Letter to the Editor

Sugars, carbonyls and smoke

The influences of tobacco ingredients on the composition of cigarette smoke, and the ensuing effects on smoke toxicity, are important and active areas of research. That is why two very similar papers on sugars as ingredients appeared side-by-side in a recent volume of Food and Chemical Toxicology. The first paper was a review by Talhout et al. on the effects of sugar ingredients on the mainstream cigarette smoke composition of carbonyl compounds; the second was a review and experimental study by me on the effect of sugar ingredients specifically on formaldehyde in smoke (Talhout et al., 2006; Baker, 2006). The latter was the ninth in a series that I and various colleagues in British American Tobacco have published over the last three years on the pyrolysis of tobacco ingredients and the effects on smoke chemistry and toxicity (Baker and Smith, 2003; Baker and Bishop, 2004; Baker et al., 2004a,b,c; Baker and Bishop, 2005; Baker et al., 2005, 2006; Baker, 2006.) With one exception, the review by Talhout et al. and our reviews and experimental studies come to somewhat different conclusions. Our conclusions are

- Commonly used cigarette ingredients at maximum levels used commercially do not alter the toxicity of cigarette smoke, based on all known results using all the bioassays currently available for assessing smoke.
- With one exception, cigarette ingredients have little effect on those smoke constituents that may be relevant to smoking-related diseases, when added at up to the maximum levels used in commercial cigarette manufacture. The smoke constituents are specifically the 44 ‘Hoffmann analytes’ measured by various regulatory authorities around the world.
- The one exception is sugar ingredients, which can increase the yields of mainstream formaldehyde by up to 60% when added to tobacco at maximum commercial use levels. The sidestream yields of formaldehyde are not affected by the addition of sugars to tobacco. Furthermore, the toxicity of mainstream smoke is not affected by the addition of sugars to tobacco.
- The addition of sugars also produced some effects, both increases and decreases, in the mainstream yields of six of the seven other Hoffmann carbonyl smoke constituents, including acetaldehyde and acrolein. These effects were generally small, less than 16% at maximum use levels, were not consistent or reproducible, and lost their significance when the long-term analytical variability was taken into account.

Talhout et al.’s conclusions and assertions are

- Sugars increase the levels of formaldehyde, acetaldehyde, acetone, acrolein and 2-furfural in smoke.
- Sugars significantly contribute to the adverse health effects of tobacco smoking.
- The sweet taste obtained by adding sugars are particularly appreciated by starting adolescent smokers.
- Sugars generate acetaldehyde, which has addictive properties and acts synergistically with nicotine in rodents.

I agree with Talhout et al. that sugars increase the levels of formaldehyde in mainstream smoke and have gone to some lengths myself to publish the results of extensive studies to that effect. However, it should be borne in mind that from extensive bioassay studies done over many years, described in detail or cited in my papers, there is no evidence to imply that this is accompanied by an increase in smoke toxicity. I also agree that there is some evidence that sugars can increase the levels of 2-furfural in mainstream smoke, discussed below. However, I do not agree with their other conclusions. Why the differences? Who is right?

Talhout et al. are simply mistaken in some of their statements. For example, in their ‘Sugars in tobacco products’ section they cite four references to state: ‘During the manufacturing process of a tobacco product, up to 13% w/w of sugars and sweeteners are intentionally added to tobacco’. This statement is at variance with the information in their Table 1, which indicates that 4.0% sucrose is the maximum level of any sugar added. Furthermore, two of the references cited give no information on the level of sugars added (Leffingwell, 1999; Seeman et al., 2003). A third reference (Rodgman, 2002) states that up to 2.5% w/w sugars are added (2.5 mg per g tobacco) in cigarette manufacture, not 13% w/w.
The evidence that Talhout et al. use for concluding that added sugars also increase mainstream smoke yields of acetaldehyde, acrolein, etc. is derived from pyrolysis studies summarised in their Table 2 and smoke chemistry studies summarised in their Table 3. The pyrolysis results quoted show that sugars do indeed produce such carbonyl compounds when they are pyrolysed in some laboratory pyrolysis systems. However, and as acknowledged by Talhout et al., it is very important in isolated pyrolysis experiments to simulate the combustion conditions that occur inside the burning cigarette, such as heating rate, temperature range, oxygen level and residence time in the pyrolysis zone, otherwise false results can be obtained relative to the behaviour of the ingredient in the cigarette. Several such examples are well documented (Baker and Bishop, 2004). This is particularly the case with involatile substances such as sugars (Baker and Bishop, 2005). The sugar pyrolysis studies quoted in Talhout et al.’s Table 2 are 20–50 years old, and the conditions used do not accurately simulate the combustion conditions that occur during cigarette smoking. The results should be regarded, at best, as not necessarily relevant to the behaviour in a burning cigarette. More recent pyrolysis results obtained in our laboratories, using conditions that simulate to some extent the conditions in a smouldering cigarette and a system specifically designed to measure carbonyl pyrolysis products, have shown that no acetaldehyde or acrolein is formed by pyrolysis from some sugars (Baker et al., 2005). Pyrolysis of sugars in our laboratories also generally indicates that 2-furfural is a product of pyrolysis (Baker and Bishop, 2005). There is also limited smoke chemistry data from the study to indicate that this is reflected in increased smoke yields of 2-furfural in experimental cigarettes when very high levels of some sugars are added to tobacco.

