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The Protective Effect of Ginseng and Aloe Extract against Cigarette Smoke-induced Hepatotoxicity

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ABSTRACT : *The preventive effects of ginseng and aloe extract on cigarette smoke-induced hepatotoxicity to Spague-Dawley rats were investigated. The experimental rats were exposed smoke by inhalation for 5 weeks, 3 times per day, and 15 minutes each time. Also ginseng and aloe extract (Group G+A), aloe (Group A) or ginseng (Group G) were administered to each group, but the positive control rats (Group C) were exposed smoke without any other special treatments. Group C showed decreased food intake and increased water consumption. Also the reduction of body weight and the increase in serum-AST, ALT, triglyceride and alkaline phosphatase were observed. The relative liver weights of group C were increased and the hepatic parenchyma revealed light brownish red grossly. On histopathologic observation, the hepatocytes of group C animals exhibited diffuse swelling which narrowed the sinusoidal lumen and disarrayed the hepatic cord-like arrangement. Diffuse necrosis of the hepatocytes was also observed. However, degeneration and necrosis of the hepatocytes were milder in group G+A. In the case of group A, the damage was moderate, while the group G showed marginal improvement from group C. Electronmicroscopically, peroxisome increased and mitochodria decreased in group C. Various hepatic damages related to smoking in group C revealed recovering tendency in group G+A. This study indicated that daily administration of ginseng and aloe could decrease and even prevent cigarette smoke-induced hepatotoxicity.*

Key Words : *Cigarette smoke, Ginseng, Aloe, Hepatotoxicity*

I. INTRODUCTION

There are numerous investigations on the effects of cigarette smoke to the respiratory, circulatory, digestive and nervous system (Astrup *et al.*, 1969; Clark, 1990; Diana *et al.*,1990; Graziano, 1984; Hoffman *et al.*,1990; Le Bouffant *et al.*, 1989; Rim, 1979; Sohn *et al.*, 1993). Among them, its role of carcinogenesis were studied intensively past 3 dacades (Reddy, 1990). Also, the combination of cigarette smoke and hazardous pollutant, like asbestos, showed a synergistic increase in the incidence of lung cancer. Those studies on smoking are warning its harmfulness to smokers.

Smoking regulation is a growing interesting issue with public-health dimensions because smoking is regarded as pan-social stressor to smokers and even non-smokers. Currently, cigarette consumption has increased in juveniles and women in Korea, although social attitudes begin to change slowly as smoking's harmful effects become better understood.

For thousands of years, ginseng has been used for oriental medicine with great success, though lacking a thorough understanding of its acting mechanism. It is the most valued herb and is widely used as a tonic in Korea and oriental countries. Ginseng contains at least seven differnt saponins: Rb2Rc, Rb3, Re, Rd, Rg2, and 20-glucoginsenosaponin-Rf (Han, 1986; Kim, 1990; Oura, 1975). Recent analysis showed that the most important nonsaponin component of ginseng is the antioxidant which has been shown to be the principle in improving antiaging effects (Jang, 1993; Shim, 1976). There are quiet long history of aloe used as a general remedy. The herb contains several aloin, and its derivative including alomicin, aloenin and aloesin, and saponin(Max, 1979; Reynolds, 1982; Salisburg, 1972).

Despite the wide use, there has been little research on the concerned or preventive effect of herbal stuff to cigarette-smoking toxicity. This

study was designed to assess the effects of Ginseng and/or aloe administration to cigarette smoking exposed animals

II. MATERIALS AND METHODS

1. Animals

Three-week-old Sprague Dawley rats, both sex, were purchased from Laboratory Animal Center, Bio-Safety Research Institute, Chonbuk National University, and housed in poly-propylene cages on sawdust bedding (β-chip) with commercial rodent chow pellet (Je-il) available ad libitum. The animals were allowed to acclimate for 1 week prior to initiation of the experiment and observed at least daily for clincal signs and body condition. Also food and water or the extract consumption were measured.

2. Cigarette and Extracts

The cigarette, Eighty-eight, and the ginseng extract were produced and supplied by Korea Tobacco and Ginseng Corporation. Aloe vera extract was assayed by Institute of Kim Jeong Moon Aloe according to freeze-drying method.

