REPORT

Mutagens From Heated Chinese and U.S. Cooking Oils

P. G. Shields, G. X. Xu, W. J. Blot, J. F. Fraumeni, Jr., G. E. Trivers, E. D. Pellizzari, Y. H. Qu, Y. T. Gao, C. C. Harris

Background: The lung cancer incidence in Chinese women is among the highest in the world, but tobacco smoking accounts for only a minority of the cancers. Epidemiologic investigations of lung cancer among Chinese women have implicated exposure to indoor air pollution from wok cooking, where the volatile emissions from unrefined cooking oils are mutagenic. ***Purpose:*** This study was conducted to identify and quantify the potentially mutagenic substances emitted from a variety of cooking oils heated to the temperatures typically used in wok cooking. ***Methods:*** Several cooking oils and fatty acids were heated in a wok to boiling, at temperatures (for the cooking oils) that ranged from 240 °C to 280 °C (typical cooking temperatures in Shanghai, China). The oils tested were unrefined Chinese rapeseed, refined U.S. rapeseed (known as canola), Chinese soybean, and Chinese peanut in addition to linolenic, linoleic, and erucic fatty acids. Condensates of the emissions were collected and tested in the ***Salmonella*** mutation assay (using ***Salmonella typhimurium*** tester strains TA98 and TA104). Volatile decomposition products also were subjected to gas chromatography and mass spectroscopy. Aldehydes were detected using high-performance liquid chromatography and UV spectroscopy. ***Results:*** 1,3-Butadiene, benzene, acrolein, formaldehyde, and other related compounds were qualitatively and quantitatively detected, with emissions tending to be highest for unrefined Chinese rapeseed oil and lowest for peanut oil. The emission of 1,3-butadiene and benzene was approximately 22-fold and 12-fold higher, respectively, from heated unrefined Chinese rapeseed oil than from heated peanut oil. Lowering the cooking temperatures or adding an antioxidant, such as butylated hydroxyanisole, before cooking decreased the amount of these volatile emissions. Among the individual fatty acids tested, heated linolenic acid produced the greatest quantities of 1,3-butadiene, benzene, and acrolein. Separately, the mutagenicity of individual volatile emission condensates was correlated with linolenic acid content ($r = .83$; $P = .0004$). Condensates from heated linolenic acid, but not linoleic or erucic acid, were highly mutagenic. ***Conclusions:*** These studies, combined with experimental and epidemiologic findings, suggest that high-temperature wok cooking with unrefined Chinese rapeseed oil may increase lung cancer risk. This study indicates methods that may reduce that risk. ***Implications:*** The common use of wok cooking in China might be an important but controllable risk factor in the etiology of lung cancer. In the United States, where cooking oils are usually refined for purity, additional studies should be conducted to further quantify the potential risks of such methods of cooking. [J Natl Cancer Inst 87:836-841, 1995]

Lung cancer incidence in Chinese women is among the highest in the world *(1-5).* While tobacco smoking is a major risk factor for cancer, especially in men, it is not for Chinese women (*4,6-8*). Moreover, among Chinese women who do smoke, the tendency is to smoke much less than observed for U.S. women (*6,8-10*), averaging less than eight cigarettes per day. As a possible etiologic factor, epidemiologic studies *(9.10)* of lung cancer in China have implicated indoor air pollutants from cooking-oil vapors. In Shanghai, specifically, the use of unrefined rapeseed oil for wok cooking, compared with soybean oil, was associated with an odds ratio of 1.4 *(95%* confidence interval [CI] = 1.1-1.8) (9). The excess risk also was associated with exposure to wok emissions, measured by the degree of house smokiness and complaints of eye irritation. Rapeseed oil is known in the United States as canola oil, a refined oil with low erucic fatty acid coctent. In China, rapeseed oils having either low- or high-erucic acid content are used for cooking, but refined oils were seldom available or used.

Condensates of volatile emissions from oils cooked in a wok were mutagenic in several in vitro short-term test systems (*11*). Other oils, such as peanut oil. were not. It has been found that the mutagenicity of heated Chinese rapeseed oil condensate is inhibited by the addition of butylated hydroxyanisole to the oil before cooking or when the oil is hydrogenated. These findings suggest that the mutagenicity is related to oxidation of fatty acids. linolenic acid in particular.

In Shanghai. women generally cook with Chinese rapeseed oil and, to a lesser extent, soybean oil. Customarily, about

**Affiliations of authors:* P. G. Shields, G. E. Trivers, C. C. Harris (Laboratory of Human Carcinogenesis), W. J. Blot. J. F. Fraumeni, Jr. (Epidemiology and Biostatistics Program). Division of Cancer Etiology. National Cancer Institute. Bethesda. Md.

