Chinese "Herbal" Cigarettes Are as Carcinogenic and Addictive as Regular Cigarettes

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Abstract

Objective: **To examine the Chinese tobacco industry's claim that herbal cigarettes are less harmful than regular cigarettes.**

Methods: **The study design was a cross-sectional survey. One hundred thirty-five herbal cigarette smokers and 143 regular smokers from one city in China completed a questionnaire on smoking behavior and provided a urine sample. The main outcome measures were cotinine and *trans*-3′-hydroxycotinine in all samples, and polycyclic aromatic hydrocarbon metabolites (PAH; 1-hydroxypyrene, naphthols, hydroxyfluorenes, and hydroxyphnanthrenes) and the tobacco specific nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-butanol (NNAL) and NNAL-glucuronide in randomly selected 98 samples (47 from the herbal smokers' group and 51 from the regular smokers' group). Values were normalized by creatinine to correct for possible variability introduced by dilution or concentration of the urine.**

Results: **Health concern was among the main reasons that smokers switched to herbal cigarettes from regular cigarettes. Smokers reported increased consumption after switching to herbal cigarettes from regular cigarettes. For all the four markers analyzed (cotinine, *trans*-3′-hydroxycotinine, total NNAL, and total PAHs), we observed no significant difference in the levels ($P = 0.169$, $P = 0.146$, $P = 0.171$, and $P = 0.554$, respectively) between smokers of herbal cigarettes and smokers of regular cigarettes. Both total NNAL and total PAHs were significantly correlated with cotinine and *trans*-3′-hydroxycotinine ($P < 0.001$ for all four correlations).**

Conclusions: **Our findings showed that herbal cigarettes did not deliver less carcinogens than regular cigarettes. The public needs to be aware of this fact, and the Chinese tobacco industry should avoid misleading the public when promoting herbal cigarettes as safer products.**

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Introduction

In Western countries, the term "herbal cigarettes" often refers to cigarettes that are made of a mixture of different herbs and that contain no tobacco or nicotine. In China, the China National Tobacco Corporation began in the late 1970s to develop tobacco cigarettes that also contain Chinese medicinal herbs, which it also calls "herbal cigarettes" (1). In the manufacture of these herbal cigarettes, extracts of Chinese medicinal herbs are mixed with or sprayed on leaf tobacco (2) A host of Chinese herbs have been used as cigarette additives, from the commonly known Ginseng to much less known ones such as Jiaogulan (2).[5] Most of these herbs are common ingredients in traditional Chinese medicine and are used for therapeutic purposes or as dietary supplements. Since the first herbal cigarette brand in China, Changle, was marketed by the Beijing Cigarette Factory (affiliated with the China National Tobacco Corporation) in 1979 (2), many herbal cigarette brands have been developed and marketed in China. In the 1990s, herbal cigarettes began to gain popularity in China. The two brands that have achieved the most sales success in China were Jinsheng and Wuyeshen, which sold more than 20 billion cigarettes in 2008, accounting for more than 1% of all the cigarettes produced in China.[6,7,8] [For comparison, Lucky Strike had a 1.1% share of the U.S. market in 1965 (3) and Virginia Slims had 2.6% in 2000.[9]] Most herbal brands in China, including Jinsheng and Wuyeshen, have the same machine-determined yield of tar as regular cigarettes (15 mg).

Although the market share of herbal cigarettes is still relatively small in China, herbal brands are quickly

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expanding their market there and into the global market. Jinsheng's export markets in 2008 included the Philippines, Singapore, Indonesia, Malaysia, Cambodia, Myanmar, Canada, and Taiwan.[10] In 2003, Jinsheng was so successful in the Philippines that it accounted for 90% of imported cigarettes in Manila.[11] Zhongnanhai, the first herbal brand with a low-tar rating (at 1, 3, 5, 6, and 8 mg), has achieved considerable success in Japan and can also be found in the markets of the United States, Singapore, Malaysia, Taiwan, Hong Kong, and Macao.[12]

Many claims of health benefits for smokers of herbal cigarettes were made by the Chinese tobacco industry. For example, Jinsheng claims a host of benefits, including less coughing and sputum, nourishment of the kidneys and the lungs, and boosting of sexual drive.[13] The health claims Jinsheng made can also be conveniently found in a card inserted in some cigarette packages.[13] Wuyeshen claims >60% reduction in cancer-causing nitrosamines, including tobacco-specific nitrosamines, and the inhibition of benzo(*a*)pyrene carcinogenicity.[14]

Several studies have attempted to evaluate the health benefits of smoking herbal cigarettes by either measuring the yields of tobacco-specific nitrosamines in mainstream tobacco smoke with smoking machine or cellular response to tobacco smoke in *in vitro* experiments (4-7). No studies have directly measured the levels of carcinogens from herbal cigarettes in smokers' bodies. The present study examines, for the first time, the level of metabolites of several key tobacco constituents in herbal cigarette smokers' urine. In contrast to the claims made by the Chinese tobacco companies that herbal cigarettes are safer than regular cigarettes, we find no difference in the levels of nicotine or carcinogens in smokers' bodies between these two types of cigarettes.

