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Influence of tea and coffee on biomonitoring of toluene exposure

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Background The intake of some benzoic acid-containing foods or drinks such as green tea and coffee is known to increase urinary hippuric acid (HA) concentrations, and, unless this can be accounted for, may result in false-positive findings during the biological monitoring of toluene exposure.

Aims To investigate the influence of green tea and coffee ingestion on urinary HA concentrations.

Methods Time-weighted average exposures to toluene were monitored by measuring urinary HA in 245 car painters in 2005 and again in 2006. Samples of both urine and blood were collected during work hours. All the participants were also asked about their alcohol intake, smoking and dietary and beverage habits, especially green tea and coffee. To clarify the relationship between green tea and coffee ingestion, workers were prohibited from consuming green tea and coffee for 1 day before the health check-up in 2006.

Results The frequency of positive urinary HA concentrations (>1.0 g/l) in heavy consumers of green tea and/or coffee was significantly higher than that of the non-consumer or light consumers (OR 2.34, 95% CI 1.15–4.74). Prohibiting green tea and coffee ingestion was effective in decreasing the frequency of falsely elevated urinary HA concentrations ($P < 0.01$).

Conclusions The consumption of green tea and/or coffee can result in an overestimation of urinary HA concentrations and cause false-positive results during the biological monitoring of workers exposed to low doses of toluene.

Key words Biological monitoring; catechin; chlorogenic acid; coffee; green tea; hippuric acid.

Introduction

Toluene has been extensively used as an industrial solvent and biological exposure monitoring for it is common.

Urinary hippuric acid (HA) is widely measured as a biological marker of occupational exposure to toluene. In Japan, the six monthly estimation of urinary HA has been obligatory in occupational health surveillance since 1989, and a urinary HA level of >1.0 g/l is abnormal according to the Japanese Regulation on Prevention of Organic Solvent Poisoning. Due to improved hygiene standards in Japan, occupational exposure to toluene is not high [usually a maximum of 100–150 parts per million (p.p.m.)]. Urinary HA concentrations are increased not only by toluene exposure but also by the intake of food and drink containing benzoic acid [1–3]. For example, blueberries, grapes, apples, strawberries, plums, wine [4] and cider [5] are precursors of HA in urine. Therefore, it is often difficult to ascertain whether positive results are specifically due to toluene exposure, especially where there is low-dose exposure to toluene.

In our workplace, the levels of exposure to toluene are low (airborne toluene < 1.0 p.p.m.). Despite toluene workers being advised that the intake of foods containing benzoic acid should be strictly prohibited before biological monitoring, >30% of total HA measurements show a high HA concentration (>1.0 g/l) in urine [2]. The authors interviewed workers and noticed that one of them who showed a positive urinary HA concentration (>1.0 g/l) had consumed five or six cups of green tea or coffee before his medical check-up. Some kinds of tea and coffee produce HA as a metabolite which is excreted in urine [6,7]. We therefore hypothesized that the intake of green tea and coffee might be a factor in false-positive urinary HA and investigated the relationship between the consumption of green tea and coffee and urinary HA concentrations.

Methods

This study was carried out in the painting sections of an automobile factory from April 2005 to April 2007. In the first year, 245 of 250 workers (all males) agreed to

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Table 1. Urinary HA concentrations by smoking, alcohol drinking and tea and/or coffee consumption

	HA (g/l)				
	n (%)	GM	GSD	<1.0 (g/l), *n* (%)	>1.0 (g/l), *n* (%)
All participants	245 (100)	0.34	8.74	199 (81)	46 (19)
Smoking					
Non-smokers	83 (34)	0.31	8.17	71 (29)	12 (5)
Smokers	162 (66)	0.36	8.84	128 (52)	34 (14)
Alcohol drinking					
Teetotallers	53 (22)	0.45	7.59	40 (16)	13 (6)
Drinkers	192 (78)	0.32	8.68	159 (65)	33 (13)
Tea or coffee consumption					
No or light	165 (67)	0.28***	8.50	143 (58)	22 (9)**
Heavy	80 (33)	0.52***	8.95	56 (23)	24 (10)**

GM, geometric mean; GSD, geometric standard deviation.

