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EFFECT OF EXPOSURE TO GREEN COFFEE DUST EXTRACT ON AIRWAY REACTIVITY

E. Žuškin[1], I. Dreshaj[2], M. Jakupi[2] and M. A. Haxhiu[2]

»Andrija Štampar« School of Public Health, Medical Faculty, University of Zagreb[1] and Institute of Clinical Physiology, Medical School, University of Kosovo, Prishtina[2]

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An experimental study on the effect of exposure to green coffee dust water-extract on airway responses to bronchoconstrictive drugs was carried out in eleven anaesthetized mongreal dogs. Inhalation of green coffee dust extract caused an increase in respiratory frequency (FR), minute volume (MV), lung resistance (RL) and dynamic elastance (Edyn), and a slight decrease in tidal volume (V_T). Changes were greater in comparison to changes following saline inhalation, although the differences were not statistically significant ($P > 0.05$). Inhalation of green coffee dust extract did not change significantly the sensitivity of bronchial system to aerosolized acetylcholine (ACh). Responses to ACh following pretreatment with saline or green coffee dust extract were similar in all respiratory parameters. The findings with pure green coffee dust water-extract suggest that bronchospasm in coffee workers is not due to the pharmacological activity of the water soluble agent in the dust, or due to increased bronchial reactivity.

Allergic symptoms such as asthma, rhinitis, conjuctivitis or others have been reported in coffee workers (1—5). Furthermore, epidemiological studies in coffee workers demonstrated that occupational exposure to green or roasted coffee is likely to contribute to the development of chronic respiratory symptoms and lung function changes in exposed workers (6, 7). Pharmacological studies on isolated guinea pig tracheal spirals have shown that green coffee alergen induced dose-dependent contraction, while roasted coffee allergen induced concentration-dependent relaxation of uncontracted and histamine-contracted tissues (8). A recent study of *Žuškin and co-workers,* (9) demonstrated that bronchoprovocation testing with green coffee allergen provoked an immediate asthmatic reaction in 44.4% of tested subjects with acute obstructive

changes mostly in smaller airways. Furthermore, it is assumed that exposure to green coffee may cause airway hyperreactivity by increasing airway permeability, thereby allowing higher concentrations of inhaled materials to reach »target« cells.

The present study was undertaken in order to study the effect of exposure to green coffee dust extract on airway responses to bronchoconstrictive drugs.

MATERIAL AND METHODS

The study was carried out on eleven adult healthy mongreal dogs of both sexes with the mean body weight of 17 kg (range 9—25 kg). Anaesthesia was induced with ketamin hydrochloride (4 mg/kg) given intramuscularly, and alpha chloralose (80 mg/kg) administered intravenously.

The animals were intubated and placed in the lateral position. A catheter was inserted into the femoral artery to measure blood pressure (BP) and heart rate (HR). Another catheter was inserted into the peripheral vein for systemic administration of saline during the experiment, and supplementary doses of chloralose were given as needed to supress epicanthal reflex, but to keep an intact corneal reflex.

To the intubated animals a three-way valve was attached to the tracheal tube. One pathway was used for administration of aerosols. From the other pathway, air flow ($\dot{V}$) was measured by a heated Fleisch pneumotachograph and Statham differential pressure transducer. Tidal volume (V_T) was obtained by electronically integrating the flow signal. The esophageal pressure (Poes) was monitored with the pressure transducer connected to a fluid-filled plastic catheter (2 mm in diameter) positioned in the lower third of the esophagus.

Flow, volume and pressure signals were recorded on a four-channel Watanabe recorder for subsequent analysis. From these records, $\dot{V}$, V_T, respiratory frequency (RF), HR and BP were read, and minute ventilation (MV), lung resistance (RL), and dynamic elastance (Edyn) were calculated. The change of Poes required for each 100 ml of V_T (Edyn = $= \frac{\text{Poes (cm } H_2O)}{V_T \text{ (ml)}} \times 100$) was calculated as an index of the airway and air space constriction. The reported values were means of 5—10 successive breaths.