Materials and Methods

Sampling Protocol. All subjects were smokers smoking cigarettes of Chinese brands living in one city in China. One hundred eighty herbal cigarette smokers and 180 regular cigarette smokers were recruited through three district community centers. (Because all herbal brands are still very localized in China currently and all of the herbal smokers in our study smoked the same brand that was produced locally, we chose not to disclose the name of brand to protect our local collaborators from the retaliation by the local tobacco company.) Regular cigarette smokers smoked cigarettes with 14 or 15 mg machine-measured tar yields per cigarette. Herbal cigarette smokers were smokers of a local popular herbal brand with 15 mg of machine-measured tar yield. Several inclusion criteria were applied: (*a*) Subjects had to be male smokers (because few women smoke in China); (*b*) subjects had to be between the ages of 18 and 65 y, with no diagnosis of cancer, heart disease, or major respiratory diseases; (*c*) subjects had to smoke on average at least 5 cigarettes per day; (*d*) subjects had to have been smoking the current brand for at least 3 mo; and (*e*) when brand-mixing was present, smokers had to smoke either regular or herbal brands at least 90% of the time.

Each subject signed a consent form and completed a questionnaire. At the end of the questionnaire, a 25-mL urine sample was collected.

The protocol was approved by the University of California San Francisco Committee on Human Research and the China Center for Disease Control and Prevention Committee on Human Subjects.

Laboratory Analysis of Tobacco Smoke Compounds in Smokers' Urine. The urine samples were frozen and shipped to San Francisco General Hospital for analysis in the Tobacco Biomarker Core Facility of the UCSF Helen Diller Family Comprehensive Cancer Center. Cotinine and *trans*-3′-hydroxycotinine, both metabolites of nicotine; 4-(methylnitrosamino)-1-(3-pyridyl)-butanol (NNAL) and NNAL-glucuronide, metabolites of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone, a tobacco specific nitrosamine and one of the most potent carcinogens in tobacco smoke (8); and metabolites of polycyclic aromatic hydrocarbons (PAH), which represent a class of combustion products that include a number of carcinogens, were measured. All analytes were measured using liquid chromatography: cotinine and *trans*-3′-hydroxycotinine; NNAL and NNAL-glucuronide, reported as total NNAL (9); and metabolites of the PAHs, including 1-hydroxypyrene, naphthols, hydroxyfluorenes, and hydroxyphenanthrenes, reported as total PAHs (10). Concentrations of cotinine, *trans*-3′-hydroxycotinine, total PAHs, and total NNALs were normalized by urine creatinine to correct for variations due to dilution or concentration of urine. Per-cigarette levels of normalized total PAHs, total NNAL, cotinine, and *trans*-3′-hydroxycotinine were estimated by dividing the concentrations by the number of cigarettes the subject reported smoking per day.

Every sample was analyzed for the levels of cotinine and *trans*-3′-hydroxycotinine (for a total of 360 samples). A random sample of 60 samples from each group of smokers (for a total of 120 samples) was analyzed for PAHs and NNAL. Nine subjects were dropped because of incomplete demographic information in the questionnaire. Three samples were excluded from the results due to abnormally low levels of creatinine. Twenty-seven subjects who claimed to smoke herbal cigarettes and 19 who claimed to smoker regular cigarettes were dropped from the study because their urine samples indicated cotinine levels (< 50 μg/L; ref. 11) of a typical nonsmoker. Seven smokers of regular cigarettes were dropped from the study because the main brand they smoked had a tar level of light cigarettes (<14 mg). In sum, the results reported in this article are based on 278 samples for cotinine and *trans*-3′-hydroxycotinine and 93 samples for PAHs and NNAL.