G. X. Xu. Y. H. Qu. Y. T. Gao. Shanghai Cancer Institute. Shanghai, People's Republic of China.

E. D. Pellizzari, Research Triangle Institute. Research Triangle Park, N.C.

Correspondence to: C. C. Harris. M.D.. National Institutes of Health. Bldg. 37, Rm. 2C01, Bethesda. MD 20892.

See "Notes" section following "References."

25-100 mL of cooking oil, depending on the type of food being prepared, is placed in the wok and then heated to approximately 280 'C. This high heating temperature results in the generation of a large amount of smoke from the oil that can imtate the eyes and mucous membranes. Thus, kitchen windows are commonly left open, even in the winter. Cooking foods at lower temperatures causes the food to acquire a "bad" taste, whereas cooking at high temperatures tends to reduce this problem.

In this report, we have analyzed volatile emissions from several cooking oils heated to the temperatures typically used in Chinese wok cooking. Included in these analyses is a preliminary characterization of the mutagenicity of these compounds.

Methods

Chemicals and cooking oils. Chinese cooking oils (unrefined Chinese rapeseed. peanut. sesame, and soybean) were purchased from retail Shanghai markets. Different lots were tested for mutagenic condensates. Unrefined Chinese rapeseed oil will be referred to as Chinese rapeseed oil in this report. Canola oil (Proctor and Gamble, Cincinnati, Ohio), a refined North American rapeseed oil. was purchased from a supermarket in Bethesda. Md. Linolenic acid, linoleic acid, and erucic acid were purchased from Sigma Chemical Co. (St. Louis. Mo.). All chemicals were reagent grade.

Preparation of condensates. A wok lid was modified by introducing three holes—two for the attachment of filter holders and one for a thermometer. Two glass filters (#49; Shanghai Huon Guan Paper Corp., Shanghai, China) were used in each filter holder. Cooking oils were placed in the wok (20 mL for volatile organic compound analysis and 100 mL for mutagenicity studies) and heated rapidly with a spherical heating mantle (1000 mL; 380 W) until the designated temperature was reached (Chinese rapeseed: 275-280 'C [with and without butylated hydroxyanisole: Sigma Chemical Co.], canola oil: 275-280 'C, peanut oil: 260-265 'C, soybean oil: 260-265 'C, linolenic acid: 240 'C, linoleic acid: 240 'C, and erucic acid: 240 'C), coinciding with either the release of smoke for oils. the typical Shanghai cooking temperatures. or boiling points for the fatty acids. The wok was then covered, and suction was applied through the filters via a pump (20-30 L/minute). After cooking for 20 minutes. condensates from the four filters were extracted with acetone (10 mL) at room temperature. The condensate extract was then filtered with #1 filter paper (Whatman Ltd., Maidstone, U.K.) and evaporated at 60 'C under a stream of nitrogen. The wok was washed with liquid detergent after each use. Condensates were stored at –70 'C.

Salmonella mutation assay. The assay was performed according to the method of Maron and Ames (*12*). Briefly. test condensates were diluted with dimethyl sulfoxide in the presence (or absence) of S9 liver homogenates (prepared from male Sprague-Dawley rats that had been given injections of Aroclor 1254) and preincubated (20 minutes at 37 'C) in glass culture tubes. ***Salmonella*** *typhimurium* tester strains TA98 and TA104 were utilized. The bacteria were incubated under selective conditions on agar plates for 48 hours at 37 'C.

Determination of volatile organic compounds. The identification of the major components in oil vapor samples was accomplished by manually elucidating their mass spectroscopic fragmentation patterns and comparing them with published spectra (*13*). Oil vapors were cryogenically trapped, subjected to gas chromatography (model 3700; Varian Associates. Inc., Lexington. Mass.) using thermal desorption onto a DB-624 fused silica capillary column (30 mm x 0.32 mm internal diameter. 2.7 mL/minute flow rate; 240 'C) and analyzed with a magnetic sector mass spectrophotometer (model 2091; Pharmacia LKB Nuclear, Gaithersburg. Md.). Internal standatti-normalized responses from duplicate analyses of each standard were fit to a second-order calibration curve. Concentrations for 1,3-butadiene and benzene were calculated from the gas chromatography and mass spectroscopy responses for the analyte (normalized to the response of the internal standard) and the coefficients of the calibration curve. Larger volumes (*200* mL) of the wok background and canister background samples were analyzed along with a National Institutes of Standards and Technology standard reference mixture (SRM #1804) containing 1.3-butadiene and benzene. The recoveries were 96% and 92%. respectively.

Determination of aldehyde and ketone content. Aldehydes and ketones were collected from heated oil emissions above the wok. using Sep-Pak DNPH-Silica canridges (Waters Chromatography. Millipore. Bedford, Mass.). The cartridges were extracted with acetonitrile (6 mL) in a volumetric flask. Extracts were analyzed by isocratic high-performance liquid chromatography (50% acetonitrile. 10% methanol. and 40% water mobile phase on a Sphcrisorb ODS column 25 cm x 4.6 mm internal diameter) and analyzed by UV (365 nm) spectroscopy. Calibration standards were used for identification (retention time) and to construct a linear calibration curve.

