Pergamon

Food and Chemical Toxicology 37 (1999) 125–134

Food and Chemical Toxicology

Mutagenicity and Aromatic Amine Content of Fumes from Heated Cooking Oils Produced in Taiwan

TAI-AN CHIANG[1]*, WU PEI-FEN[2], LIAO SU YING[1], LI-FANG WANG[3] and YING CHIN KO[4]

[1]Department of Industrial Safety and Hygiene, Tajen Junior College of Pharmacy, No. 20, Wei-Shin Road, Shin-Era, En-Pu, Ping-Tung, [2]Department of Medical Technology, China Junior College of Medical Technology, No. 89, Wen-Hwa 1st Street, Jen-Te, Tainan, [3]School of Chemistry, Kaohsiung Medical College, Kaohsiung, No. 100, Shih-Chuan 1st Road, Kaohsiung and [4]Department of Public Health, Kaohsiung Medical College, Kaohsiung No. 100, Shih-Chuan 1st Road, Kaohsiung, Taiwan ROC

(Accepted 26 May 1998)

Abstract—According to toxicological studies, there are several unidentified mutagens derived from cooking oil fumes appearing in kitchens of Chinese homes where women daily prepare food. Data are limited to an analysis of aromatic amines from cooking oil fumes, which are known to be carcinogenic for bladder cancer. Fume samples from three different commercial cooking oils frequently used in Taiwan were collected and analysed for mutagenicity in the *Salmonella*/microsome assay. Aromatic amines were extracted from the samples and identified by HPLC and confirmed by gas chromatography/mass spectrometry (GC/MS). Extracts from three cooking oil fumes were found to be mutagenic in the presence of S-9 mix. All samples contained 2-naphthylamine (2-NA) and 4-aminobiphenyl (4-ABP). Concentrations of 2-NA and 4-ABP were 31.5 and 35.7 $\mu g/m^3$ in fumes from sunflower oil, 31.9 and 26.4 mg/m^3 in vegetable oil, and 48.3 and 23.3 $\mu g/m^3$ in refined-lard oil, respectively. Mutagenicities of the three cooking oil condensates were significantly reduced ($P < 0.05$) by adding the antioxidant catechin (CAT) into the oils before heating. Significant difference existed between the amounts of aromatic amines with and without adding CAT ($P < 0.05$). These results indicate that exposure to cooking oil fumes in Taiwan might be an important but controllable risk factor in the aetiology of bladder cancer.

Keywords: carcinogenic; mutagenicity; aromatic amines; cooking oil fumes.

Abbreviations: 4-ABP = 4-aminobiphenyl; BHA = butylated hydroxyanisole; B[*a*]A = benzo[*a*]anthracene; B[*a*]P = benzo[*a*]pyrene; CAT = catechin; DB[*ah*]A = dibenz[*ah*]anthracene; GC/MS = gas chromatography/mass spectrometry; HAA = heterocyclic amines; 2-NA = 2-naphthylamine; PAH = polyaromatic hydrocarbon.

INTRODUCTION

Several aromatic amines have been implicated as human bladder carcinogens, including 2-naphthylamine (2-NA) (Schulte *et al.*, 1986), 4-aminobiphenyl (4-ABP) (Hueper, 1969), benzidine (Meigs *et al.*, 1986), 4,4′-methylenedianiline (Schulte *et al.*, 1987), 4,4′-methylenebis (2-chloroaniline) (Ward *et al.*, 1988), *o*-toluidine (Rubino *et al.*, 1982) and 4-chloro-*o*-toluidine (Stasik, 1988). According to earlier studies, 2-NA and 4-ABP are considered particularly important as aetiological agents inducing human bladder cancer associated with cigarette smoking (Gorrod and Manson, 1986) and occupational exposure (Riffelmann *et al.*, 1995).

Numerous studies have indicated that smokers exhibit higher haemoglobin adducts of aromatic amines than non-smokers (Bryant *et al.*, 1988; Vineis *et al.*, 1990; Weston *et al.*, 1991). The level of adducts in non-smokers is positively associated with their exposure to environmental tobacco smoke (Maclure *et al.*, 1989). Roughly 50% of attributed risk for bladder cancer is associated with

*Corresponding author.

0278-6915/99/$ - see front matter
PII S0278-6915(98)00081-7

cigarette smoking, which seems to indicate that there remains some exposure to aromatic amines that is not associated with tobacco smoke.

Early Western investigations (Gere, 1982; Teschke *et al.*, 1989) indicated that air samples from restaurant kitchens were mutagenic in *Salmonella typhimurium* strains TA98 and TA100, as were fumes arising from cooking certain foods (Lofroth *et al.*, 1991; Rappaport *et al.*, 1979). Recently, according to research from mainland China and Taiwan, polycyclic aromatic hydrocarbons (PAHs), benzo[*a*]pyrene (B[*a*]P), dibenz[*ah*]anthracene (D[*ah*]A) and benz[*a*]anthracene (B[a]A) were extracted from rapeseed, sunflower, vegetable, and refined-lard oils (Chiang *et al.*, 1997; Li *et al.*, 1994). Several PAHs are considered to be aetiological agents for lung adenocarcinoma among Chinese women. In our previous studies, some mutagens were not identified and confirmed by comparing with the amounts of mutagenicity between cooking oil fumes and identified PAHs (Chiang *et al.*, 1997, 1998; Wu *et al.*, 1998a). Epidemiological studies have observed an elevated incidence of cancers among non-smoking women with long-term exposure to cooking oil fumes (Gallagner *et al.*, 1964; King and Haenszel, 1973), and excess bladder cancer was reported among cooks who had occupational exposure to cooking oil fumes daily (Schoenberg *et al.*, 1984). The aromatic amines were suspected aetiological factors for contracting bladder cancer among these people. There are limited data about the arylamine content of fumes from cooking oils. We analysed the mutagenicity of the frequently used oils (sunflower, vegetable and refined-lard oils) during the past 10 yr in Taiwan. Five aromatic amines, 2-NA, 4-ABP, benzidine, *o*-toluidine and 4,4′-methylenebis (2-chloroaniline), were analysed. In addition, catechin (CAT) was added to cooking oils before heating to clarify the effect of this antioxidant on mutagenicity and arylamine concentrations of fumes produced by the heated cooking oils.