Statistical Analysis. Survey questions were analyzed using χ^2 test. Levels of biomarkers were analyzed using

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Table 1. Demographic characteristics of the subjects

	Smokers of herbal cigarettes	Smokers of regular cigarettes	*P*
Sample size, *n*	135	143	
Age (y), median (IQR)	48 (38-56)	48 (39-54)	0.567*
Cigarettes per day on average			
Median (IQR)	20 (15-20)	20 (15-20)	0.962*
Education, *n* (%)			
Junior high school and below	70 (52)	77 (54)	
Secondary technical school	41 (30)	42 (29)	
Junior college	20 (15)	18 (12)	
College and above	4 (3)	6 (4)	0.621†
Employment status, *n* (%)			
Employed	81 (60)	94 (66)	
Unemployed	54 (40)	49 (34)	0.979†
Monthly income (yuan), *n* (%)			
<500	19 (14)	30 (21)	
500-999	40 (30)	41 (29)	
1,000-1,999	58 (43)	52 (36)	
2,000-4,999	17 (12)	18 (12)	
≥5,000	1 (1)	2 (1)	0.567†
Change in daily consumption after switching from regular cigarettes (14-15 mg) to herbal cigarettes, %			
Increased daily consumption	47	—	
Decreased daily consumption	30	—	
No change in daily consumption	23	—	
Cotinine and *trans*-3′-hydroxycotinine, median (IQR)			
Sample size	134	142	
Cotinine (μg/mg creatinine)	12.8 (5.57-22.2)	14.3 (8.00-23.7)	0.169*
Cotinine (ng/mL)	1,142 (476-2,175)	1,538 (666-2,463)	0.047*
trans-3′-Hydroxycotinine (μg/mg creatinine)	33.0 (9.88-61.4)	41.1 (15.6-65.7)	0.146*
trans-3′-Hydroxycotinine (ng/mL)	2,799 (732-6,346)	3,732 (1,518-7,230)	0.058*
Total PAHs and total NNAL, median (IQR)			
Sample size	44	49	
Total PAHs (pmol/mg creatinine)	172 (87.1-245)	159 (126-225)	0.554*
Total NNAL (pmol/mg creatinine)	0.454 (0.256-0.862)	0.410 (0.291-0.649)	0.171*

*Based on Mann-Whitney signed rank test.
†Based on χ^2 test.

a Mann-Whitney rank sum test. Calculations were done with Stata 10.1.

Results

Demographic information for the subjects is presented in Table 1. Herbal cigarette smokers and regular cigarette smokers did not differ in age, number of cigarettes smoked per day, educational level, employment status, or income.

Urine Levels of Cotinine, *trans*-3′-Hydroxycotinine, Total PAHs, and Total NNAL. Adjusted for creatinine, neither the levels of cotinine ($P = 0.169$) nor *trans*-3′-hydroxycotinine ($P = 0.146$) were significantly different between herbal smokers and regular smokers (Table 1; Fig. 1). [Unadjusted cotinine and *trans*-3′-hydroxycotinine (ng/mL) were lower in herbal cigarette smokers; $P = 0.047$ and $P = 0.058$, respectively.] The levels of total PAHs ($P = 0.554$) and total NNAL were not statistically different between the two groups ($P = 0.171$; Table 1; Figs. 2 and 3).

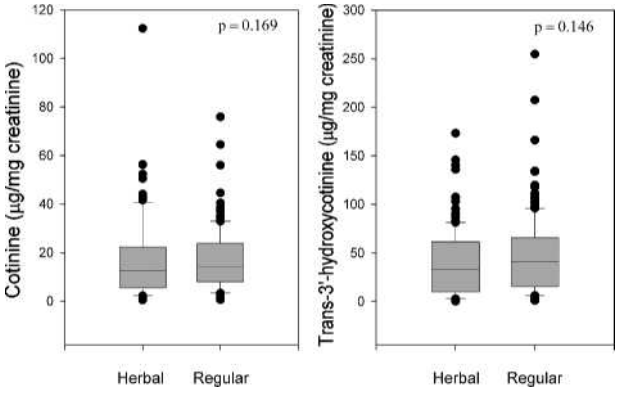

Figure 1. There is no significant difference in the levels of cotinine and *trans*-3′-hydroxycotinine (normalized by creatinine to account for differences in urine concentration) between herbal smokers and regular smokers.

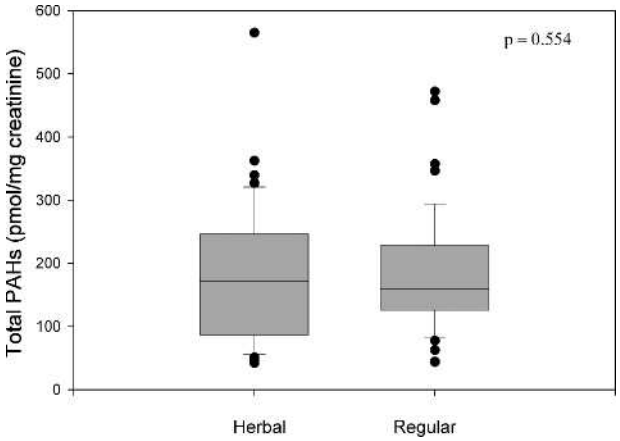

Figure 2. There is no significant difference in PAHs between herbal smokers and regular smokers.