3. Treatment of Animals

Rats were randomly allotted into 5 group; nonsmoke-exposed group (Group N), smoke-exposed group (Group C), smoke-exposed and ginseng administered group (Group G), smoke-exposed and aloe administered group (Group A), smoke-exposed and ginseng-aloe administered group (Group G+A). Each group has 10 rats, both female and male, respectively. Extracts of Ginseng (50 mg/kg B.W./day) and/or aloe (15 mg/kg B.W./day) mixed in drinking water were administered for 5 weeks. All animals of each smoke-exposed group were inhaled to the smoke for 15 minutes and three times per day for 5 weeks at a smoking chamber (19x52x69cm) which was manufactured by this Institute. On last day of experiment, rats were euthanized. Ether was used to induce anesthesia for collection of blood from the abdominal vena cava as well as for euthanasia.

4. Blood Chemistry

Serum samples were analyzed using a blood autoanalyzer (Hitachi 747) for the following parameters: alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), cholesterol, triglyceride, glucose, total protein, bilirubin, blood urea nitrogen (BUN), creatinine, albumin, high density lipoprotein.

5. Pathology

After euthanasia, animals were immediately necropsied and body and liver weights were recorded. Samples from the liver were fixed in 10 % neutral buffered formalin, then processed routinely, sectioned at 5 microns, stained with hematoxylin and eosin, and examined by light microscope. Some tissues were minced into 1 mm cubes and fixed in glutaraldehyde, then processed routinely for electronmicroscopy. The sections were stained with uranyl acetate and lead citrate and observed under transmission electron microscope.

6. Statistical analysis

Statistical significance of the results was determined by paired student t-test and were considered significant at $p<0.05$.

III. RESULTS AND DISCUSSION

There was no death, but notable signs of each group were moderately increased respiratory rate and locomotion for 3-4 minute following smoking exposure, which was commensurate with results of Gairola (1991). Thereafter, these signs disappeared gradually and no difference was observed between negative control and each treated group.

Total animal body weights of all groups were slightly increased during experimental term. However, body weights of only smoke-exposed group (Group C), both sex, were significantly lower ($p<0.05$) than those of nonsmoking group (Group

Table I. Body Weights and Relative Liver Weights* of SD Rats on Sacrifice

sex		Groups				
		N	C	G	A	A+G
Male	Body(g)	346.51±48.24	312.48±51.57a	331.45±61.54	325.71±54.19	337.39±56.78
	Liver(%)	3.23± 0.12	3.44± 0.38	3.28± 0.19	3.35± 0.27	3.26± 0.15
Female	Body(g)	249.36±51.42	221.47±48.19[a]	237.71±56.43	236.35±41.58	242.39±45.68
	Liver(%)	3.36± 0.24	3.49± 0.46	3.35± 0.13	3.41± 0.36	3.32± 0.48

Values are expressed as mean ±S.D.
* : Relative liver weight (organ/body weight)x100(%)
a : Significantly different from N group (P<0.05)

Table 2. Serum Biochemical Values of SD Rats

Parameter/Groups	N	C	G	A	A+G
Alk. Phos.	495.5±151.3	514.8±139.2	420.7±121.8	472.6±141.6	446.5±113.2
Bilirubin	0.2± 0.0	0.3± 0.0	0.3± 0.0	0.3± 0.0	0.3± 0.0
AST(SGOT)	200.3± 14.9	254.5± 18.7	185.7± 13.8	211.4± 19.5	221.7± 15.7
ALT(SGPT)	75.4± 1.9	122.6± 4.8	93.6± 2.4	85.2± 3.1	88.6± 3.7
Total Protein	7.1± 0.3	7.4± 0.6	7.2± 0.7	7.5± 0.5	7.3± 0.8
Albumin	3.9± 0.1	4.1± 0.2	2.6± 0.1	3.9± 0.2	3.8± 0.3
Cholesterol	90.6± 2.3	55.3± 1.8	78.4± 2.2	59.5± 3.1	78.4± 3.5
Triglyceride	47.5± 2.1	116.7± 3.1	77.6± 2.9	94.3± 1.7	51.6± 2.1
BUN	20.4± 3.1	22.3± 1.8	21.3± 2.3	21.6± 1.6	20.5± 2.6
Creatinine	0.6± 0.0	0.6± 0.0	0.6± 0.0	0.6± 0.0	0.5± 0.0
Glucose	10.8± 0.3	10.7± 0.2	10.3± 0.4	10.6± 0.1	10.5± 0.3
Phosphorus	9.1± 0.5	8.7± 0.4	8.1± 0.0	7.6± 0.8	8.1± 0.2
Amylase	496.3± 37.4	512.3± 31.6	507.5± 27.6	521.3± 31.3	492.8± 35.2
Uric acid	3.1± 0.2	2.8± 0.1	2.9± 0.0	2.9± 0.1	2.9± 0.0
HDL Cho.	48.5± 0.8	43.1± 0.5	53.5± 1.1	39.5± 1.2	52.4± 2.3

Values are expressed as mean ±S.D.