Talhout et al. in practice base their conclusions on added sugars producing increased levels of acetaldehyde, acrolein, etc. from two of the additive – smoke chemistry studies included in their Table 3: Thornton and Massey, 1975 and Shelar et al., 1992. Both those studies used very large quantities of added sugars, much higher than maximum levels used on commercial cigarettes. For example, Table 3 quotes Shelar et al. as adding up to 12% by weight of fructose, glucose or sucrose to tobacco in their experiments (they actually added up to 16%), which produced increases of 6–36% in the smoke acetaldehyde yields relative to a control cigarette with no added sugar. Thornton and Massey added even higher levels of sugars, up to 16.8%. As indicated in Talhout et al.’s Table 1, maximum levels of fructose, glucose and sucrose added in practice to commercial cigarettes are 2.6, 2.6 and 4.0% by weight, respectively. Researchers sometimes add abnormally large quantities of ingredients to experimental cigarettes to deliberately maximise any effects in order to clarify precursor – product routes and chemical mechanisms. The results from such studies on experimental cigarettes should not be regarded as having commercial relevance. Using Shelar et al.’s data, and assuming that any generation of carbonyls from added sugars would be linear with amount added, which is the case from Shelar et al.’s linear correlations quoted in Talhout et al.’s Table 4, the increases in mainstream smoke acetaldehyde at maximum commercial use levels would be 2–8%. This level of increase of carbonyls in smoke would not be statistically significant even using the most modern measurement procedures. In a third study included in their Table 3, a more typical maximum commercial level of sugar was added to the tobacco, 5.4% invert sugar, and reported increases relative to the control cigarette were +0.6 to −0.9% for acetaldehyde, and +0.2 to −0.2% for acrolein, in other words no significant effect (National Cancer Institute, 1977).

Other additive – smoke chemistry studies (not included in their Table 3) that show no consistent, significant effects of added sugars on the levels of smoke acetaldehyde, acrolein, etc. when using actual maximum levels as used in commercial cigarettes are the extensive studies of Rustemeier et al. (2002) and Baker et al. (2004b), as well as Baker (2006). Furthermore, in 2002 Seeman at al. reviewed the entire body of scientific literature relating to sugars in tobacco and the generation of acetaldehyde in mainstream smoke. They concluded that sugars do not contribute to the production of acetaldehyde in mainstream smoke, on a weight-by-weight basis, greater than the overall formation of acetaldehyde from the tobacco itself. They also concluded that acetaldehyde in mainstream smoke was generated from natural tobacco polysaccharides such as cellulose.

As pointed out by Talhout et al., the data of Shelar et al. do show good linear correlations of formaldehyde, acetaldehyde, acetone and acrolein with added sugar for fructose, glucose and sucrose added up to 16% of tobacco weight. This does not agree with our results, which show linear correlations for formaldehyde yields only and up to 10.5% added sugar in several cigarette series, but little or no correlations with the other carbonyl compounds (Baker, 2006). Talhout et al. also quote results reported by Zilkey et al. (1982) that show weak linear correlations of acetaldehyde, acrolein and total aldehydes with sugars naturally present in tobacco of 25 cigarettes, ranging from 0% to 20%. It may be that for very high levels of sugars there is a relationship between total sugar and other carbonyl compounds. However, at the levels of sugars added commercially to cigarettes, any such relationship with added sugar is not evident amongst the general variability of the analytical measurements.

