table 1 shows that all manufacturers add invert sugar (QNE-value typically 2%) and sucrose (QNE-value typically 3%).

In addition to mono- and disaccharides, natural tobacco contains considerable amounts of polysaccharides, such as cellulose, pectins, and starch (Schlotzhauer and Chortyk, 1987; Fox, 1993; Rodgman, 2002; Seeman et al., 2002). Some of these polysaccharides, like cellulose, are used as tobacco additive (see Table 1) (Fox, 1993). Typical blended cigarettes contain about 10% of cellulose, 10% of pectins, and 2% of starch (Fox, 1993; Leffingwell, 1999; Seeman et al., 2002). Thus, carbohydrates may comprise over 40% of the tobacco and accordingly largely determine the chemical composition of tobacco smoke (Leffingwell, 1999; Weeks, 1999; Rodgman, 2002). Although this review primarily focuses on mono- and disaccharides, the differences in pyrolyzation of polysaccharides and simple sugars will be addressed to estimate their relative contribution to mainstream smoke.

2.2. Function of sugars in tobacco

The tobacco companies claim that ingredients are added to tobacco products to aid the production process or to realize brand specifications (Vleeming et al., 2005). For instance, the website of BAT states: “Food-type ingredients and flavorings are added to balance the natural tobacco taste, to replace sugars lost in the curing process, and to give individual brands their characteristic flavor

Table 1
Amounts and functions of sugars, sugar containing additives and polysaccharides added to tobacco as reported by five major tobacco manufacturers on their websites (market in brackets)

Additive	Quantities not exceeded (% w/w) and function of sugar				
	BAT (Dutch)	PM (Dutch)	RJRT (World)	Gallaher (World)	JTI (Europe)
Glucose	0.005(a)	–	<0.001(a)	2.6(a)	0.7(a),(b)
Fructose	–	–	–	2.6(a)	0.0001(a),(b)
Invert sugar	3.2(c)	1.9(a),(b)	0.003(a)	2.4(a),(b)	1.5(a),(b)
Sucrose	0.84(c)	3.4(a),(b)	3.0(c)	3.0(a),(b)	4.0(a),(b)
Brown sugar	1.3(c)	–	3.0(c)	–	–
Honey	0.8(c)	–	2.3(c)	0.1(a)	0.1(a)
Glucose (corn) syrup	1.2(c)	–	3.8(a)	0.1(a)	0.4(a),(b)
Molasses, sugar cane	0.3(c)	–	–	0.1(a)	0.3(a)
Fig juice	0.04(a)	–	0.3(c)	0.1(a)	0.03(a)
Prune juice	1.4(c)	–	0.5(c)	0.1(a)	0.3(a),(d)
Cellulose	1.3(e)	–	3.6(f)	4.8(e)	1.5(f)

Selection of sugars was based on: (1) reported by at least two manufacturers, and (2) reported QNEs over 0.1% for at least two manufacturers or over 1% for at least one manufacturer.
(a) Flavor; (b) humectant; (c) casing ingredient; (d) plum juice; (e) Binder; (f) formulation aid.
BAT: British American Tobacco (British American Tobacco, 2004), PM: Philip Morris (Philip Morris International Inc., 2004), RJRT: R.J. Reynolds Tobacco Company (R.J. Reynolds Tobacco Company, 2005), Gallaher: Gallaher Group Plc. (Gallaher Group Plc., 2005), JTI: Japan Tobacco International (JT International, 2005).

and aroma. Other ingredients have more technological functions such as to control moisture, to protect against microbial degradation, and to act as binder or filler.'' (British American Tobacco, 2004). According to five main tobacco manufacturers, sugars serve as binder, casing ingredient, flavor, formulation aid or humectant (see Table 1).

Indeed, sugars are important for tobacco smoke flavoring (Leffingwell, 1999; Weeks, 1999; Seeman et al., 2003), considering for instance the differences in smoke flavor between flue-cured, bright tobaccos (high-sugar levels) and air-cured, Burley tobaccos (virtually no sugars) (Schlotzhauer and Chortyk, 1987). The tobacco industry probably also adds sugars to mask the bad harsh taste and the irritability of tobacco smoke. Finally, and not mentioned by tobacco companies, sugars are pro-addictive compounds. These consumption-enhancing effects of sugar will be addressed in Section 6.

3. Fate of sugars upon combustion

Due to the high content of sugars in tobacco products, their fate during smoking has been thoroughly investigated. As most of the naturally present sugars are nonvolatile, only minor amounts of sugars (approximately 0.5% of glucose and sucrose) are transferred unchanged into the mainstream smoke (Gager et al., 1971a,b; Fox, 1993; Rodgman, 2002; Byrd et al., 2004). The larger part of the sugars will combust, pyrolyze or participate in pyrosynthesis processes (Schlotzhauer and Chortyk, 1987; Fox, 1993; Baker, 1999; Byrd, 2004).