Respiratory changes were recorded following inhalation of normal saline, acethylcholine (ACh) or green coffee dust water-extract aerosolized by a Bird Micronebulizer with an air flow of 8 L/min. Each dog was first exposed to aerosolized saline for two minutes and respiratory parameters were recorded at different time intervals over 30-minute postexposure period. After exposure to saline, bronchoconstriction was

induced by two minute inhalation of aerosolized ACh dissolved in saline (0.1—20.0 mg/ml). Increasing concentrations of ACh were administered in the lower airways via a side of three-way valve until a clear bronchoconstriction response was achieved.

In order to investigate the effect of green coffee dust on bronchial reactivity, 60 grams of green coffee power was mixed with 600 ml of saline. The green coffee dust used in the study was collected in a coffee processing industry. Coffee extract was aerosolized during 120 minutes and respiratory function was measured at different time intervals during exposure. Immediately after cessation of green coffee aerosol inhalation, response to ACh was obtained in the identical manner as after saline administration.

Values of respiratory parameters (RF, V_T, MV, Edyn and RL) were analysed during control period before exposure, and at different time intervals after exposure to saline, ACh or green coffee dust extract (1, 5, 15 and 30 minutes after inhalation).

RESULTS

Table 1 shows the responses of RF, V_T, MV, RL and Edyn at one minute after inhalation of saline, green coffee dust extract and different doses of ACh administered after saline or green coffee dust extract aerosols. Inhalation of green coffee dust extract caused an increase in RF, MV, RL and Edyn, and a slight decrease in V_T in relation to saline. However, the differences between responses to saline and green coffee dust extract were not statistically significant ($P > 0.05$).

Figures 1 and 2 show relative mean changes in RF, V_T, Edyn and RL as percentages of control values at one minute after inhalation of different ACh concentrations (0.2—20.0 mg/ml) following pretreatment with saline or green coffee dust extract. Inhalation of ACh after saline caused changes in RF ranging from a decrease of 2% to an increase of 134% at ACh concentration of 20.0 mg/ml. Following saline inhalation, there was a relative decrease in V_T ranging from 12% to 33%; in MV changes varied from a decrease of 14% to an increase of 48%. After inhalation of saline, there was a relative increase in RL ranging from 18% to 172% and in Edyn ranging from 26% to 261%. After coffee dust extract inhalation there was an increase in RF ranging from 5% to 77% at ACh concentration of 20.0 mg/ml. V_T and MV decreased: values for V_T varied from 8% to 43% and for MV from 2% to 12%. RL and Edyn increased with increase of ACh concentration: relative increase varied for RL from 19% to 127% and for Edyn from 17% to 242%.

Table 2 shows changes in RF, V_T, MV, RL and Edyn following inhalation of saline, green coffee dust extract and 20.0 mg/m of ACh after saline or green coffee dust extract. Data are presented at 1, 5, 15 and

Table 1

Responses to saline (S), green coffee dust extract (C) and to different doses of ACh after saline or green coffee dust extract inhalation. Data are presented at one minute following inhalation of normal saline, green coffee dust extract or ACh ($\bar{X} \pm SE$).

Respiratory parameters	Acetylcholine (mg/ml)											
			0.2		0.6		2.0		6.0		20.0	
	S	C	S	C	S	C	S	C	S	C	S	C
RF (breath/min)	16.9 ± 1.6	29.1 ± 5.5	16.6 ± 2.3	31.7 ± 8.3	17.7 ± 2.3	30.6 ± 9.4	22.3 ± 5.0	35.1 ± 9.7	23.1 ± 5.5	40.6 ± 9.8	39.6 ± 5.8	51.6 ± 7.1
V_T (ml)	263 ± 24	224 ± 18	231 ± 26	202 ± 24	240 ± 30	207 ± 24	218 ± 26	186 ± 31	211 ± 24	165 ± 30	176 ± 24	127 ± 20
MV (l/min)	4.36 ± 0.47	6.16 ± 1.03	3.75 ± 0.54	5.74 ± 1.22	4.26 ± 0.71	5.44 ± 1.28	4.55 ± 0.79	5.72 ± 1.37	4.71 ± 1.02	5.60 ± 1.05	6.47 ± 0.96	6.03 ± 1.05
RL (cm H_2O/L/s)	8.80 ± 1.20	12.7 ± 2.3	10.5 ± 1.4	15.2 ± 1.9	10.4 ± 1.3	15.1 ± 2.0	11.9 ± 1.2	17.8 ± 2.0	13.3 ± 1.1	21.0 ± 2.8	23.9 ± 6.6	28.8 ± 5.8
Edyn (cm H_2O/V_T x 100)	2.3 ± 0.5	4.1 ± 0.9	2.9 ± 0.7	5.3 ± 1.0	3.0 ± 0.7	4.8 ± 0.8	3.6 ± 0.6	7.2 ± 1.1	4.0 ± 0.6	9.3 ± 2.3	8.3 ± 1.8	14.0 ± 3.3