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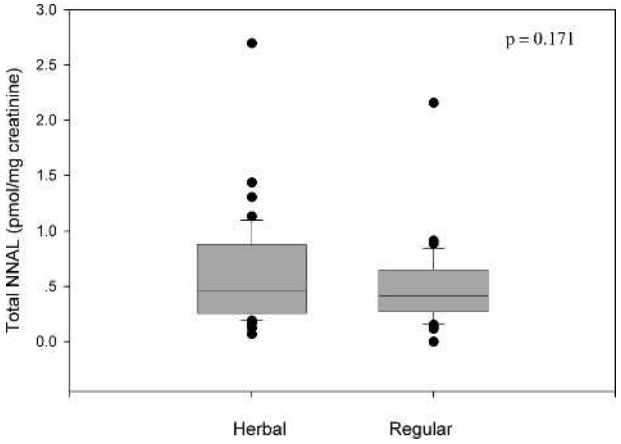

Figure 3. There is no significant difference in NNAL between herbal smokers and regular smokers.

Results per cigarette showed the same patterns (details not shown). Both NNAL and PAHs significantly correlated with cotinine (NNAL: $r_s = 0.535$, $P < 0.001$; PAHs: $r_s = 0.668$, $P < 0.001$) and *trans*-3′-hydroxycotinine (NNAL: $r_s = 0.539$, $P < 0.001$; PAHs: $r_s = 0.674$, $P < 0.001$; scatter plots of cotinine versus NNAL and PAHs shown in Fig. 4). Using a multiple regression model (results not shown), the relationships did not depend on the type of cigarettes the subjects smoked.

Cigarette Switching. There was no significant difference in daily cigarette consumption between regular and herbal smokers (Table 1). Of the 135 herbal smokers, 106 (86%) had switched from regular cigarettes, a median of 6.25 years earlier [interquartile range (IQR), 4-10 years]. Smokers reported increased numbers of cigarettes smoked per day after switching to herbal cigarettes from regular cigarettes (Table 1). The most often cited reason for switching to herbal cigarettes was "better taste" compared with regular cigarettes (47%). Health concern was the second most popular reason reported for switching (24%; Table 2). "Convenience of purchase" and "support for a local product and business" accounted for 21% and 15% of the responses, respectively. There are two opposite concerns about the price: Some smokers switched because the current brand was more affordable, whereas others switched because the current brand was more expensive and "good for face" when offering cigarette to others, which is a common social etiquette in China. Additionally, "no fake cigarettes" was reported by 4% of the respondents as the reason for switching to herbal cigarettes.

Discussion

The present study is the first that examines the level of tobacco toxins in the bodies of smokers of Chinese herbal cigarettes. We examined the major metabolites of nicotine and two groups of tobacco carcinogens among smokers of herbal cigarettes. There was no detectable difference in the levels of nicotine or total NNAL, the metabolite of the main tobacco specific carcinogen 4-(methylnitrosamino)- 1-(3-pyridyl)-1-butanone, or PAHs between herbal cigarette smokers and regular cigarette smokers.

Smokers of herbal cigarettes had lower concentrations of unadjusted cotinine and *trans*-3′-hydroxycotinine in the urine, but not after normalizing for creatinine. This result may suggest slightly lower intake of nicotine from their cigarettes or more concentrated urine among herbal cigarette smokers. The reason for lower nicotine is unclear because we did not measure the nicotine content of the various types of cigarettes. The primary toxicity of nicotine is sustaining addiction, and it is doubtful that very small differences in nicotine exposure, as were seen in our study, would have any meaningful effect on the addiction potential of the cigarettes. In any event, measures for tobacco smoke carcinogen biomarkers show no evidence whatsoever of lower exposure in herbal cigarette smokers, suggesting no less cancer risk.

Although our results show that herbal cigarette smokers have similar levels of carcinogens in their bodies as regular cigarette smokers, we could not test the industry claim that the herbal additives inhibit the toxicity of these carcinogens. We could not locate any published studies that examined or supported such claims.