Statistical methods. Spearman's rank correlation coefficients were used to assess the relationship between linolenic acid and condensate mutagenicity. *P* values result from two-sided tests.

Results

Mutagenicity testing using the Salmonella mutation assay with tester strain TA98 and S9 liver homogenates confirmed that unrefined Chinese rapeseed condensates are mutagenic (Table 1); the number of mutants (i.e., revertants) per plate increased fourfold and a dose–response effect was observed until cytotoxicity occurred. The condensates were not mutagenic without ***S9*** liver homogenates, indicating a requirement for metabolic activation (data not shown). Individual condensates were not mutagenic using the tester strain TA104, with or without ***S9*** (data not shown). Soybean oil was weakly mutagenic, but peanut oil. sesame oil, lard, and canola oil were not under these conditions.

We hypothesized that the condensate mutagenicity was related to linolenic acid content because of previous data showing that mutagenicity could be eradicated with hydrogenation of the oil *(11)* and that linolenic acid is the fatty acid in cooking oil with the greatest number of

Table 1. Mutagenicity of cooking oil condensates: TA98 *Salmonella* mutation assay*

Dose, mg/plate	Chinese rapeseed	Soybean	Peanut	Lard	Canola	Sesame	Linoleic	Linolenic	Erucic
Vehicle†	19 ± 1	23 ± 6	28 ± 5	17 ± 7	26 ± 7	27 ± 5	17 ± 4	24 ± 3	19 ± 2
0.1	42 ± 9‡	23 ± 9	21 ± 5	20 ± 4	22 ± 4	22 ± 4	24 ± 6	85 ± 4‡	24 f 4
0.33	111 ± 16‡	45 ± 7	26 ± 2	22 ± 6	19 ± 3	23 ± S	33 ± 5	415 ± 26$	24 ± 10
1.0	157 ± 10‡	68 ± 8‡	25 ± 3	27 ± 3	30 ± 3	23 ± 4	20 ± 2	29 ± 10	24 f 7
3.33	29 ± 8	15 ± 3	15 ± 3	24 ± 8	24 ± 11	14 ± 8	18 ± 5	10 ± 2	22 ± 3
10.0	44 ± 2	9 ± 4	19 ± 3	18 ± 5	21 ± 3	17 ± 2	12 ± 2	0 f 1	29 ± 6
Positive§	136 ± 11	181 ± 16	147 ± 16	145 ± 25	152 ± 1	150 ± 9	135 ± 10	123 ± 15	183 ± 10

*No. of revertants; mean of triplicates ± SD.
†Vehicle control = dimethyl sulfoxide. 0.1 mL/plate.
‡Positive result (>twofold increase in revertants over the vehicle control)
§Positive control = 2-aminoanthracene, 0.5 mg/plate.

double bonds (n = 3). Further, mutagenic Chinese and nonmutagenic **U.S.** (canola) rapeseed oils have much higher contents of linolenic acid compared with other nonmutagenic oils, such as peanut (9.8%, 11.3%, and 0.6%, respectively [unpublished data]). Our tests indicated that linolenic acid was highly mutagenic (Table 1). Moreover, when linolenic acid was added to the peanut oil before heating, the results became positive. **A** correlation with the number of revertants was found for the concentration of linolenic acid present either in native oils or when added as a supplement in different proportions to peanut oil (Fig. 1; Spearman's rank correlation coefficient $r = .83$; $P = .0004$). In contrast, linoleic acid and erucic acid were not mutagenic (Table 1).