Upon pyrolysis, sugars caramelize and break down into a mixture of organic acids and a variety of aldehydes (Creighton and Hirji, 1988; Shelar et al., 1992). The reactions involved, varying from chemical degradation and polymerization to condensation, are complex and the chemical identity of the final reaction products is poorly known (Tomasik, 1989). First, thermally induced enolization and dehydration reactions generate osuloses (α-dicarbonyl compounds), the key intermediates of thermal caramelization (Fig. 1) (Tomasik, 1989; Ledl and Schleicher, 1990; Hollnagel and Kroh, 2002). These osuloses may cyclise to furan derivatives (Tomasik, 1989). The principal degradation product in caramel is 5-hydroxymethyl furfural (an intramolecular condensation product of deoxyhexosulose) (Fadel and Farouk, 2002). The formed osuloses may also decompose into acids and aldehydes (Tomasik, 1989; Ledl and Schleicher, 1990).

Tobacco contains a variety of amines (ammonium compounds, amino acids, proteins) that are naturally present or have intentionally been added in considerable amounts (Leffingwell, 1999; Britt et al., 2004; Indiana Prevention

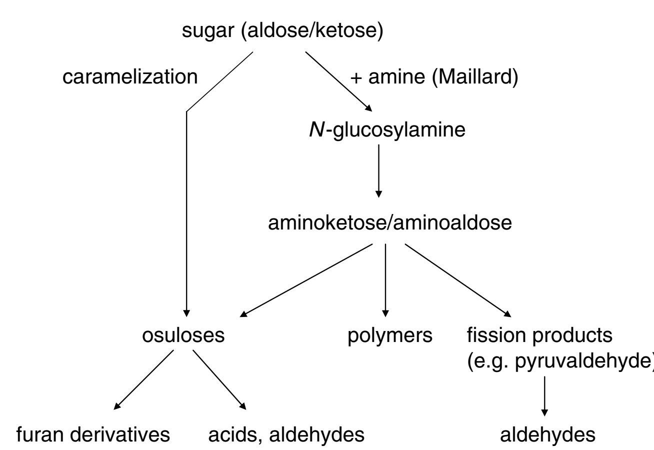

Fig. 1. Products formed from sugars via caramelization and via reaction with amines (Maillard reaction).

Resource Center, 2005). In addition to thermal caramelization, reducing sugars participate with such amines in a complex set of reactions that are collectively known as the Maillard reaction (Tomasik, 1989; Fadel and Farouk, 2002). Like in food processing, during smoking sugars react with amines to yield brown-colored Maillard reaction products that 'improve' the taste of tobacco smoke (Ledl and Schleicher, 1990; Coleman and Perfetti, 1997; Rodgman, 2002; Britt et al., 2004). In tobacco, Maillard reactions result in 1.5–2.0% w/w amino-sugar compounds (Leffingwell, 1999; Britt et al., 2004).

The initial step in the Maillard reaction involves condensation of a carbonyl group of a reducing sugar with an amino group, and results in *N*-substituted glycosylamines (Fig. 1). These compounds are thermally unstable and quickly undergo isomerization by Amadori rearrangement (if the sugar is an aldose) or Heynes rearrangement (if the sugar is a ketose) to give aminoketoses and aminoaldoses, respectively (Ledl and Schleicher, 1990; Coleman and Chung, 2002). Various compounds are formed from these aminoketoses and aminoaldoses (Tomasik, 1989; Ledl and Schleicher, 1990; Coleman and Perfetti, 1997), for example osuloses (as described above), melanoidin polymers, and fission products, such as diacetyl (2,3-butanedione), acetol (1-hydroxy-2-propanone) and pyruvaldehyde, which can react further to other aldehydes (Tomasik, 1989; Fadel and Farouk, 2002). In the following sections, the effects of the addition of sugars to tobacco on mainstream smoke, smoking behavior and consumer's health will be described.

4. Combustion of tobacco sugars: pyrolysis and products in mainstream smoke

Three methods are usually employed to investigate the identity of the compounds formed during the combustion process of a tobacco additive (Fox, 1993; Byrd, 2004; Byrd et al., 2004):

(1) Pyrolyzation of a single additive in absence of tobacco and subsequent analysis of the pyrolysis products. This technique is useful as a first screening of potential pyrolysis products, their thermal stability and the temperature at which they are formed (Baker and Bishop, 2004). However, the pyrolysis conditions only approximate the burning cigarette with regard to temperature and atmosphere and make no allowance for the presence of other tobacco and/or smoke components that may interact with the sugars (Fox, 1993; Byrd, 2004; Byrd et al., 2004).