***$P < 0.001$, **$P < 0.01$.

participate. Urine and blood were sampled during occupational health surveillance. Urinary HA concentrations were measured by high-performance liquid chromatography without creatinine correction because the Japanese Regulation on the Prevention of Organic Solvent Poisoning does not require creatinine concentration measurement.

All participants gave informed consent before having their blood drawn. Furthermore, their smoking habits, alcohol intake and tea or coffee consumption were confirmed in a medical interview by doctors just before the health check. Non-smokers were defined as those of <10 pack-years according to the Blinkman index. Teetotallers were defined as those who had not drunk any kind of alcohol in the last 10 years. Workers who consumed three or more cups of tea or coffee per day were defined as heavy consumers, and those drinking less than three cups a day were defined as light consumers.

The study was repeated in 2006 when toluene-exposed workers were asked to avoid green tea and coffee in addition to all the other restricted foods they already knew about for 1 day before the occupational health surveillance.

This study protocol was reviewed and approved by the Ethics Committee of the University of Miyazaki.

Statistical analyses were conducted using SPSS Base 11.0J for personal computers. To test for significance, we used χ^2 for comparisons involving categorized multivariate regression analyses; *P*-values <0.05 were considered significant.

Table 2. Multivariate regression analysis of HA excretion (>1.0 g/l)

Variables	OR	95% CI
Age	1.00	0.96–1.05
Smoking	1.16	0.54–2.49
Alcohol	0.77	0.33–1.79
BMI	0.48	0.19–1.23
Tea, coffee	2.34	1.15–4.74*

BMI, body mass index.

*$P < 0.05$.

Table 3. Multivariate regression analysis for teetotallers ($n = 53$)

Variables	OR	95% CI
Age	1.12	0.98–1.28
BMI	1.01	0.07–15.8
Smoking	9.15	0.71–117
Tea, coffee	18.23	2.44–136**

**$P < 0.01$.

Table 4. Multivariate regression analysis for heavy consumers of tea and/or coffee ($n = 80$)

Variables	OR	95% CI
Age	1.05	0.97–1.14
BMI	0.8	0.22–2.87
Smoking	2.04	0.47–8.8
Alcohol	0.27	0.09–0.86*

*$P < 0.05$.

Results

The ages of the workers in 2005 ranged from 24 to 59, with a mean age of 43.5 years old. In 2005, the urinary HA concentrations in the heavy consumers of tea or coffee were significantly higher than that in the light consumers ($P < 0.001$), and the number of workers showing high levels of HA excretion (>1.0 g/l) in the heavy-consumer group was significantly higher than that in the light consumers ($P < 0.01$) (Table 1).

The consumption of tea or coffee was associated with a significant increase in HA excretion (OR 2.34, 95% CI 1.15–4.74, $P < 0.05$) in the multivariate regression analysis (Table 2).

Not drinking alcohol significantly reduced the number of people showing an increase in the HA concentrations (Tables 3 and 4) in the heavy consumers of tea and/or coffee (OR 0.24, 95% CI 0.06–0.89, $P < 0.05$) (Table 3). In teetotallers, the heavy consumption of tea or coffee was a markedly strong positive factor for urinary HA excretion (OR 9.94, 95% CI 1.73–57.20, $P < 0.01$) (Table 4).

In 2006, 194 workers from the first year were enrolled in this study, as 51 workers had dropped out because of retirement or transfer to another workplace. The number of people showing high HA excretion levels (>1.0 g/l) significantly decreased compared to 2005, from 46 to 14 ($P < 0.01$) (Table 5), after providing information about the prohibition of green tea and coffee ingestion for 1 day before collecting specimens (in addition to the limitation of other foods and drinks already known to contain benzoic acid).