N). Relative liver weights of group C increased even though they were not significant (Table 1).

Smoke exposed group (Group C) showed slight reduction in food intake and increase in drinking water consuption compare to other groups. These effects were considered as typical response to smoking exposure (Clark, 1990).

Several blood chemical parameters were altered following smoke exposure. Activities of liver-associated enzymes, ALT, AST, ALP, were elevated and triglyceride values were high in group C too. These data indicated that some degree of smoke-induced hepatic damage and functional disorder of hepatocytes, as reported previously (Mulligan, 1983). Meanwhile, Cholesterol values decreased in group C and other treated groups (Table 2).

Grossly, there was no any specific liver lesion in all of the groups. The only finding was dark-redish change of the lobular center and light brownish red color around them in group C animals. His-

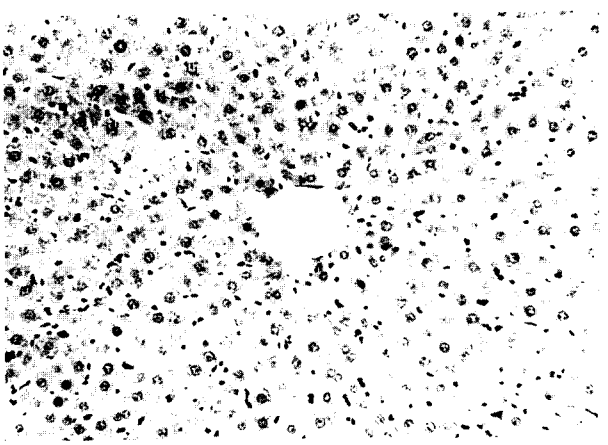

Fig. 1. Normal architecture and cord-like arrangement of hepatic parenchyma of negative control rat (N). H & E. x 200.

topathologically, the most prominent changes induced by smoking (Group C) were diffuse swelling of hepatocytes and demolished sinusoids, which resulted in derangement of hepatic cord-like ar-

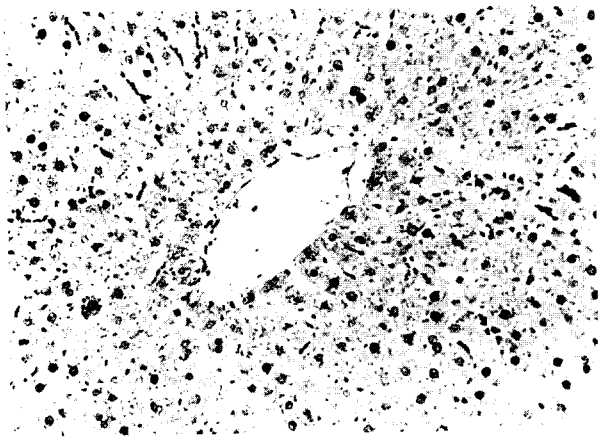

Fig. 2. Diffuse swollen and necrotized hepatic cells demolish normal hepatic arrangement and sinusoids in a positive control rat (C) exposed only to cigarette smoke. H & E. x 200.

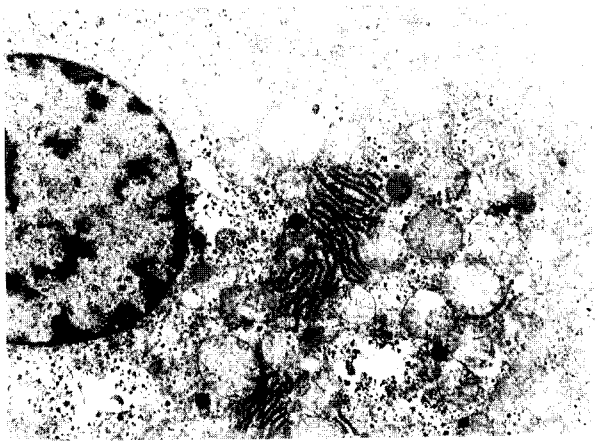

Fig. 5. N Ultrastructure of a hepatocyte contains many electron-dense peroxisomes and decreased mitochondria in the scanty cytoplasmic matrix of positive control rat (C). TEM. x12,500.