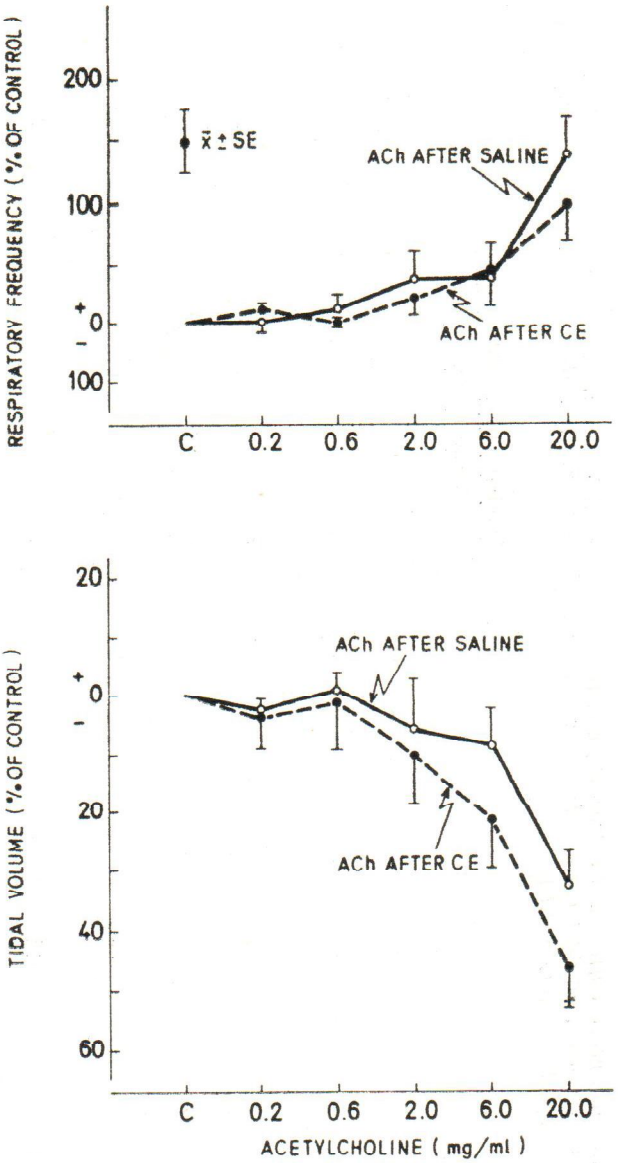

Fig. 1. *Relative mean changes in respiratory frequency (RF), and tidal volume (V_T) as percentages of control values at one minute after inhalation of different ACh concentrations (0.2—20.0 mg/ml) following pretreatment with saline or green coffee dust extract.*

Table 2

Responses to saline (S), green coffee dust extract (C) and to 20 mg/ml of ACh at different time intervals following inhalation of saline, or green coffee dust extract. Data for normal saline and green coffee dust extract are presented at one minute following inhalation ($\bar{X} \pm SE$).