MATERIALS AND METHODS

Chemicals

Three commercial hand-made cooking oils (sunflower oil, vegetable oil and refined-lard oil) were purchased at traditional Taiwanese markets. The acetone extracts of the oils and air samples before heating were checked for mutagenicity in order to confirm that the process of cooking was responsible for the mutagenicity of these oils. Each oil (0.1 litre) was poured into an iron pot and heated by an electronic heater at $300 \pm 10^{\circ}$C. In addition, we designed another experiment to clarify the effects of an antioxidant on the mutagenicity and arylamine content of cooking oil fumes. Different amounts (500 ppm, 1000 ppm and 1500 ppm) of the antioxidant CAT were added to the three cooking oils before heating, and condensates were collected. All experiments were performed in triplicate, and particulate matter arising from the hot oil was collected for 30 min on 37-mm Grade AA glass fibre filter paper, by means of a personal sampling pump (flow rate: 2 litres/min) placed 50 cm above the fuming surface (approximate position of cook's face). An air sampling study was performed while the iron pot was heated without cooking oils to confirm that the aromatic amines were not supplied from the heated environmental air or heated iron pot.

Fume extraction

The filter paper was weighed before and after sampling. Each filter paper was divided into 1-cm squares and the pieces were extracted with 200 ml acetone in a shaker. The organic extracts were filtered through Whatman No. 1 filter paper; the filtrates were concentrated to approximately 10 ml in a vacuum rotary evaporator at 40°C and then evaporated to dryness under a nitrogen stream. The residue was weighed, redissolved in the original solvent (2 ml) and stored at −80°C until the mutagenicity test and HPLC analysis were performed.

Mutagenicity test

Samples were tested for mutagenicity by the *Salmonella*/microsome test, as described by Maron and Ames (1983). Liver homogenate supernatant (S-9) was prepared from the liver of male Sprague–Dawley rats treated with Aroclor 1254, as described by Maron and Ames (1983). Test condensates were diluted in 100 ml dimethyl sulfoxide with or without 0.5 ml S-9 mix, and were gently stirred for 20 min at 37°C. Selective top agar (2 ml) was added to each tube and the mixture was stirred and layered over the surface of a minimal agar plate. The plates were incubated for 48 hr. Each condensate was tested at four concentrations (0.25, 0.5, 1.0, 2.0 mg) and the mean number $\pm$ standard deviations of revertants from the six plates was calculated. Colonies were counted by an automated colony counter.

HPLC and GC/MS analysis

Extracts of samples were passed through a Sephadex LH-20 column (15 mm i.d. × 190 mm) at a flow rate of 1.5 ml/min, with 2-propanol as the eluent. Fractions were collected by a fraction collector at 2-min intervals. An aliquot (10 μl) of each fraction was evaporated and the residue was dissolved in 1 ml acetone for aromatic amine determination by HPLC. The fractions were filtered with a 0.45-μm Millipore filter and eluted with 65% acetonitrile–water (v/v) at 1 ml/min using a Hewlett-Packard 1050 HPLC system (column type: 80 Å C_{18}, 25 cm × 4 mm i.d., 5 μm). The eluents were monitored at 230 nm. The quantitative analysis method was compared with standard calibration

curves and the peaks were deconvoluted by the program in HP-MS (Hewlett Packard Company) Chem. Station. The areas of the peaks were used to calculate the concentration of AAs. In order to confirm the arylamines existing in the three tested oil fumes, UV spectral characteristics of the HPLC peaks in each purified sample were compared with library spectra acquired from standard solutions. Furthermore, gas chromatography/mass spectrometry (GC/MS) was conducted using an HP 5890 Series II instrument equipped with split/splitless injector and a PTE 5 Supelco 30 cm × 0.25 mm column (0.2 μm). An HP-MSD 5972 mass detector was used as detector and an HP-MS Chem. Station as integrator.

RESULTS

The amount of fume particulates and acetone extracts was higher (but not significant) in vegetable oil (Table 1). The acetone extracts of the oils and air samples before heating showed no mutagenicity using the *Salmonella* mutation assay with tester strain TA98. The fume extracts of sunflower oil and vegetable oil displayed direct (–S-9) mutagenicity when the concentration was greater than 0.5 and 2.0 mg/plate, respectively (Table 2). Extracts from sunflower, vegetable and refined-lard oil fumes were found to be mutagenic in the presence of S-9 mix when the concentration was greater than 2.0 mg/plate. The mutagenicity of cooking oil condensates was dependent on the concentration and cooking-oil temperature (data not shown). Air samples collected from unheated oils were all negative in TA98 with or without S-9. Different amounts of CAT were added before heating and condensates were collected. CAT significantly inhibited the mutagenicity of all cooking oil condensates ($P < 0.05$) (Fig. 1).