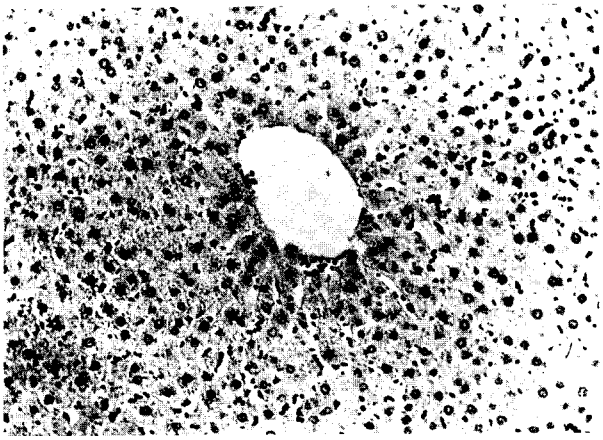

Fig. 3. Normal hepatic cells and sinusoidal remnant reappear among the degenerated hepatic parenchyma of the Aloe-treated rat (A). H & E. x 200.

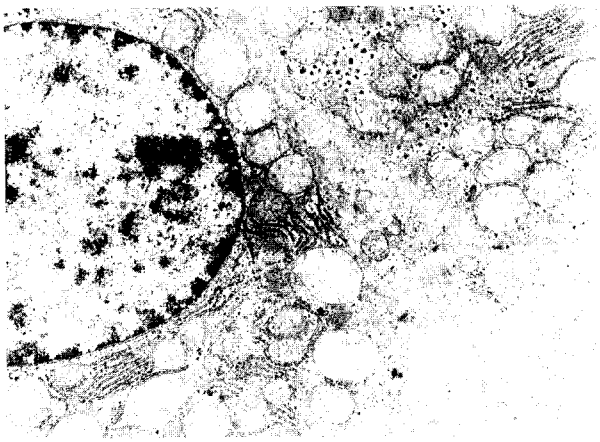

Fig. 6. Most peroxisomes disappear from dense cytoplasmic matrix accompanying increased mitochondria in Aloe + Ginseng-treated rat (A + G). Tem. x12,500.

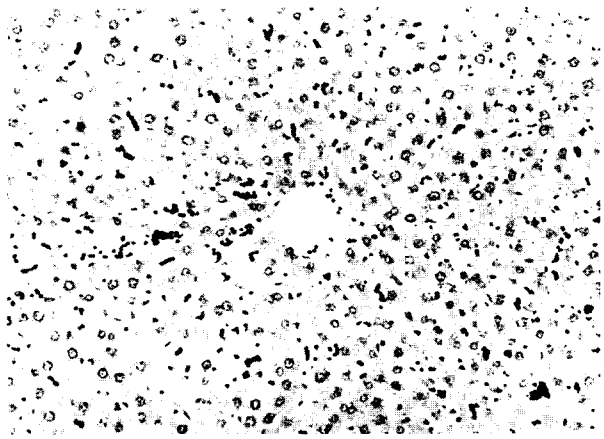

Fig. 4. Close to normal cellular pattern and architecture of hepatic parenchyma remain in Aloe + Ginseng-treated rat (A + G). H & E. x 200.

rangement. Diffuse coagulation necrosis of parenchymal cells and hypereosinophilic cells were found very often together (Fig. 2). However, these degenerative and necrotic lesions were highly repaired in group G+A (Fig. 4) but still mild lesions were shown in group A (Fig. 3) but moderate lesions were observed in group G comparing with that of group C. Electronmicroscopically, the numbers of peroxisomes of hepatocyte increased, whereas the numbers of mitochondria decreased in group C(Fig. 5). The numbers and sizes of peroxisomes and mitochondria in group G+A were almostly same as did in group N (Fig. 6). These pathological findings may provide a clear results of liver dysfunction following toxicity of cigarette

smoking.

This study suggests that cigarette smoke induces various liver damages and daily administration of ginseng and aloe can decrease and even prevent cigarette smoke-induced hepatotoxicity.

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