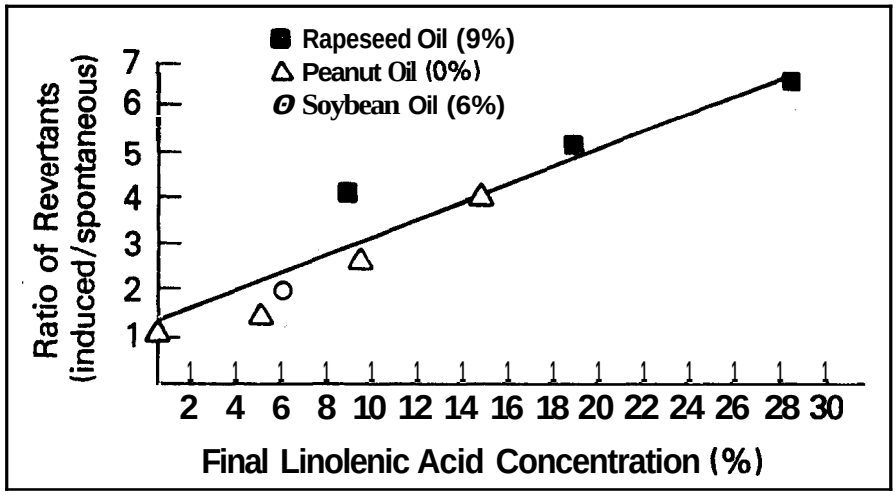

Fig. 1. Dose–response curve showing that the concentration of linolenic acid is correlated with the number of revertants in the *Salmonella* mutation assay ($r = .83$; P = .0004). Oils were tested either alone or with the addition of increasing amounts of linolenic acid. Parentheses indicate starting concentration of linolenic acid in native oils. Data represent the highest number of revertants found for each of the oils tested (see Table 1).

Qualitative analyses of volatile organic compounds from heated Chinese rapeseed, canola, soybean, and peanut oils were undertaken by gas chromatography and mass spectroscopy (Fig. 2). The analysis identified 54 major and minor compounds among the four oils, most of which were present in all oils. There were semiquantitative and quantitative differences in volatile organic compounds emitted from the heated cooking oils. The Chinese rapeseed oil tested here had the highest content of major peaks and substantially more minor peaks. Canola oil was similar, but soybean and peanut oils had substantially less. Quantitatively, a similar pattern was observed for 1,3-butadiene and benzene (Table 2) compared with the semiquantitative differences for total peaks. For all oils, 1,3-butadiene, acetaldehyde, n-pentane, acrolein, propanol, n-hexane, propionaldehyde, and benzene were observed. Of particular note, the emission of 1,3-butadiene and benzene was approximately 22-fold and 12-fold higher, respectively, from heated unrefined Chinese rapeseed oil than from heated peanut oil (Table 2).

Heating the oils in a wok at lower temperatures resulted in qualitatively less volatile organic compounds, as evidenced by much smaller peak heights (data not shown). Quantitatively, compared with Chinese rapeseed oil heated to 275 °C, there were fourfold and 14-fold lower levels of 1,3-butadiene and onefold and sevenfold lower levels of benzene when the oils were heated at **240** °C and **185** °C, respectively (data not shown). Linolenic acid, in contrast, at its boiling point (240 °C) emitted sevenfold higher levels of 1,3-butadiene and 76-fold higher levels of benzene, compared with Chinese rapeseed oil also heated to 240 °C. Linoleic acid, however, emitted only twofold higher levels of 1.3-butadiene and 12-fold higher levels of benzene, compared with the Chinese rapeseed oil (at 240 °C). Erucic acid emitted threefold lower levels of 1,3-butadiene and sixfold lower levels of benzene. The addition of butylated hydroxyanisole (0.1% vol/vol) to Chinese rapeseed oil before heating lowered the emission of total volatile organic compounds and reduced the emissions of 1,3-butadiene by 50% and benzene by 73% (Table 2).

Aldehyde emissions from the cooking oils also were determined (Table 2). In general, Chinese rapeseed oil emitted the most aldehydes, while peanut oil emitted the least. Acrolein was produced from all the heated oils, although there were no appreciable differences among the oils except for peanut oil, which was substantially lower. Linolenic acid produced at least **two** times more acrolein than any oil. There were no appreciable differences in formaldehyde emission among the oils and acids.

Discussion

Our findings, together with carcinogenesis bioassays and epidemiologic studies, suggest that wok cooking with Chinese rapeseed oil may pose a lung cancer risk in Chinese women. We observed that heated cooking oils emit a variety of toxic agents, some of which are known as potential or probable human or laboratory animal carcinogens (*5,14-20*) or mutagens (*14,21,22*), including 1,3-butadiene, benzene, acrolein. formaldehyde, and acetaldehyde. Some of these compounds may cause acute neurologic, respiratory. and dermatologic effects. *n*-Hexane is associated with chronic neurologic effects (23). It is noteworthy that some agents (e.g., acrolein and aldehydes) cause eye irritation. coinciding with the report of eye irritation related to wok cooking and lung cancer (9). Unrefined Chinese cooking oil. which has been associated with lung cancer risk (9) and mutagenicity (*11*), had the greatest amount of volatile decomposition products, but levels were only somewhat higher than **U.S.** canola oil. Peanut oil emitted substantially less.