We found significant correlations between total NNAL or total PAHs and the metabolites of nicotine (cotinine and *trans*-3′-hydroxycotinine). The correlations persisted after stratifying for the type of cigarette smoked. Our findings support previous research that NNAL and cotinine are significantly correlated among smokers (12, 13). This result suggests that cotinine and *trans*-3′-hydroxycotinine in smokers' urine are indicative of the levels of total NNAL and total PAHs in Chinese herbal and regular smokers due to smoking.

Herbal smokers who switched to herbal cigarettes from regular cigarettes reported increased cigarette consumption after switching. Because of the cross-sectional design, the current study was not able to examine the effect of this increased consumption on the nicotine and carcinogen intake from tobacco smoke. It would be of interest for future studies, especially with short-term or long-term switching experimental designs, to examine whether it was the health messages and/or the herbal additives that triggered this increased consumption.

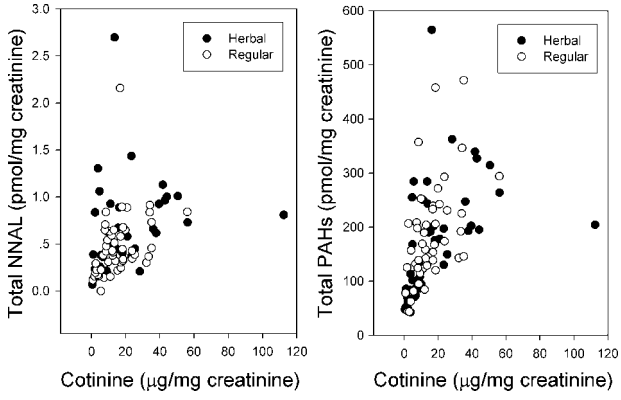

Figure 4. Scatter plots of cotinine versus total NNAL ($r_s = 0.535$, $P < 0.001$) and total PAHs ($r_s = 0.668$, $P < 0.001$) show that higher levels of cotinine are associated with higher levels of carcinogens.

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Table 2. Reasons for herbal cigarette smokers to switch from regular cigarettes (14-15 mg tar) to current herbal brands

Ranking of reasons	Specific reasons	Response, *n* (%)
1	Better taste	50 (47)
2	Health concerns	26 (24)
3	Convenience of purchase	22 (21)
4	Support for local product and business	15 (15)
5	Price	10 (9)
6	No fake cigarettes of current brand	4 (4)

NOTE: Of 135 subjects who smoked herbal cigarettes, 106 answered this multiple-choice question. Percentages do not add up to 100% because respondents were allowed to report more than one reason.

Many of the herbal constituents in herbal cigarettes present therapeutic benefits if used alone (generally taken orally, rather than burned and smoked). When burned with processed tobacco and inhaled, these herbal constituents are likely to undergo complex physical and chemical changes. Of the three main herbal brands in China, Wuyeshen, Jinsheng, and Zhongnanhai, we did not find any literature evaluating the health benefits of Jinsheng and Zhongnanhai. Three studies examined the safety claims of Wuyeshen (5-7). One study found reduction of tobacco-specific nitrosamines in mainstream smoke compared with regular cigarettes (7). The other two studies found lower toxicologic effects from test animals smoking Wuyenshen and reduced deaths in mouse embryonic cells and human endothelial cells in *in vitro* experiments (4-6). None of these studies were conducted by independent researchers: one was by a researcher from the tobacco company that manufactured Wuyeshen (7), and the others by researchers with close ties with the tobacco industry (5, 6). A full independent evaluation of the final products, which is yet to be undertaken, would be necessary before any conclusion can be reached to support claims of therapeutic effects of herbal cigarettes.

The marketing of herbal cigarettes as safer products by the Chinese tobacco industry, although unfounded, has been effective; we found health concern to be the second most reported reason for smokers to switch to herbal cigarettes (Table 2).

In 2001, Jinsheng and Zhongnanhai were among the 36 most prestigious brands selected by the China National Tobacco Corporation out of hundreds of brands in China.[15] With a strong foothold in several provinces in China, several herbal brands are being exported to Japan, Korea, countries in Southeast Asia, and North America (1).[9,12] Because of the health benefits the marketing implies and the fact that smokers in many of these countries are more health conscious, herbal cigarettes are, albeit slowly, gaining popularity in these countries. Local regulatory agencies should be aware of the unsubstantiated health claims and take measures to restrict the marketing of herbal cigarettes.

Disclosure of Potential Conflicts of Interest

N. Benowitz has testified as an expert witness for the plaintiffs on issues surrounding nicotine addiction in several lawsuits against the tobacco industry. The other authors have nothing to disclose.

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