(2) Burning (smoking) the tobacco that contains a specific amount of the additive and subsequent analysis of selected smoke components. The substantial loading of tobacco with the additive that is mostly required to obtain significant results may, however, affect the burning characteristics of the tobacco (Fox, 1993; Byrd, 2004; Byrd et al., 2004). Also, this method cannot determine whether the additive is a precursor or an enhancer of a certain smoke component (Torikaiu et al., 2005). These problems can be circumvented by:

(3) Burning the additive in the tobacco matrix, but labeled as radioactive isotope. The low quantities used here do not affect the burning characteristics of the tobacco (Byrd, 2004; Byrd et al., 2004), but the method is sophisticated and expensive (Fox, 1993).

4.1. Pyrolysis of single ingredients and simple mixtures

Table 2 describes the results of pyrolysis studies (two of the studies have been performed by tobacco companies). Pyrolysis of sugars or sugar-amino acid mixtures was performed at one temperature, often in inert atmospheres. Such study designs poorly reflect the conditions of burning cigarettes with oxygen levels ranging from 0% to 14% and the temperature in the burning zone ranging from ambient temperature to 900 °C (Stohs et al., 1997; Stotesbury et al., 1999; Baker and Bishop, 2004; Torikai et al., 2004). Since each entry reflects only part of the actual pyrolyzation process in cigarettes, it is important to consider a range of measurements that have been performed at different temperatures.

Various sugar pyrolysis products are reported with yields that depend on the pyrolysis temperature. Typical high temperature pyrolysis products are the polyaromatic hydrocarbons (PAHs) (Sanders et al., 2003). Indeed, PAHs are detected in the studies performed at >650 °C, but not in those performed <460 °C (see Table 2). In the lower temperature range, sugars degrade less vigorously, resulting in pyrolyzation products that resemble more closely the original sugar structure (Table 2).

With increasing temperature, less furan, furfural and 5-hydroxymethylfurfural is formed, whereas the yields of aliphatic aldehydes (such as acetaldehyde and acrolein) increase. Glucose, fructose and sucrose result in the same pyrolysis products, but the yields are different, e.g. fructose yields more furfural than glucose or sucrose, whereas glucose yields relatively more 5-hydroxymethyl furfural.

A large variety of products, including aldehydes, ketones, acids, pyrazines and pyridines, results from the Amadori reaction between sugars and amino acids. For instance, acrylamide is generated from asparagine and glucose (Friedman, 2003; Yaylayan et al., 2003), and furfural is generated from alanine and glucose (Yaylayan and Keyhani, 2000). The products from sugar-amine pyrolysis partly overlap with those of simple sugar pyrolysis, because the Maillard reaction includes catalyzed caramelization of sugars (Tomasik, 1989; Ledl and Schleicher, 1990; Fadel and Farouk, 2002).

The pyrolysis products of polysaccharides and simple sugars are similar, but their yields differ (Fox, 1993; Rodgman, 2002; Seeman et al., 2002; Sanders et al., 2003). As compared to cellulose, pyrolysis of simple sugars yields

Table 2
Pyrolysis products of sugars and sugar-amino acid mixtures (i.e. no tobacco matrix)