Our study revealed that condensates of the volatile emissions from Chinese rapeseed oil, soybean oil, and linolenic acid are mutagenic in the *Salmonella* mutation assay. Comparable data from other studies are limited, but volatile emissions from several cooked foods (e.g., beef) have previously been found to be mutagenic *(2425).* as were samples of restaurant kitchen air *(2627).* Furthermore, some studies in western countries indicate

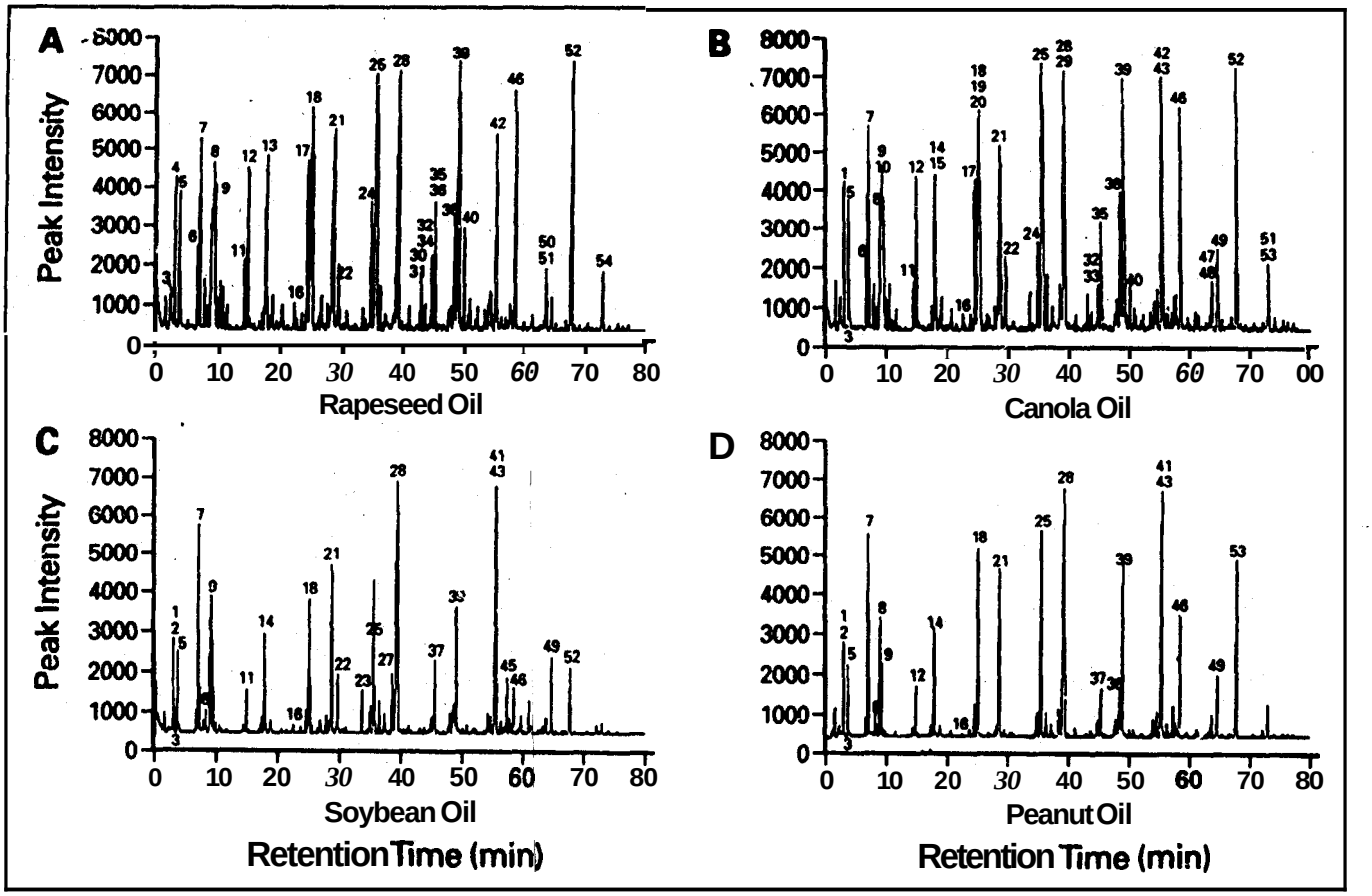

Fig. 2. Gas chromatography and mass spectroscopy analysis of volatile emissions of cooking oils heated in a wok. The cooking temperatures were chosen on the basis of typical cooking temperatures in Shanghai and/or when the oils began to emit smoke. Chinese rapeseed oil (A) and U.S. canola oil (B) were heated at 275 °C. Chinese soybean oil (C) and Chinese peanut oil (D) were heated at 260-265 °C. Smaller peaks. except for 1.3-butadiene and benzene. were not identified. The peaks that were identified are numbered and correspond to n-butane (1), butene isomer (2), 1.3-butadiene (3), I-butene (4), acetaldehyde (5). I-pentene (6), n-pentane (7), acrolein (8). propanol (9). 1.3-pentadiene isomer (10), I-hexene (11), n-hexane (12), *n*-butanol (13), *n*-butanal (14), methyl vinyl ketone (IS). benzene (16), 1-heptene (17), n-heptane (18), C_7H_{12} isomers (19), C_7H_{14} isomers (20), *n*-pentanal (21), 1-pentene-3-ol (22), toluene (23). 1-octene (24), *n*-octane (25), *trans*-4-octene or C_8H_{16} isomer (26). 1-pentanol (27), *n*-hexanal (28), C_8H_{14} isomer (29), cyclopentane and carbaldehyde (30), C_2-alkyl benzene (31), I-nomne (32), C_8H_{12} isomer (33), C_7H_8O isomer (34), *n*-nonane (35), C_9H_{18} isomer (36), 2-hexenal (37), *n*-butylcyclopentane (38). *n*-heptanal (39), C_9H_{16} isomer (40), *trans*-2-heptanal (41). unsaturated hydrocarbons (42), $C_{10}H_{18}$ isomer (43). $C_{11}H_{24}$ isomers (44) octa-1,7-diene-3-ol (45), *n*-octanal (46), 1-decene (47). $C_{11}H_{24}$ isomers (48), *trans*-2-octenal (49), unsaturated hydrocarbons (50), $C_{11}H_{22}$ isomers (51), *n*-nonanal (52). $C_{12}H_{22}$ isomers (53). and unsaturated hydrocarbons (54).

Table 2. Detection of volatile organic compounds in cooking oil emissions

Sample	I. 3-Butadiene*	Benzene*	Formaldehyde, µg/L†	Acetaldehyde. µg/L†	Acrolein. µg/L†
Rapeseed oil	504	2391	71.2	306.9	391.8
Rapeseed oil + buiylated hydroxyanisole, 0.1%	247	663	10.0	40.0	36.0
Canola oil	200	664	30.2	94.6	320.0
Soybean oil	57	450	39.1	112.7	442.7
Peanut oil	23	203	22.8	45.1	49.0
Peanut oil + linolenic acid. 10%	123	626	49.0	147.0	247.0
Peanut oil + linolenic acid. 20%	725	21 200‡	—	—	—
Linolenic acid	3390	184 000‡	43.3	239.0	867.4
Linoleic acid	279	23 300‡	52.3	102.4	286.9
Erucic acid	48	347	—	—	—

*Calculated using National Institute of Standards and Technology reference standard: expressed as ng/L.
† — = not tested.