HPLC analysis showed that all extracts of cooking oil fumes contained 2-NP and 4-ABP (Fig. 2) and was confirmed by UV spectral (Fig. 3) and GC/MS (Figs 4 and 5). The average concentrations of 2-NP and 4-ABP were 31.5 and 35.7 $\mu g/m^3$ in sunflower oil, 31.9 and 26.4 $\mu g/m^3$ in vegetable oil,

Table 1. Comparison of the amounts of fume particulates from various cooking oils heated at 300 ± 10°C for 30 min

Oil	Fume particulate (mg/m^3)	Acetone extracts (mg/m^3)
Sunflower	25.1 ± 2.3	20.7 ± 1.8
Vegetable	28.3 ± 2.8	22.4 ± 2.0
Refined-lard	26.8 ± 2.1	20.6 ± 1.6

Table 2. The mutagenicity of acetone extracts of fume particulates from various oils in *Salmonella typhimurium* TA98 with or without S-9 mix

Concn (mg)	Revertants/plate†					
	–S9			+S9		
	Sunflower	Vegetable	Refined-lard	Sunflower	Vegetable	Refined-lard
0.25	24 ± 1	16 ± 3	15 ± 2	62 ± 2*	35 ± 1	30 ± 1
0.5	30 ± 1*	21 ± 1	18 ± 1	85 ± 2+*	45 ± 2	35 ± 2
1.0	41 ± 1*	26 ± 1	21 ± 2	118 ± 3*	55 ± 3+*	40 ± 1
2.0	55 ± 3*	30 ± 2*	25 ± 1	158 ± 4*	69 ± 3*	51 ± 2*

*Positive result (mutagenicity was twofold higher than the spontaneous response).
†The spontaneous revertants of TA98 were 14 ± 1 (–S-9) and 25 ± 2 (+S-9), respectively; positive control, 2-NA (1 μg/plate): 917 ± 44, and 4-ABP (1 μg/plate): 870 ± 28.

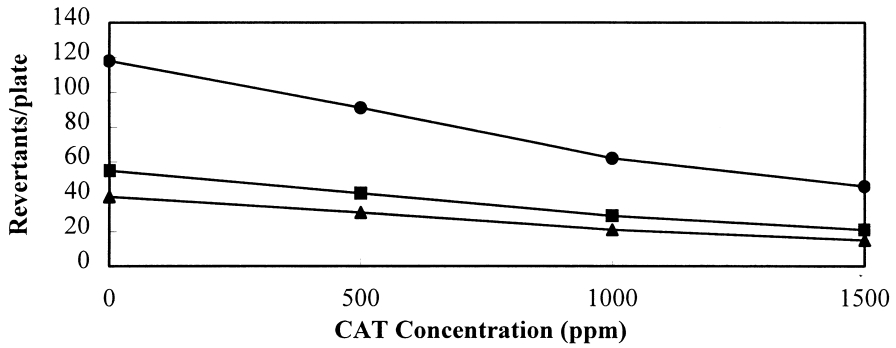

Fig. 1. Effect of CAT on cooking oil condensates (1.0 mg/plate) mutagenicity in the *Salmonella* mutation assay (TA98 + S-9).