Sugar	Pyrolysis conditions and major products (yield in mg/g sugar or otherwise as indicated)
Fructose	840 °C in N_2 (Higman et al., 1970). Benzene 5.3; phenol 4.8; toluene 2.8; furfural 2.4; indene 2.1; styrene, xylenes 1.4; naphthalene 1.1; *p*-methylstyrene 0.7; ethylbenzene 0.7; alkyl-naphthalene 0.4; *o*-cresol 0.3; *m*-cresol, *p*-cresol 0.3; 5-methylfurfural 0.2; B[*a*]P 0.1 800 °C in N_2/air (Schlotzhauer et al., 1982). Furfural 38.6; 5-hydroxymethylfurfural 19.5 Rapidly heated to 650 °C in N_2 (Gilbert and Lindsey, 1957). Main PAHs (μg/g): acenaphthylene 1.0; fluorene 1.2; anthracene 1.4; pyrene 0.4; fluoranthrene 1.1; 3-methylpyrene 0.1; 1:2-benzanthracene 1.2; 3:4-benzpyrene 0.3 Heated to 900 °C at 6 °C/min. in He (Burton, 1976). Rel. amount (temperature of max. formation): formaldehyde 1680 (225 °C); acetaldehyde 96 (325 °C); acrolein 480 (425 °C); acetone 176 (325 °C); 2-butanone 188 (325 °C)
Glucose	Heated at 460 °C for 5 s; Curie-point pyrolysis[a] (Ohnishi and Kato, 1977). 1,6-Anhydro-β-D-glucopyranose (levoglucosan) 23; 1,6-anhydro-ß-D-glucofuranose 12; 5-hydroxy-methylfurfural 11; furfural 8 840 °C in N_2 (Higman et al., 1970). Phenol 6.2; benzene 4.6; toluene 2.6; naphthalene 1.4; furfural 1.3; styrene, xylenes 1.3; *m*-cresol, *p*-cresol 1.2; indene 1.1; *o*-cresol 1.1; ethylbenzene 0.8; *p*-methylstyrene 0.8; alkyl-naphthalene 0.6; 5-methylfurfural 0.4; acenaphthylene 0.2; B[*a*]P 0.05 Rapidly heated to 650 °C in N_2 (Gilbert and Lindsey, 1957). PAHs (μg/g): acenaphthylene 1.3; anthracene 0.4; pyrene 0.7; fluoranthrene 0.5; 1:2-benzanthracene 0.4; 1:2-benzpyrene 0.1; 3:4-benzpyrene 0.3 Heated to 250, 350 and 500 °C in stationary He (Kato, 1967). Relative amount of product at 250, 300 and 500 °C: acetaldehyde: 1.8, 5.2, 5.6; acetone: 1.7, 2.6, 3.1; furan: 2.1, 2.9, 1.1; diacetyl: 0.5, 1.0, 2.0; propionaldehyde: 0.8, 1.0, 1.5; furfural: 11.7, 12.5, 3.3; acrolein: 0.7, 1.5, 4.3; 5-methylfurfural: 1.9, 1.9, 0.5 Heated to 900 °C at 6 °C/min. in He (Burton, 1976). Rel. amount (temperature of max. formation): formaldehyde 238 (225 °C); acetaldehyde 255 (375 °C); acrolein 800 (400 °C); acetone 830 (400 °C); 2-butanone 875 (400 °C)
Sucrose	800 °C in N_2/air (Schlotzhauer et al., 1982). Furfural 27.7; 5-hydroxymethylfurfural 19.5 700 °C for 10 s in N_2 (Schlotzhauer et al., 1985). Total volatiles from pyrolysate (%): 2-fural-dehyde 67%; 5-methyl-2-furaldehyde 4%; 3-methylfuran 3%; 1,3-cyclo-pentane-dione 2%; 2-furan-methanol 2%; furancarboxylic acid methyl ester 2% Rapidly heated to 650 °C in N_2 (Gilbert and Lindsey, 1957). PAHs (μg/g): acenaphthylene 0.2; fluorene 0.1; anthracene 0.7; pyrene 0.2; fluoranthrene 0.4; 3-methylpyrene 0.2; 1:2-benzanthracene 0.4 Heated for 10 s at different *T*'s in N_2 (Schlotzhauer et al., 1986). 5-Hydroxymethylfurfural formed: 61 (350 °C); 83 (450 °C); 76 (550 °C); 66 (650 °C); 47 (750 °C) and 37 (850 °C) Heated to 900 °C at 6 °C/min in He (Burton, 1976). Rel. amount (temperature of max. formation): formaldehyde 920 (200 °C); acetaldehyde 140 (375 °C); acrolein 148 (325 °C); acetone 270 (425); 2-butanone 250 (375 °C)
Glucose-amino acids	Glucose-Ala heated to 210 °C at 50 °C/ms for 20 s (Yaylayan and Keyhani, 2000). Glycolaldehyde, pyruvaldehyde, furanmethanol, acetol, furfural, 2,3-pentanedione, 3-hydroxy-2-butanone, 2,3-butanedione Glucose-Asp to 300 or 700 °C at 10 °C/min in air[a] (Coleman and Perfetti, 1997). Ketones, furans, acetic acid, pyrroles, pyridines, methylpyridines, pyrazines Glucose-Leu to 300 or 700 °C at 10 °C/min in air[a] (Coleman and Perfetti, 1997). Ketones, 3-methyl-butanal, furans, acetic acid, pyrazines, 3-methylbutanoic acid, pyrroles Glucose-Pro 840 °C in He (Britt et al., 2004). mg/g mixture: pyrrole 6.4; benzene 5.8; benzonitrile quinoline 2.1; isoquinoline 0.49; phenanthracene 0.45 Glucose-Thr to 300 or 700 °C at 10 °C/min in air[a] (Coleman and Perfetti, 1997). Ketones, furans, acetic acid, pyridines, pyrazines, propanoic acid, pyrroles Glucose-Val to 300 or 700 °C at 10 °C/min, air[a] (Coleman and Perfetti, 1997). Ketones; 2-methyl-propanal; furans; pyrazines; 2-methylpropanoic acid

[a] TC: study sponsored by tobacco company.

more (substituted) furfurals and less anhydrosugars, like levoglucosan (Ohnishi and Kato, 1977; Schlotzhauer et al., 1982, 1985; Evans et al., 1996; Sanders et al., 2003). In addition, it seems that simple sugars generate more formaldehyde (Burton, 1976), but less acetaldehyde, acetone (Kato, 1967; Burton, 1976), and acrolein (Burton, 1976). It is difficult to estimate the difference in total yield of pyrolysis products of simple sugars versus polysaccharides, because the few comparative studies available report only part of the products. Since conclusive studies[1] on the effect of (labeled) polysaccharides on the composition of cigarette mainstream smoke are also not available, the relative contribution of pyrolyzation products of sugars versus other carbohydrates to the composition of tobacco smoke cannot be properly evaluated.