‡Estimated concentration: exceeds highest standard.

that restaurant cooks have elevated risks of lung cancer (*28*,*29*), even when risks are adjusted for tobacco use.

Several lines of evidence suggest an important role for linolenic acid. Specifically, mutagenicity was associated with linolenic acid concentration. and the mutagenicity was reduced by hydrogenation or by adding butylated hydroxy-

anisole to the oil before cooking. Also, heating pure linolenic acid resulted in the greatest production of mutagenic, volatile decomposition products. Linolenic acid is known to cause bad odors (*30*), which can be reduced by hydrogenation or the addition of antioxidants, and might explain the customary use of high-temperature cooking (275-280 °C) in Shanghai. However, the presence of linolenic acid does not fully explain the mutagenicity results because Chinese rapeseed oil is mutagenic, while U.S. canola oil is not, although they have similar linolenic acid contents. Furthermore, soybean oil is weakly mutagenic even though it has less linolenic acid than canola oil. We suspected that the erucic acid content or other characteristics of Chinese rapeseed plants, including additives or refining processes, may be involved, although none of these factors consistently explained the effects when we tested different lots of refined Chinese rapeseed oil or linolenic acid (data not shown). Therefore, the most plausible explanation for these findings is that canola oil contains specific inhibitors to oxidation or that Chinese rapeseed oil contains promutagenic compounds in addition to linolenic acid.

Among the chemicals detected in the cooking oil emissions, 1,3-butadiene has been classified as a probable (group 2A) human carcinogen by the International Agency for Research on Cancer (*5,31*) and a suspected human carcinogen by the American Conference of Governmental Industrial Hygienists (20). At exposures as low as 6.5 ppm, this compound is a lung carcinogen in laboratory mice (*15,16,19*), although rats are typically resistant (*32*). The interspecies variation is likely related to differences in metabolic activation and detoxification (*33-35*). Epidemiologic evidence to date has not documented a lung cancer risk related to 1.3-butadiene exposure (*36*), although some studies suggest an excess of hematologic malignancies (*17,37*). Other volatile decomposition products of the cooking oils may contribute to lung cancer risks. While benzene is an established human leukemogen (*14*). its association with lung cancer is not clear, although an increased risk has been reported in benzene-exposed Chinese workers (*18*) and experimental studies also indicate that benzene may be a lung carcinogen (38). Some studies (*39-42*) have related formaldehyde to lung cancer, but the evidence is inconclusive. Acrolein is mutagenic in a number of different test systems (*14,21,22*), but human studies are lacking.