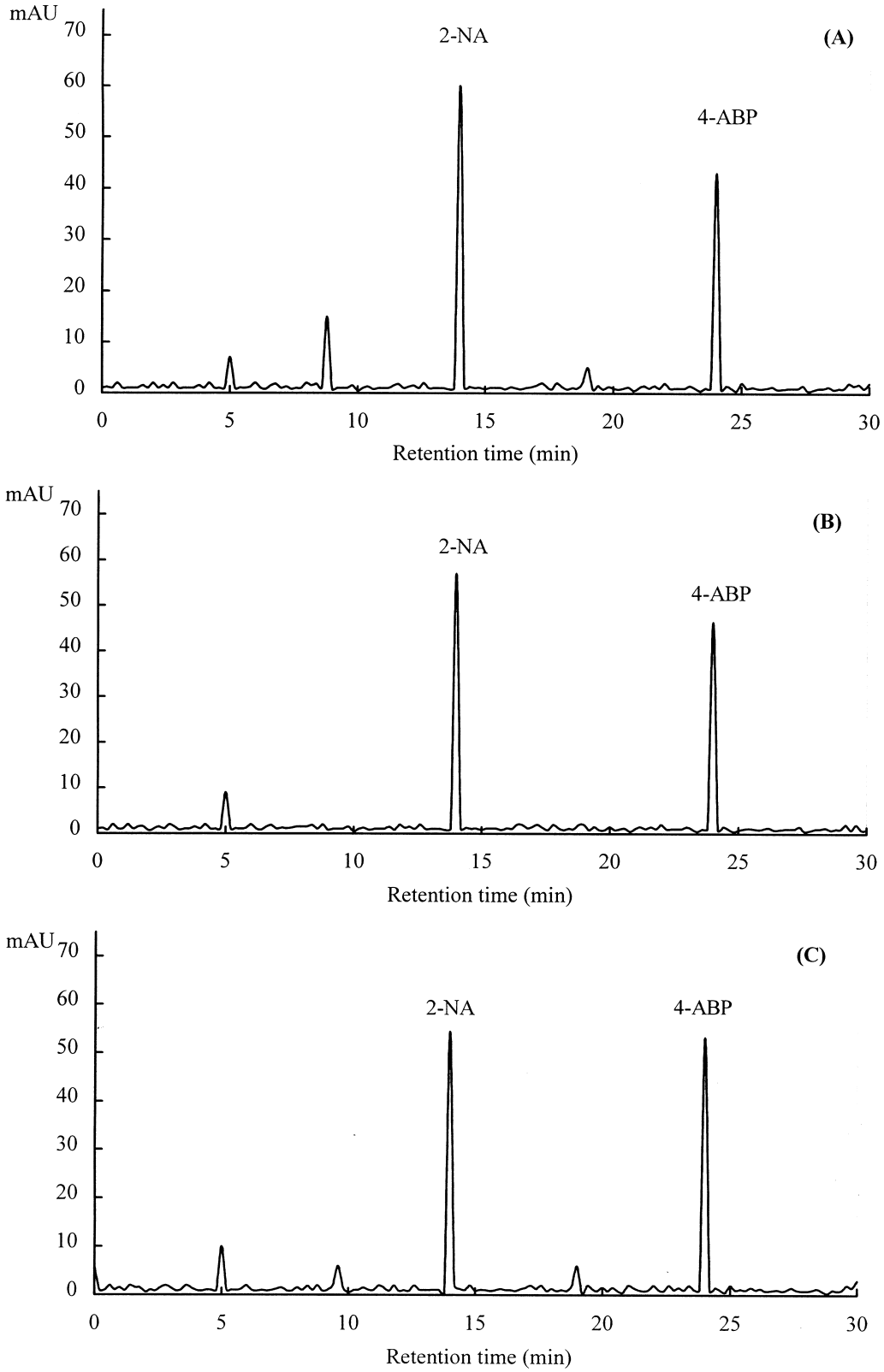

Fig. 2. Chromatography of acetone extracts of fumes from heated sunflower oil (A), vegetable oil (B) and refined-lard oil (C) detected by HPLC.

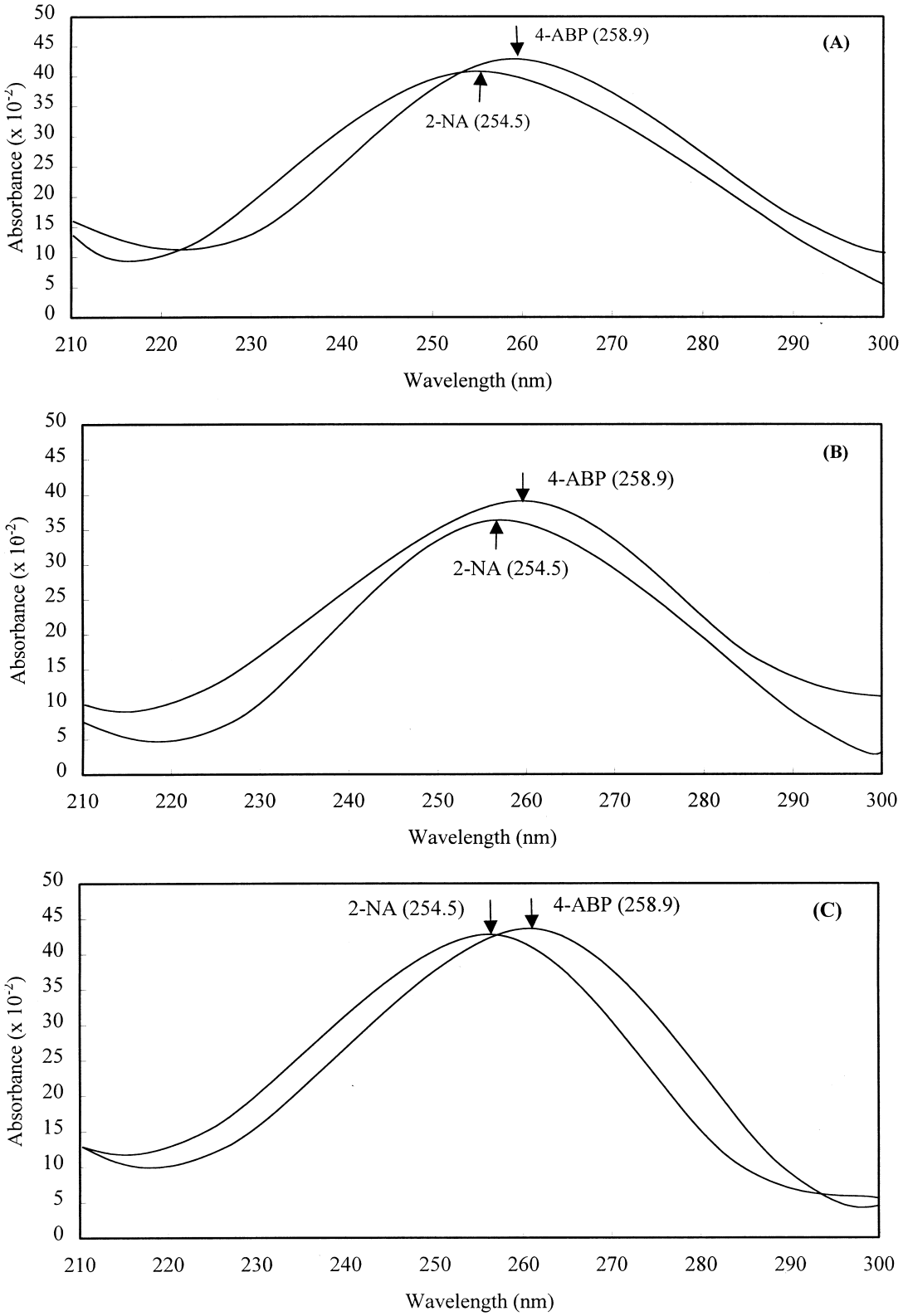

Fig. 3. UV spectra of acetone extracts of fumes from heated sunflower oil (A), vegetable oil (B) and refined-lard oil (C) monitored by photodiode array by HPLC.