[1] Only one study ((National Cancer Institute, 1980) cited in (Paschke et al., 2002)) gives detailed information on the effect of added cellulose on mainstream smoke.

4.2. Combustion products of sugar additives in mainstream smoke

Burning the (labeled) additive in the tobacco matrix in a smoking machine and subsequent analysis of the mainstream smoke components gives more accurate information on the actual pyrolysis process than the pyrolysis studies on a single ingredient (see Section 4.1). One should, however, realize that the data thus obtained do not imply that the detected products solely originate from sugars.

Table 3 (mainly based on studies performed by tobacco companies) shows that the addition of sugars to tobacco primarily enhances the level of aldehydes and ketones, especially formaldehyde, acetaldehyde, acetone, acrolein, 2-furfural and other furans. For instance, as compared to the Burley reference cigarette, the addition of 12% w/w of sugar (a representative concentration in tobacco, see Section 2.1) to a Burley tobacco increased (depending on the type of sugar and tobacco) the mainstream smoke levels of formaldehyde (40–148%), acetaldehyde (6–36%), acetone (11–52%), acrolein (20–73%), and total carbonyl (14–36%) (Shelar et al., 1992). Precursor–product relationships of these components are described in Section 5. Studies with mixtures of additives on smoke components support the observation (Table 3) that the addition of sugars to tobacco significantly increases the pyrolytic formation of formaldehyde. Baker and co-workers reported statistically significant increases (up to 73%) in formaldehyde levels in mainstream smoke for all mixtures containing over 1% w/w sugars (but not in corn syrup) (Baker et al., 2004a,b,c). Similarly, a 60–65% increase in the concentration of formaldehyde in mainstream smoke was observed following the addition of a corn syrup sugar mixture containing 4.2–6.3% w/w sugar (Rustemeier et al., 2002; Baker et al., 2004b).

Table 3 further shows that the addition of sugars to tobacco enhances the concentration of total acids in mainstream smoke. This is in agreement with the results obtained by Elson et al. (1972), who showed that the smoke pH-value of a cigarette containing 17.8% of sugar ranges around 4.0, whereas the smoke pH of a cigarillo containing only 0.5% of sugar exceeds the value of 8.5. As a result of the lower pH, mainstream smoke of tobacco enriched with sugars will contain lower levels of free-base nicotine (see Table 3 and Section 6.1) (Willems et al., 2006). Finally, Table 3 indicates that sugar combustion products have primarily been found in sidestream smoke. As specific data on sidestream smoke components are not available, the effect of combustion/pyrolysis of sugars on the composition of sidestream smoke is not further addressed.

Table 3
Effect of added sugars on the composition of cigarette mainstream smoke (MSS)