Some of the chemicals detected in cooking-oil emissions are also evident in cigarette smoke. In particular, 1,3-butadiene (*43*) has been reported at levels ranging from 19 µg to 75 µg per cigarette in mainstream smoke, depending on whether the cigarette smoke is filtered. The amount of 1,3-butadiene generated from heating Chinese rapeseed oil under the conditions reported here, however, is approximately 0.6 µg. Therefore, for 1,3-butadiene and also for benzene, acrolein, and the other detectable volatile products, the lifetime exposure from wok cooking appears to be substantially less than that for a heavy smoker. However, these calculations may underestimate the exposure and risk because they do not sufficiently consider peak exposures during the initial generation of volatile compounds.

This study suggests several methods that could reduce exposures to volatile organic compounds and mutagenic substances from heated cooking oils. These methods include cooking at lower temperatures, addition of antioxidants, hydrogenation during refining, and increasing ventilation during cooking. Further studies are needed to clarify the relationship of cooking oil vapors, other environmental exposures, and genetic susceptibilities to lung cancer in Chinese populations. Studies also are needed in the United States that will evaluate a lung cancer risk associated with exposure to cooking oils, especially in different ethnic and racial groups, including Americans of Chinese descent. Finally, the effects of cooking specific foods and the volatilization of other potential mutagens and carcinogens should be investigated.

References

(1) 'Cancer incidence in five continents. Volume V. IARC Sci Publ 88:1-970, 1987

(2) Jin F, Devesa SS, Zheng W, et al: Cancer incidence trends in urban Shanghai, 1972-1989. Int J Cancer 53:764-770, 1993

(3) Fraumeni JF Jr, Mason TJ: Cancer mortality among Chinese Americans, 1950-69. J Natl Cancer Inst 52,659-665, 1974

(4) MacLennan R, Da Costa J. Day NE, et al: Risk factors for lung cancer in Singapore Chinese, a population with high female incidence rates. Int J Cancer 20:854-860, 1977

(5) International Agency for Research on Cancer: Cancer Incidence in Five Continents. vol VI. Lyon: IARC, 1992, pp 1-1080

(6) Mumford JL, He XZ, Chapman RS, et al: Lung cancer and indoor air pollution in Xuan Wei, China. Science 235:217-220, 1987

(7) Hinds MW, Stemmermann GN, Yang HY, et al: Differences in lung cancer risk from smoking among Japanese, Chinese and Hawaiian women in Hawaii. Int J Cancer 27:297-302, 1981

(8) Gao YT, Blot WJ, Zheng W. et al: Lung cancer and smoking in Shanghai. Int J Epidemiol 17:277-280, 1988

(9) Gao YT, Blot WJ. Zheng W. et al: Lung cancer among Chinese women. Int J Cancer 40604-609,1987

(10) Wu-Williams AH, Dai XD, Blot W, et al: Lung cancer among women in north-east China. Br J Cancer 62:982-987, 1990

(11) Qu YH. Xu GX, Zhou JZ, et al: Genotoxicity of heated cooking oil vapors. Mutat Res 298:105-111, 1992

(12) Maron DM. Ames BN: Revised methods for the *Salmonella* mutagenicity test. Mutat Res 113:173-215, 1983

(13) Eight Peak Index of Mass Spectra. Mass Spectra Data Center, I974

(14) International Agency for Research on Cancer: IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Overall Evaluations of Carcinogenicity: an Updating of IARC Monographs, vols 1-42. Lyon: IARC. 1987

(15) Melnick RL, Huff J. Matanoski GM: Carcinogenicity of 1,3-butadiene [letter] [see comment citations in Medline]. Lancet 340:724-725, 1992

(16) Melnick RL. Huff J: 1,3-Butadiene: toxicity and carcinogenicity in laboratory animals and in humans. Rev Environ Contam Toxicol 124:111-144, 1992

(17) Landrigan PJ: Critical assessment of epidemiologic studies on the human carcinogenicity of 1,3-butadiene. Environ Health Perspect 86:143-147, 1990

(18) Yin SN. Hayes RB. Linet MS: A cohort study of cancer among benzene-exposed workers in China: overall results. Am J Ind Med. In press

(19) Huff JE. Melnick RL. Solleveld HA, et al: Multiple organ carcinogenicity of 1,3-butadiene in B6C3F1 mice after 60 weeks of inhalation exposure. Science 227:548-549, 1985

(20) 1993-1994 Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, Ohio: Am Conf Govt Indust Hygienists 1993, pp 1-124

(21) Curren RD. Yang LL, Conklin PM. et al: Mutagenesis of xeroderma pigmentosum fibroblasts by acrolein. Mutat Res 209: 17-22.1988

(22) Wilson VL. Foiles PG, Chung FL. et al: Detection of acrolein and crotonaidehyde DNA adducts in cultured human cells and canine peripheral blood lymphocytes by 32P-postlabeling and nucleotide chromatography. Carcinogenesis12:1483-1490, 1991