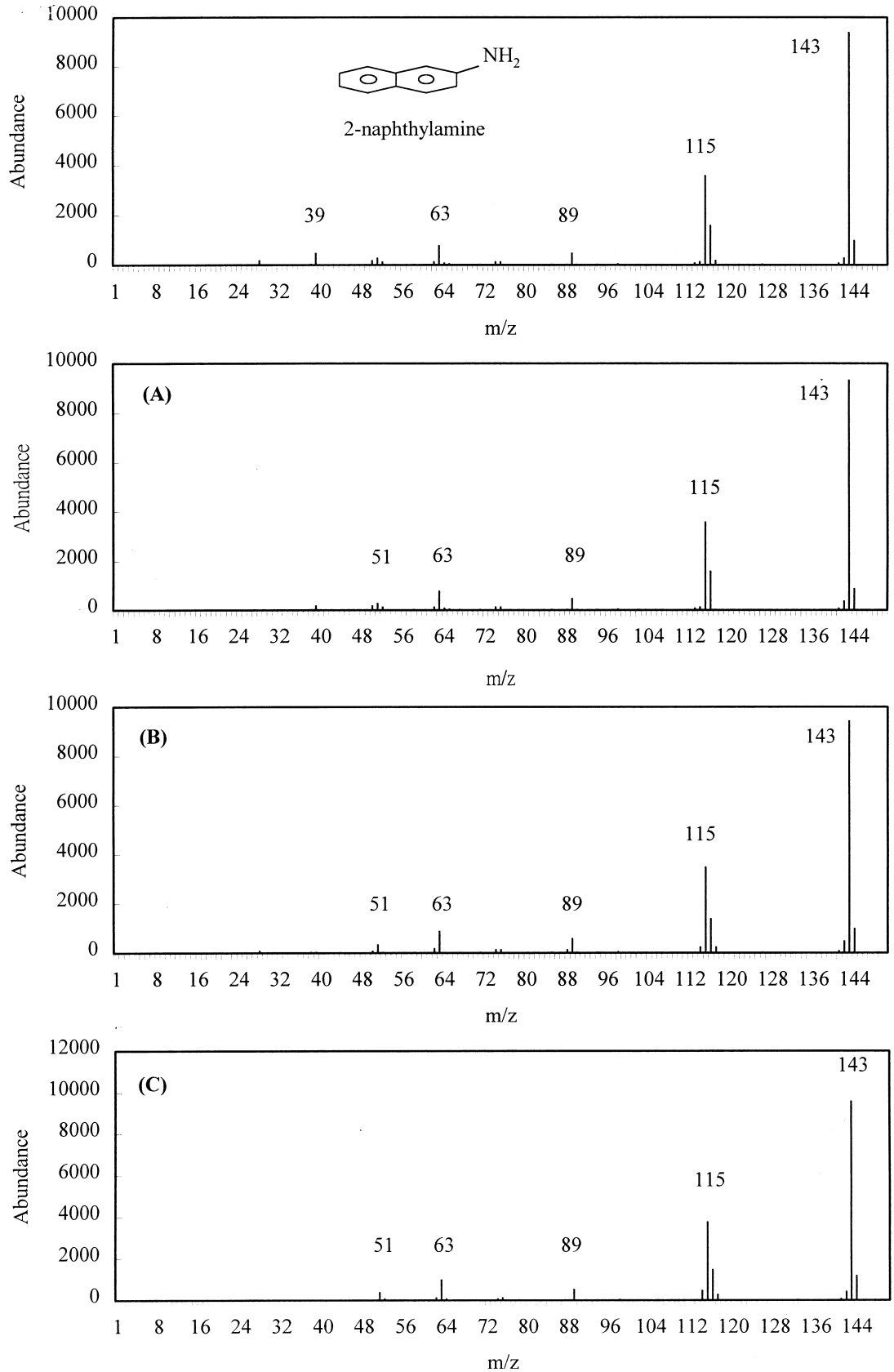

Fig. 4. Mass spectra of 2-naphthylamine of acetone extracts of fumes from heated sunflower oil (A), vegetable oil (B) and refined-lard oil (C) monitored by GC.