Sugar	Amount added (% w/w), type of tobacco and selected MSS components (mg/cig; % difference from control)
Fructose	12.8, Burley[a] (Thornton and Massey, 1975). Total nicotine alkaloids 2.2 (−30%); total carbonyls 4.4 (+10%); volatile carbonyls 2.2 (+16%); volatile aldehydes 0.53 (−12%); 2-furfural 0.089 (+68%); total acids 2.7 (+14%); volatile acids 1.2 (+17%) 12, low-mid stalk Burley tobacco[a] (Shelar et al., 1992). Formaldehyde 0.025 (+53%); acetaldehyde 0.57 (+13%); acetone 0.35 (+32%); acrolein 0.16 (+37%); total carbonyl 1.1 (+22%); volatile nicotine 0.083 (−30%) 12, mid-upper stalk Burley[a] (Shelar et al., 1992). Formaldehyde 0.020 (+80%); acetaldehyde 0.64 (+10%); acetone 0.34 (+12%); acrolein 0.14 (+20%); total carbonyl 1.1 (+13%); volatile nicotine 0.20 (−29%)
Glucose	10.5, Burley[a] (Thornton and Massey, 1975). Total nicotine alkaloids 2.6 (−2.0%); total carbonyls 4.2 (+5.0%); volatile carbonyls 2.0 (+5.3%); volatile aldehydes 0.50 (−17%); 2-furfural 0.067 (+26%); total acids 2.5 (+6.9%); volatile acids 1.1 (+5.7%) 16.8, Burley[a] (Thornton and Massey, 1975). Total nicotine alkaloids 2.2 (−35%); total carbonyls 4.3 (+7.5%); volatile carbonyls 2.1 (+10%); volatile aldehydes 0.54 (−10%); 2-furfural 0.080 (+51%); total acids 2.5 (+6.0%); volatile acids 1.2 (+11%) 16.1, air-cured[a] (Thornton and Massey, 1975). Available ^{14}C-nicotine directed into MSS: 37% (−15%) 12, low-mid stalk Burley[a] (Shelar et al., 1992) Formaldehyde 0.028 (+72%); acetaldehyde 0.646 (+26%); acetone 0.41 (+52%); acrolein 0.16 (+36%); total carbonyl 1.2 (+36%); volatile nicotine 0.090 (−23%) 12, mid-upper stalk Burley[a] (Shelar et al., 1992) Formaldehyde 0.020 (+80%); acetaldehyde 0.78 (+36%); acetone 0.43 (+40%); acrolein 0.16 (+36%); total carbonyl 1.4 (+37%); volatile nicotine 0.19 (−33%) ^{14}C-glucose in Burley[a] (Gager et al., 1971b). ^{14}-C pyrolysis products (%) in MS gas phase 4.7 (acetone 0.08; acetaldehyde 0.05; 2-methylfuran 0.02; 2-butanone 0.02; furan 0.01; propionaldehyde, acrolein, crotonaldehyde, benzene < 0.01); MS TPM 1.7; SS gas phase 45.8; SS TPM 3.7; butt 41.0
Invert sugar	5.4, tobacco blend[b] (National Cancer Institute, 1977 cited in Paschke et al., 2002). Nicotine 1.8 (−3.6%); acetaldehyde 1.26 (+0.6%); acrolein 0.11 (+0.2%); isoprene 0.46 (−9.5%); HCN 0.34 (−8.5%); formaldehyde 0.03 (+22%); NO_x 0.44 (+5.8%) 5.4, Burley blend (National Cancer Institute, 1977 cited in Paschke et al., 2002). Nicotine 2.9 (−19%); phenol 0.11 (−33%); acetaldehyde 1.1 (−0.9%); acrolein 0.08 (−0.2%); isoprene 0.47 (−5.4%); HCN 0.33 (−13%); formaldehyde 0.02 (−10%); NO_x 0.63 (−11%) 5.1, 1R1 Kentucky Ref[a] (Jenkins et al., 1980). ^{14}-C pyrolysis products (%) in MS gas phase 13.6; MS TPM 9.1; SS gas phase 63.8; SS TPM 7.8; butt 5.7
Sucrose	12, low-mid stalk Burley[a] (Shelar et al., 1992). Formaldehyde 0.023 (+40%); acetaldehyde 0.55 (+9%); acetone 0.35 (+31%); acrolein 0.20 (+73%); total carbonyl 1.13 (+25%); volatile nicotine 0.075 (−36%) 12, mid-upper stalk Burley[a] (Shelar et al., 1992). Formaldehyde 0.028 (+148%); acetaldehyde 0.62 (+6%); acetone 0.34 (+11%); acrolein 0.18 (+52%); total carbonyl 1.2 (+14%); volatile nicotine 0.18 (−36%) ^{14}C-sucrose in Burley blend[a] (Gager et al., 1971b). ^{14}-C pyrolysis products (%) in MS gas phase 5.9 (acetone 0.1: 2,5-dimethylfuran 0.07; acetaldehyde 0.06; acetonitrile 0.04; 2-methyl-furan 0.03; 2-butanone 0.03; 2,3-butanedione 0.01; furan 0.01; propionaldehyde, acrolein, benzene, 3-buten-2-one, crotonaldehyde < 0.01); MS TPM 3.0; SS gas phase 51.6; SS TPM 3.8%; butt 40.6

[a] TC: study sponsored by tobacco company.
[b] Flue-cured, Burley, Maryland, Turkish, reconstituted sheet.

5. Relation between the sugar content of tobacco and smoke composition

In addition to the previously mentioned studies where one specific amount of sugar was added to tobacco, others have investigated the effect of increasing amounts of sugar in tobacco on the mainstream smoke level of several aldehydes. This is important since the precursor–product relationships between ingredients and smoke components should be clearly established before measures can be taken to diminish the concentration of toxic ingredients in the frame of tobacco control. Benchmark studies are mainly performed to assess the effect of sugars in various tobacco brands on the smoke components generated. Such studies, however, neglect that the level of smoke components also depends on the type of tobacco. This can be circumvented by testing the effect of different amounts of sugar added to a single type of tobacco (preferably Burley that contains virtually no natural sugars). The results of these approaches for aldehydes are discussed below.