(23) Section four: Chemical compounds II. *In* Hamilton and Hardy's Industrial Toxicology, 4th ed (Finkel AJ, ed). Boston: Wright-PSG. 1983, pp 197-237

(24) Rappaport SM. McCartney MC. Wei ET: Volatilization of mutagens from beef during cooking. Cancer Lett 8:139-145, 1979

(25) Lofroth G, Stensman C, Brandhorst-Satrkom M: Indoor sources of mutagenic aerosol par-

ticulate matter: smoking, cooking and incense burning. Mutat Res 261:21-28, 1991
(26) Gere A: Decrease in essential fatty acid content of edible fate during the frying process. Z Ernahrungswiss 21:191-201, 1982
(27) Teschke K. Hertzman C. Van Netten C. et al: Potential exposure of cooks to airborne mutagens and carcinogens. Environ Res 50:296-308, 1989
(28) Coggon D, Pannett B. Osmond C, et al: A survey of cancer and occupation in young and middle aged men. I. Cancers of the respiratory tract. Br J Ind Med 43:332-338, 1986
(29) Dubrow R, Wegman DH: Cancer and occupation in Massachusetts: a death certificate study. Am J Ind Med 6207-230.1984
(30) Mounts T L Odor considerations in the use of frying oils. J Am Oil Chem Soc 56:659-663, 1979
(31) IARC Working Group on the Evaluation of Carcinogenic Risks to Humans: Occupational Exposures to Mists and Vapours From Strong Inorganic Acids; and Other Industrial Chemicals, vol 54. Lyon: IARC. 1992. pp 1-336
(32) Owen PE, Glaister JR, Gaunt IF. et al: Inhalation toxicity studies with 1.3-butadiene. 3. Two year toxicity/carcinogenicity study in rats. Am Ind Hyg Assoc J 48:407-413,1987
(33) Kohn MC, Melnick R L Species differences in the production and clearance of 1.3-butadiene metabolites: a mechanistic model indicates predominantly physiological, not biochemical. control. Carcinogenesis 14:619-628, 1993
(34) Csanady GA. Guengerich FP. Bond J A Comparison of the biotransformation of 1.3-bumdiene and its metabolite, butadiene monoepoxide, by hepatic and pulmonary tissues from humans, rats and mice [published erratum appears in Carcinogenesis 14:784, 1993]. Carcinogenesis 13:1143-1153, 1992
(35) Sabourin PJ, Burka LT. Bechtold WE. et al: Species differences in urinary butadiene metabolites: identification of 1,2-dihydroxy-4-(N-acetylcysteinyl)butane, a novel metabolite of butadiene. Carcinogenesis 13:1633-1638, I992
(36) Matanoski GM. Santos-Burga C. Schwartz L: Mortality of a cohort of workers in the styrene-butadiene polymer manufacturing industry (1943-1982). Environ Health Perspect 86:107-117, 1990
(37) Santos-Burga C, Matanoski GM, Zeger S, et al: Lymphohematopoietic cancer in styrene-butadiene polymerization workers [see comment citation in Medline]. Am J Epidemiol 136:843-854, 1992
(38) Huff JE, Haseman JK. DeMarini DM. et al: Multiple-site carcinogenicity of benzene in Fischer 344 rats and B6C3F1 mice. Environ Health Perspect 82:125-163, 1989
(39) Gardner MJ. Pannett B, Winter PD. ei al: A cohort study of workers exposed to formaldehyde in the British chemical industry: an update. Br J Ind Med 50:827-834, 1993
(40) Stayner LT. Elliott L, Blade L, et al: A retrospective cohort mortality study of workers exposed to formaldehyde in the garment industry. Am J Ind Med 13:667-681, 1988
(41) Blair A, Stewart P, O'Berg M. et al: Mortality among industrial workers exposed to formaldehyde [see comment citation in Medline]. J Natl Cancer Inst 76:1071-1084, 1986
(42) Bertazzi PA, Pesatori AC. Radice L, et al: Exposure to formaldehyde and cancer mortality in a cohort of workers producing resins. Scand J Work Environ Health 12:461-468, 1986
(43) Brunnemann KD, Kagan MR, Cox JE. et al: Analysis of 1.3-butadiene and other selected gas-phase components in cigarette mainstream and sidestream smoke by gas chromatography-mass selective detection. Carcinogenesis 11:1863-1868, 1990

Notes

We thank Dr. Richard Sans for his expertise in the *Salmonella* mutation assay. Ms. Elise Bowman-for assistance in the preparation of cooking oil condensates, and Ms. Dorothea Dudek for editorial assistance.

Manuscript received November 11, 1994; revised March 10, 1995: accepted March 27. 1995.