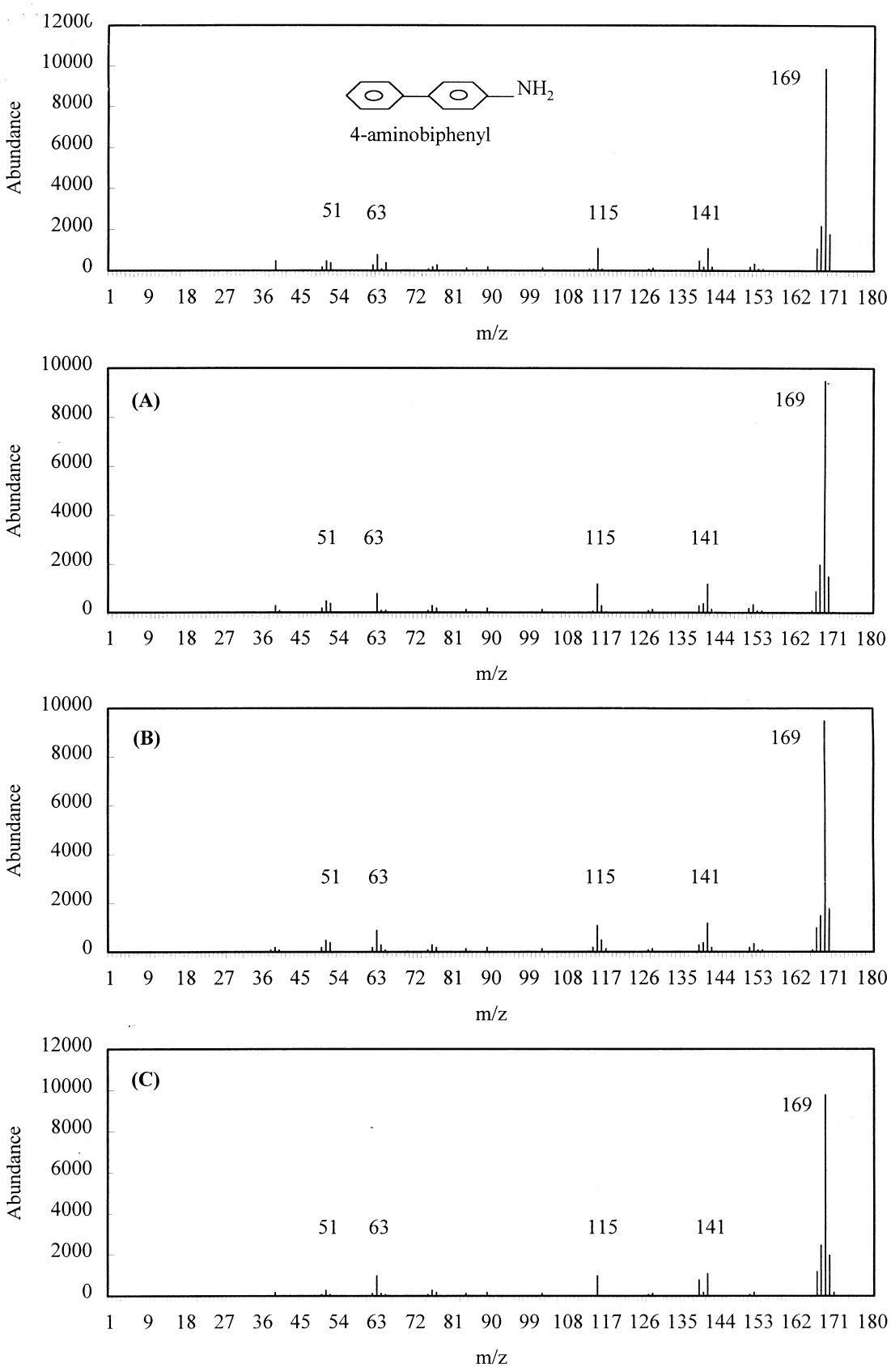

Fig. 5. Mass spectra of 4-aminobiphenyl of acetone extracts of fumes from heated sunflower oil (A), vegetable oil (B) and refined-lard oil (C) monitored by GC.

and 48.3 and 23.3 $\mu g/m^3$ in refined-lard oil, respectively (Table 3). Quantitative analyses of arylamines derived from condensates of cooking oils plus different amounts of CAT were also undertaken. The amounts of arylamines were significantly reduced when CAT was added at concentrations of 500, 1000 and 1500 ppm, respectively ($P < 0.05$). Vegetable oil had the highest reduction rate of arylamine concentrations, followed by refined-lard oil and sunflower oil.

DISCUSSION

In earlier studies, several PAH mutagens [DB[*ah*]A, B[*a*]P in mainland China (Li *et al.*, 1994), and DB[*ah*]A, B[*a*]P, B[*a*]A in Taiwan (Chiang *et al.*, 1997)] and volatile organic compounds (Shields *et al.*, 1995) were found in cooking oils. We analysed frequently used oils (sunflower, vegetable and refined-lard oils) in Taiwan and successfully identified two aromatic amines (2-NA and 4-ABP) from these oil fumes. Numerous studies have been conducted which indicate that exposures to aromatic amines were highly associated with occupational exposure (Riffelmann *et al.*, 1995) and environmental tobacco exposure (Maclure *et al.*, 1989). The epidemiological studies were in accordance with this conclusion (Bulbulyan *et al.*, 1995; Naito *et al.*, 1995; Vineis *et al.*, 1994) and also indicated that excess bladder cancer among cooks might be due to occupational exposure to cooking oil fumes (Schoenberg *et al.*, 1984). The results provide experimental evidence that cooking oil fumes containing aromatic amines might elevate the risk of contracting bladder cancer. The carcinogenicity of 2-NA and 4-ABP were confirmed by IARC (1992) and ACGIH (1993) and considered as human carcinogens. Although not all the arylamines in fumes emitted will be respired, this still may be a potential risk factor of contracting bladder cancer in cooks and women who perform cooking tasks and inhale cooking oil fumes daily.

The formation of polycyclic aromatic compounds in fumes derived from cooking oils has been identified in earlier studies (Chiang *et al.*, 1997; Li *et al.*, 1994; Wu *et al.*, 1998b). The polycyclic aromatic compounds of arylamines in cooking oil fumes needs further analysis because the arylamines are not likely to be produced solely from the fatty acids but with nitrogen atoms. The first possible source of the nitrogen atoms in the arylamines may be contributed from nitrogen dioxide in the atmospheric environment like the formation of nitropyrene from PAHs (Matsushita, 1980). The second possible contribution of nitrogen atoms may be the addition of nitrogen in cooking oils to prevent the oxidation of fatty acids by oil producers in Taiwan (Chiang *et al.*, 1997). The third hypothesis is that arylamines may be produced by heterocyclic aromatic amines (HAAs) which have been identified in some amino acids pyrolysates and which are structurally very similar to arylamines (Sugimura, 1982). According to our study, several amino acids such as phenylalanine, glycine and creatinine were detected in cooking oils (unpublished data). Formation of HAAs in heated cooking oils may be precursors of arylamines in fumes derived from cooking oils (Bryant *et al.*, 1987). Further risk assessment, including the relationship between personal exposure to arylamines and bladder cancer, is needed.