A benchmark study by Seeman et al., sponsored by Philip Morris, on a large number of commercial US cigarettes suggested that the concentration of reducing sugars in the tobacco was not correlated to the concentration of acetaldehyde in mainstream smoke (Seeman et al., 2003). The authors proposed that mainstream smoke acetaldehyde was mainly derived from naturally occurring polysaccharides, such as cellulose, since the pyrolysis of cellulose generates larger amounts of low molecular weight aldehydes than the pyrolysis of reducing sugars (see Section 4.1). The lack of a correlation between the tobacco sugar content and the concentration of aldehydes in mainstream smoke was confirmed by the Imperial tobacco company in a benchmark study of forty different cigarette brands (Phillpotts et al., 1975).

In contrast to these benchmark studies, Zilkey et al. (1982), using 25 cigarettes that were blended from several types of bright and Burley tobacco (no sugar added), showed clear relations between sugar levels in tobacco and the concentration of aldehydes in mainstream smoke. In this study, the reducing sugars in tobacco ranged from 0% to 20%, whereas the range of the mainstream smoke level (μg/cig) of acetaldehyde, acrolein and total aldehydes was 163–1003, 14–75 and 303–1292, respectively. Using these data, the coefficient of determination (i.e. r^2-value) of the association between reducing sugars and acetaldehyde, acrolein and total aldehydes was 0.53, 0.46, and 0.55, respectively. After exclusion of the three data points of cigarettes that were equipped with a charcoal filter (instead of a cellulose acetate filter), the r^2-value of the associations increased to 0.61, 0.59, and 0.64, respectively. This indicates that, in addition to the tobacco type, the design characteristics of the cigarette determine the chemical composition of mainstream smoke. In contrast to the proposition of Seeman et al. (see above), the concentration of cellulose in tobacco was not correlated to smoke levels of acetaldehyde, acrolein and total aldehydes (r^2-values of 0.05, 0.002, and 0.1, respectively).

Studies performed by R.J. Reynolds Tobacco confirm that sugar in tobacco increase the level of tobacco smoke aldehydes (Shelar et al., 1992). Fructose, glucose, and sucrose were added in increasing amounts (4%, 8%, 12%, and 16% w/w) to either low-mid stalk Burley tobacco (K1) or mid-upper stalk Burley tobacco (K2). The results show significant correlations between the levels of fructose, glucose, sucrose in tobacco and the smoke level of formaldehyde, acetaldehyde, acetone, and acrolein (see Table 4). As the sugars in this study were all tested in the same tobacco type, the calculated correlation coefficients were higher than those obtained from the data of Zilkey et al. (1982).

In summary, conflicting results have been reported on the relation between the concentration of sugars in tobacco and mainstream smoke aldehyde levels. Clearly, the study with different types of tobacco (but no additives or differences in cigarette design) gives better correlations than the benchmark studies, and those studies using increasing amounts of sugars tested in one type of tobacco give the best correlations. It is therefore concluded that benchmark studies, with their variety in both tobacco composition and design characteristics of the cigarettes, are not optimal to study the effect of the combustion of particular ingredients. When increasing concentrations of sugars are tested in one type of tobacco, significant linear increases of several aldehydes are clearly established.

Table 4
Correlations (expressed as r^2-values) between levels of sugars in tobacco and smoke components calculated from the data of Shelar et al. (1992)

Tobacco type/sugar (range in % w/w)	Correlation between sugar and smoke component (r^2-value)			
	Formaldehyde	Acetaldehyde	Acetone	Acrolein
K1/fructose (0.1–12.4)	0.93	0.68	0.88	0.95
K2/fructose (0.1–10.0)	0.93	0.85	0.88	0.92
K1/glucose (0.1–15.6)	0.95	0.95	0.97	0.90
K2/glucose (0.0–13.6)	0.68	0.69	0.45	0.47
K1/sucrose (0.1–14.2)	0.95	0.36	0.59	0.98
K2/sucrose (0.0–13.2)	0.97	0.66	0.68	0.90

K1: low-mid stalk Burley tobacco; K2: mid-upper stalk Burley tobacco.

For K1: increase (μg/cig) per weight percent of sugar added: 0.8–1.2 (formaldehyde; control 16.0), 3.3–10.5 (acetaldehyde; control 506.7), 6.4–11.2 (acetone; control 268.9), and 3.8–9.1 (acrolein; control 117.5). For K2, increase (μg/cig) per weight percent of sugar added: 0.6–1.8 (formaldehyde; control 11.2), 13.0–20.5 (acetaldehyde; control 577.6), 7.4–11.5 (acetone; control 306.3), and 3.7–7.9 (acrolein; control 117.8).

6. Effects of tobacco sugars on tobacco consumption

The toxicity of certain smoke compounds, generated upon combustion/pyrolysis products of sugars in tobacco is generally known. Two other specific effects of sugars that are related to the facilitation of tobacco use are less known and will be addressed in this section in more detail.