Table 5. Urinary HA concentrations before and after intervention

	GM	GSD	HA (<1.0) *n* (%)	HA (>1.0) *n* (%)
Before	0.34	3.1	199 (81)	46 (19)**
After	0.16	10.55	180 (93)	14 (7)**
Dropout				51 (21)

**$P < 0.01$.

Discussion

Our study found that the consumption of green tea and/or coffee causes false-positive results during biological monitoring of toluene. While it is known that the consumption

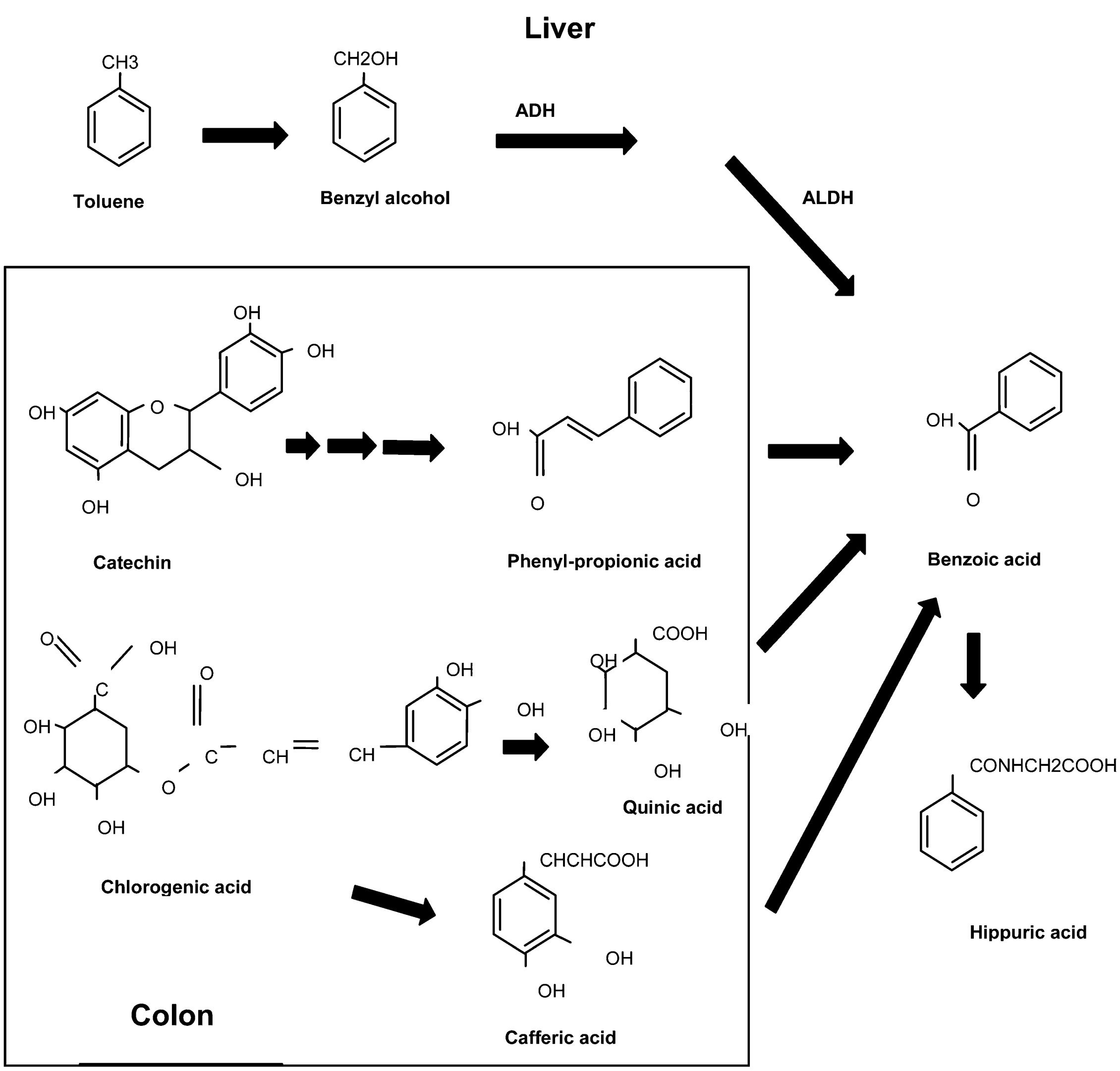

Figure 1. Metabolic pathway of toluene, catechin and chlorogenic acid in humans.

of benzoate-containing foods and soft drinks might affect urinary HA levels [2,3], the effect of green tea and coffee is not as widely recognized. In spite of strictly prohibiting the intake of such items before biological monitoring, we found that some urinary HA concentrations were often elevated during health surveillance.

It is not widely known that the intake of green tea and coffee is related to the excretion of HA in urine, even though it is well known that green tea and coffee are major sources of dietary catechin and chlorogenic acid, respectively [7–9]. However, there are a few reports that they are both converted to benzoic acid by bacterial flora in the colon, though they are not absorbed into the small intestine [6–8], and finally converted into HA in urine [6–8,10] (Figure 1).

The weakness of our paper is that it was difficult to measure the amounts of catechin and chlorogenic acid in green tea or coffee ingested. The previous reports say that 1 l of coffee provides 500–600 mg of chlorogenic acid [11] and the urinary HA during green tea consumption (6 g/day) is 4.22 mmol/24 h [8]. In addition, half of the ingested chlorogenic acid and <45% of the ingested catechin are converted to HA [7,8]. Further studies measuring their levels will be necessary to confirm to what extent the dose–response is related to HA.

Our educational intervention contributed significantly to decreasing the number of people showing positive HA excretion (Table 5). That is, prohibiting the intake of green tea and coffee before health surveillance was very effective in decreasing the frequency of false positives. It is important that we disseminate this new finding that preventing toluene workers from consuming green tea and coffee is effective in maintaining the accuracy of biological monitoring.