These three cooking oils contain more than 60% of unsaturated fatty acids which oxidize at high temperatures to produce pyrolysates (Tsai *et al.*, 1993). The study confirms that fumes from cooking oils are mutagenic towards the *S. typhimurium* strain TA98, and that successful inhibition to the level of mutagenicity can be achieved by adding catechin. Butylated hydroxyanisole (BHA) is the most commonly used antioxidant in cooking oils. Several studies have indicated that BHA induces tumorigenesis in rat species (Bran, 1975; Whysner *et al.*, 1994). CAT, extracted from tea leaves and grape seeds, shows a significant increase in oil stability but is less harmful for humans (Gordon and Kourimska, 1995; Hirose and Iwama, 1984). The

Table 3. Concentrations ($\mu g/m^3$) of aromatic amines in fume particulates of various cooking oils

Oils	2-Naphthylamine	4-Aminobiphenyl
Sunflower	31.5 ± 0.5	35.7 ± 0.2
Sunflower + CAT† (500 ppm)*	24.2 ± 0.6	25.6 ± 0.6
Sunflower + CAT (1000 ppm)	20.6 ± 0.4	23.6 ± 0.4
Sunflower + CAT (1500 ppm)	18.2 ± 0.4	20.8 ± 0.6
Vegetable	31.9 ± 0.6	26.4 ± 0.4
Vegetable + CAT (500 ppm)*	21.8 ± 0.4	19.0 ± 0.4
Vegetable + CAT (1000 ppm)*	20.2 ± 0.6	16.4 ± 0.4
Vegetable + CAT (1500 ppm)*	17.0 ± 0.4	16.0 ± 0.6
Refined-lard	48.3 ± 0.8	23.3 ± 0.4
Refined-lard + CAT (500 ppm)*	34.2 ± 0.6	16.4 ± 0.4
Refined-lard + CAT (1000 ppm)*	30.6 ± 0.6	14.1 ± 0.3
Refined-lard + CAT (1500 ppm)*	24.4 ± 0.6	10.4 ± 0.2

CAT = catechin
*Difference between three cooking oil fumes with and without CAT, $P < 0.05$, by Kruskal–Wallis, ANOVA.

significant reduction in concentration of arylamines from cooking oil fumes appears because CAT decreases the pyrolysis reaction of fatty acids (Wu *et al*., 1998). Further study is required to clarify the interactions between CAT and cooking oils and to determine a standard concentration for addition to cooking oils. The permissible concentrations of antioxidants by the Administration of Food and Sanitation differ for various chemicals and range from 200 to 1300 ppm.

In conclusion, in this study we demonstrate that cooking oil fumes are mutagenic and contain two carcinogenic aromatic amines. The Taiwan Government and oil producers have both made an effort to assure the purity and safety of oils following the polychlorinated biphenyl oil poisoning incident which occurred in Taiwan (Hsieh *et al*., 1996), but little attention has been paid to the mutagenicity or carcinogenicity of cooking oil fumes. Cooking at lower oil temperatures, improving ventilation and adding antioxidants, may be useful methods to reduce the production of carcinogenic cooking oil fumes.

REFERENCES

ACGIH (1993) Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. (1993–1994) American Conference of Governmental Industrial Hygienists, Cincinnati, OH.

Bran A. L. (1975) Toxicology and biochemistry of BHA and BHT. *Journal of the American Oil Chemists Society* **52,** 372–375.

Bryant M. S., Skipper P. L., Tannenbaum S. R. and Maclure M. (1987) Hemoglobin adducts of 4-aminobiphenyl in smokers and nonsmokers. *Cancer Research* **47,** 602–608.

Bryant M. S., Vineis P., Skipper P. L. and Tannenbaum S. R. (1988) Hemoglobin adducts of aromatic amines: associations with smoking status and type of tobacco. *Proceedings of the National Academy of Sciences of the U.S.A*. **85,** 9788–9791.

Bulbulyan M. A., Figgs L. W. and Zahm S. H. (1995) Cancer incidence and mortality among beta-naphthylamine and benzidine dye workers in Moscow. *International Journal of Epidemiology* **24,** 266–275.

Chiang T. A., Wu P. F. and Ko Y. C. (1998) Prevention of exposure to fumes produced by hot cooking oil in Taiwanese kitchens. *Environmental and Molecular Mutagenesis* **31,** 92–96.

Chiang T. A., Wu P. F., Wang L. F., Li C. H. and Ko Y. C. (1997) Mutagenicity and polycyclic aromatic hydrocarbon content of fumes from heated cooking oils produced in Taiwan. *Mutation Research* **381,** 157–161.

Gallagner R. P. and Elwood J. M. (1964) Cancer mortality among Chinese, Japanese, and Indians in British Columbia, 1964–73. *Monographs of the National Cancer Institute* **53,** 89–94.

Gere A. (1982) Decrease in essential fatty acid content of edible fats during the frying process. *Zeitschrift für Ernahrungswissenschaft* **21,** 191–201.

Gordon M. H. and Kourimska L. (1995) The effect of antioxidants on changes in oils during heating and deep frying. *Journal of the Science of Food and Agriculture* **68,** 347–353.

Gorrod J. W. and Manson D. (1986) The metabolism of aromatic amines. *Xenobiotica* **16,** 933–955.

Hirose Y. and Iwama F. (1984) Antioxidant isolated from grape seed optical isomer mixtures of catechin. *Journal of the Japanese Oil Chemists Society* **33,** 435–438.

Hsieh S. F., Yen Y. Y., Lan S. J., Hsieh C. C., Lee C. H. and Ko Y. C. (1996) A cohort study on mortality and exposure to polychlorinated biphenyls. *Archives of Environmental Health* **51,** 417–424.

Hueper W. C. (1969) *Occupational and Environmental Cancer of the Urinary System*. Yale University Press, New Haven.

IARC (1992) *IARC Monographs on the Evaluation on Carcinogenic Risk to Humans. Vol. 54. Occupational exposures to mists and vapors from strong inorganic acids and other industrial chemicals*. International Agency for Research on Cancer, Lyon.