On their conclusion that added sugars increase the toxicity of smoke, Talhout et al. present no specific toxicological evidence to support that conclusion. Our studies and reviews of extensive studies reported in the scientific literature have shown that they do not increase smoke toxicity, using all biosays commonly employed for such purposes: rodent inhalation of total smoke, mouse-skin painting with smoke particulate matter, two in vitro genotoxicity biosays and one in vitro cytotoxicity biosay of smoke particulate matter. Individually, each of these individual
biological assessments may have some limitations, for example Röper et al. (2002) have shown that the vapour phase of smoke is an important contributor to the in vitro bioassay responses, in addition to the smoke particulate phase. Whole smoke assessment techniques for use with in vitro bioassays are under development (e.g., Massey, 2002; Phillips et al., 2005) but are not currently available for use in systematic studies. The assays used in assessing the effects of tobacco ingredients on smoke toxicity are the tests that are recommended in the UK. Guidelines for the assessment of new tobacco ingredients (Report of the Scientific Committee on Tobacco and Health, 1998). Collectively, the results from the bioassays are consistent and in general agreement that adding sugars has no measurable effect on the smoke response. The bioassays mirror recommendations covering toxicological assessment of a large range on consumer products and provide broad information on the potential effects of tobacco ingredients on the toxicological profile of cigarette smoke. Within this toxicological framework there is no evidence to support the hypothesis that added sugars play a major role in influencing cigarette smoke toxicity.

Talhout et al. also speculate in their concluding section that adding sugars may also increase sidestream yields of carbonyl smoke constituents and recommend that such measurements should be made. In fact such measurements were reported in my paper (Baker, 2006). Adding white, brown and invert sugars, as well as a mixture of fructose and glucose to tobacco at above the maximum commercial use levels had no effect on the sidestream yields of formaldehyde, acetaldehyde, acetone, acrolein, propionaldehyde or methyl ethyl ketone. Sidestream yields of crotonaldehyde were increased by 12–14% with two of the four sugars.

Talhout et al. assert that added sugars produce a sweet taste that is attractive to adolescent smokers. I do not believe that this is true. Sugars have been added to tobacco in some types of cigarette in some countries such as the USA and parts of Europe for over 100 years, to replace sugars lost by curing and to enhance the tobacco flavours in smoke. Unlike when sugars are added to foods, they do not create sweet tastes in the smoke. They blend with the tobacco, making a characteristic but very distinctive tobacco taste. Terms such as bitter, sweet, woody, etc. are used by expert smoke flavour panels to describe smoke sensory characteristics but the use of such terms does not imply that sugars actually make the smoke sweet in the sense that a lay smoker would understand that term. It is not true to imply that sugars and other ingredients are added to tobacco because that would make cigarettes attractive to adolescents. British American Tobacco’s view is categorically that only informed adults should take the decision to smoke. The companies support over 120 youth smoking prevention programmes in over 70 countries, and we advocate raising the UK legal age for cigarette sales from 16 to 18 years, in line with alcohol sales.

The final assertion by Talhout et al. is that sugars generate acetaldehyde, which has addictive properties and acts synergistically with nicotine. I have already pointed out that added mono- and di-saccharide sugars do not contribute to the generation of acetaldehyde in smoke. The bioavailability of mainstream smoke acetaldehyde has been extensively reviewed by Seeman et al. (2002). The studies in that review have shown that in human smokers, mainstream smoke acetaldehyde, which is largely in the gas phase of mainstream smoke, is deposited primarily in the upper respiratory tract, including the mouth. While some acetaldehyde is directly exhaled, the remaining is cleared by efficient and rapid metabolic oxidation in blood and other tissues, including the blood–brain barrier. Experimental data have demonstrated that there is no measurable increase of acetaldehyde levels in systemic blood as a consequence of smoking. Animal studies have shown that much higher acetaldehyde doses are needed than is possible from smoking to overwhelm the rapid clearance of acetaldehyde and result in increases in blood and brain acetaldehyde concentrations. Since tobacco sugars contribute little to mainstream smoke acetaldehyde, the possibility that tobacco sugar-derived mainstream smoke acetaldehyde would result in direct central nervous system effects on the smoker is even less likely.

In their review, Talhout et al. are careful to point out which studies have been conducted by tobacco companies. This is useful because the facilities in tobacco company laboratories, and the dedication and calibre of their scientific staff, are second to none. Of course, there can always be good and bad research conducted and conclusions drawn in any laboratory, whether it be tobacco company, independent research institute or health authority. The beauty of publishing full results in peer-reviewed journals is that the full information can be assessed and repeated if there is any doubt. I believe that our conclusions are the valid ones and that there is a wealth of solid evidence to substantiate them, obtained by a variety of studies over many years.

References


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