Alcohol drinking and smoking were not significantly related to urinary HA concentrations in our study (Tables 1 and 2). At moderate or high toluene-exposure levels, it is probable that alcohol drinking and smoking reduced the urinary HA concentration, as noted in previous reports [1,12]. As for their mechanism, it can be considered that alcohol shares a common metabolic pathway with toluene and smoking enhances the clearance of toluene from the blood [13]. Regarding the difference between previous reports and our results, it is probable that toluene exposure was so low that alcohol drinking and smoking did not affect the urinary HA concentration.

Although the influence of alcohol drinking on urinary HA which originates from toluene is well known [1], little is known about the relationship between the alcohol drinking and the metabolism of some foods and drinks which contain benzoic acid, such as blueberries, apples, grapes and so on, and especially green tea and coffee. According to our multivariate regression analysis, it is possible that alcohol drinking suppresses HA excretion which originates from green tea and coffee. Alcohol may inhibit the metabolic pathway of green tea and coffee in the bacterial flora of the colon, similar to the relationship between alcohol and toluene in the liver, but this remains unclear.

In conclusion, this is the first report to demonstrate the relationship between green tea and coffee and urinary HA on occupational exposure to toluene. Their intake could possibly cause toluene workers to show a false-positive result during monitoring of urinary HA concentrations. To reduce false positives on biological monitoring, we recommend prohibiting any food or drink except water for 1 day before health surveillance of workers exposed to low doses of toluene.

Key points

- The consumption of green tea and coffee is associated with a significant increase in hippuric acid excretion.
- The frequency of false-positive results for urinary hippuric acid in biological monitoring of toluene can be reduced by prohibiting the intake of green tea and coffee before biomonitoring.

Conflicts of interest

None declared.

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