King H. and Haenszel W. (1973) Cancer mortality among foreign and native born Chinese in the United States. *Journal of Chronic Diseases* **26,** 623–646.

Li S. G., Pan D. F. and Wang G. X. (1994) Analysis of polycyclic aromatic hydrocarbons in cooking oil fumes. *Archives of Environmental Health* **49,** 119–122.

Lofroth G., Stensman C. and Bradhorst-Satzkorn M. (1991) Indoor sources of mutagenic aerosol particulate matter: smoking, cooking and incense burning. *Mutation Research* **261,** 21–28.

Maclure M., Ben-Abraham Katz R., Bryant M. S., Skipper P. L. and Tannenbaum S. R. (1989) Elevated blood levels of carcinogens in passive smokers. *American Public Health Journal* **79,** 1381–1384.

Maron D. M. and Ames B. N. (1983) Revised methods for the *Salmonella* mutagenicity test. *Mutation Research* **113,** 173–215.

Matsushita H. (1980) Mutagenicity of aromatic nitro compounds and their chemical analysis, pp. 97–100. U.S.–Japan Cooperative Medical Science Programs.

Meigs J. W., Marrett L. D., Ulrich F. U. and Flannery J. T. (1986) Bladder tumor incidence among workers exposed to benzidine: a thirty-year follow-up. *Journal of the National Cancer Institute* **76,** 1–8.

Naito S., Tanaka K. and Koga H. (1995) Cancer occurrence among dyestuff workers exposed to aromatic amines. A long-term follow-up study. *Cancer* **76,** 1445–1452.

Rappaport S. M., McCartney M. C. and Wei E. T. (1979) Volatilization of mutagens from beef during cooking. *Cancer Letters* **8,** 139–145.

Riffelmann M., Müller G. and Schmieding W. (1995) Biomonitoring of urinary aromatic amines and arylamine hemoglobin adducts in exposed workers and non-exposed control persons. *International Archives of Occupational and Environmental Health* **68,** 36–43.

Rubino G. F., Scansetti G., Piolatto G. and Pira E. (1982) The carcinogenic effect of aromatic amines. An epidemiological study on the role of o-toluidine and 4,4′-methylene-bis-2-methylaniline in inducing bladder cancer in man. *Environmental Research* **27,** 241–254.

Schoenberg J. B., Stemhagen A. and Mogielnicki A. P. (1984) Case-control study of bladder cancer in New Jersey. I. Occupational exposures in white males. *Journal of the National Cancer Institute* **72,** 973–981.

Schulte P. A., Ringen K., Hemstreet G. P., Altekruse E. B., Gullen W. H., Tillet S., Allsbrook W. C. J., Crosby J. H., Witherington R., Stringer W. and Brubaker M. M. (1986) Risk factors for bladder cancer in a cohort exposed to aromatic amines. *Cancer* **58,** 2156–2161.

Schulte P. A., Ringen K., Hemstreet G. P. and Ward E. (1987) Occupational cancer of the urinary tract. *Occupational Medicine: State of the Art Reviews* **2,** 85–107.

Shields P. G., Xu G. X., Blot W. J., Fraumeni J. J. F., Trivers G. E., Pellizzari E. D., Qu Y. H., Gao Y. T. and Harris C. C. (1995) Mutagens from heated Chinese and

U.S. cooking oils. *Journal of the National Cancer Institute* **87,** 836–841.

Stasik M. J. (1988) Carcinomas of the urinary bladder in a 4-chloro-o-toluidine cohort. *International Archives of Occupational and Environmental Health* **60,** 21–24.

Sugimura T. (1982) A view of a cancer researcher on environmental mutagens. In *Environmental Mutagens and Carcinogens*, ed. T. Sugimura *et al*., pp. 3–20. Alan R. Liss, New York.

Teschke K., Hertzman C., Netten C. V., Lee E., Morrision B., Corrista A., Lau G. and Hundal A. (1989) Potential exposure of cooks to airborne mutagens and carcinogens. *Environmental Research* **50,** 296–308.

Vineis P. (1994) Epidemiology of cancer from exposure to arylamines. *Environmental Health Perspectives* **102,** 7–10.

Vineis P., Caporaso N., Tannenbaum S. R., Skipper P. L., Glogowski J., Bartsch H., Coda M., Talaska G. and Kadlubar F. (1990) Acetylation phenotype, carcinogen-hemoglobin adducts, and cigarette smoking. *Cancer Research* **50,** 3002–3004.

Ward E., Halperin W., Thun M., Grossman H. B., Fink B., Koss L., Osorio A. M. and Schulte P. A. (1988) Bladder tumors in two young males occupationally exposed to MBOCA. *American Journal of Industrial Medicine* **14,** 267–272.

Weston A., Caporaso N. E., Taghizadeh K., Hoover R. N., Tannenbaum S. R., Skipper P. L., Resau J. H., Trump B. F. and Harris C. C. (1991) Measurement of 4-aminobiphenyl-hemoglobin adducts in lung cancer cases and controls. *Cancer Research* **51,** 5219–5223.

Whysner J., Wang C. X., Zang E., Iatropoulos M. J. and Williams G. M. (1994) Dose response of promotion by butylated hydroxyanisole in chemically initiated tumours of the rat forestomach. *Food and Chemical Toxicology* **32,** 215–222.

Wu P. F., Chiang T. A. and Ko Y. C. (1998) Genotoxicity of fumes from heated cooking oil produced in Taiwan. *Environmental Research*. In press.

Wu P. F., Chiang T. A., Wang L. F., Chang C. S. and Ko Y. C. (1998a) Nitro-polycyclic aromatic hydrocarbon contents of fumes from heated cooking oils and prevention of mutagenicity by catechin *Mutation Research*. In press.