6.1. Masking of tobacco smoke harshness

Volatile basic components, such as ammonia, nicotine and other tobacco alkaloids give tobacco smoke a harsh taste, which keeps smokers from inhaling (Hoffmann and Hoffmann, 1997). During smoking, sugars generate acids that decrease smoke pH (Section 4.2), which in turn decreases the free-base nicotine level in mainstream smoke. As a result, the impact, ''nicotine strength'', harshness and irritation of the smoke will decrease as well (Elson et al., 1972; Creighton and Hirji, 1988; Shelar et al., 1992; Leffingwell, 1999; Rodgman, 2002), which is especially important for naïve smokers, as it will encourage them to develop a smoking habit. Throat impact and harshness decrease as the sugar level increases, until a plateau value of around 10% (Shelar et al., 1992). The optimum sugar to nicotine ratio in tobacco for developing smooth products was determined to be 3.3 (Shelar et al., 1992). A major drawback of the lower content of nicotine in smoke is that smokers increase their smoking frequency and inhale the smoke more deeply to enable a higher absorption of nicotine in the airways (Elson et al., 1972; Hoffmann and Hoffmann, 1997). This obviously leads to a higher exposure of smokers to toxic and carcinogenic agents.

Furthermore, combustion/pyrolysis of sugars generates caramel flavors in tobacco smoke, which give it a sweet taste that is appreciated in particular by adolescents. This sweeter taste masks the adverse bitter taste of cigarette smoke. As a result of the lower adverseness of tobacco, people (in particular adolescents, Bates et al., 1999a; Fowles, 2001; Vleeming et al., 2005) start smoking earlier, continue smoking for longer periods, and increase their tobacco use. Smoking panels confirmed that consumer acceptance of cigarette mainstream smoke is proportional to the sugar level in the tobacco (Rodgman, 2002).

6.2. Pro-addictive properties of sugar in tobacco

Although sugars have no addictive potential *per se*, sugars in tobacco act pro-addictively, because they generate acetaldehyde in tobacco smoke. Acetaldehyde and nicotine act, via a still unknown mechanism, synergistically with respect to the addictive effect of nicotine in rodents (Bates et al., 1999a; Gray, 2000; Henningfield et al., 2004; Belluzzi et al., 2005). It has been speculated that acetaldehyde reacts with biogenic amines to condensation products that inhibit monoamine oxidase, an enzyme that degrades biogenic amines, like dopamine and noradrenalin (Villegier et al., 2003; Jamal et al., 2003; Belluzzi et al., 2005). The brain levels of these aminergic neurotransmitters, known to be involved in drug addiction (Koob, 1992), increase as a result of the inhibition of monoamine oxidase.

In summary, the addition of sugars to tobacco can enhance tobacco use in at least two ways: (1) neutralization of the harsh taste of cigarette smoke and (2) generation of acetaldehyde, which increases the addictive effect of nicotine. Philip Morris and BAT, however, reject the allegations that some of their additives increase the addictive nature of cigarettes (British American Tobacco, 2004; Philip Morris International Inc., 2004).

7. Conclusions

Sugars (naturally present and/or intentionally added) have a significant effect on mainstream smoke composition, as they are one of the main ingredients of tobacco. Depending on the type of curing, sugars are regularly present naturally in levels up to 20% w/w. In addition, various sugars, particularly sucrose and invert sugar, as well as sugar mixtures (syrups, honey) are added to tobacco in amounts up to 4% w/w for each sugar.

Five major tobacco manufacturers claimed that sugars are added either as flavor, casing or humectant. The addition of sugars, however, also promotes tobacco use as certain combustion/pyrolysis products of sugars neutralize the adverse tobacco taste or even have addictive properties (acetaldehyde). Apart from the adverse health effects that result from increased tobacco consumption, high-sugar tobaccos also yield elevated levels (increases of up to 150% were reported) of toxic components in mainstream smoke. For instance, formaldehyde, acetaldehyde, acetone, acrolein, 2-furfural and other furans are very toxic or even carcinogenic.

As the combustion products of sugars appear mainly in the sidestream smoke, the sugar level in tobacco may be relevant for passive smokers as well. Further research to the effect of sugars on main- and side-stream smoke is therefore highly recommended. Also, additional comparative data are necessary to estimate the relative contribution to mainstream smoke of sugars compared to polysaccharides. Such information is essential to estimate the impact of the adverse health effect of sugars, which is important in ingredient regulation issues.

In summary, sugars in tobacco have a negative health impact on the smoker. This is an important issue for tobacco ingredient regulation and may restrict the use of sugars as additives. Furthermore, as the type of curing largely determines the final sugar level of tobacco products, the impact of such methods should also be considered when regulation measures on sugar ingredients are issued.

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