Respiratory parameters	Acethylcholine (20 mg/ml)									
	Time (minute)									
	1′		5′		15′		30′			
	S	C	S	C	S	C	S	C	S	C
RF (breath/min)	16.9 ± 1.6	29.1 ± 5.5	39.6 ± 5.8	51,6 ± 7.1	34.4 ± 5.1	49.1 ± 7.0	30.0 ± 4.3	45.1 ± 7.6	26.0 ± 3.4	43.8 ± 7.8
V_T (ml)	263 ± 24	224 ± 18	176 ± 24	127 ± 20	210 ± 21	169 ± 18	231 ± 25	181 ± 22	237 ± 20	177 ± 23
MV (l/min)	4.36 ± 0.47	6.16 ± 1.03	6.47 ± 0.96	6.03 ± 1.05	6.63 ± 0.78	7.67 ± 0.89	6.69 ± 0.88	7.24 ± 0.93	5.87 ± 0.66	6.62 ± 0.84
RL (cm H_2O/L/s)	8.80 ± 1.20	12.7 ± 2.3	23.9 ± 6.6	28.8 ± 5.8	13.3 ± 1.9	15.1 ± 2.3	12.3 ± 1.7	13.5 ± 1.7	10.0 ± 1.4	12.1 ± 1.6
Edyn (cm H_2O/V_T x 100)	2.3 ± 0.5	4.1 ± 0.9	8.3 ± 1.8	14.0 ± 3.3	4.8 ± 1.0	6.9 ± 1.3	4.2 ± 0.9	5.7 ± 0.9	3.6 ± 0.7	5.4 ± 1.0

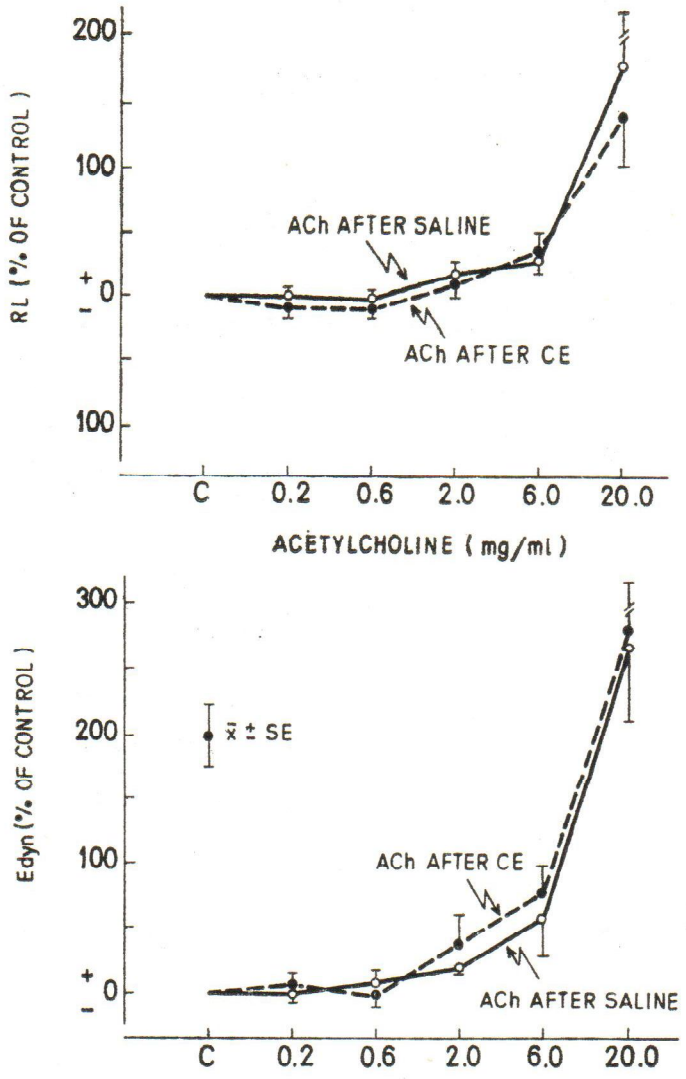

Fig. 2. *Relative mean changes in lung resistance (RL) and dynamic elastance (Edyn) as percentages of control values at one minute after inhalation of different ACh concentrations (0.2—20.0 mg/ml) following pretreatment with saline or green coffee dust extract.*

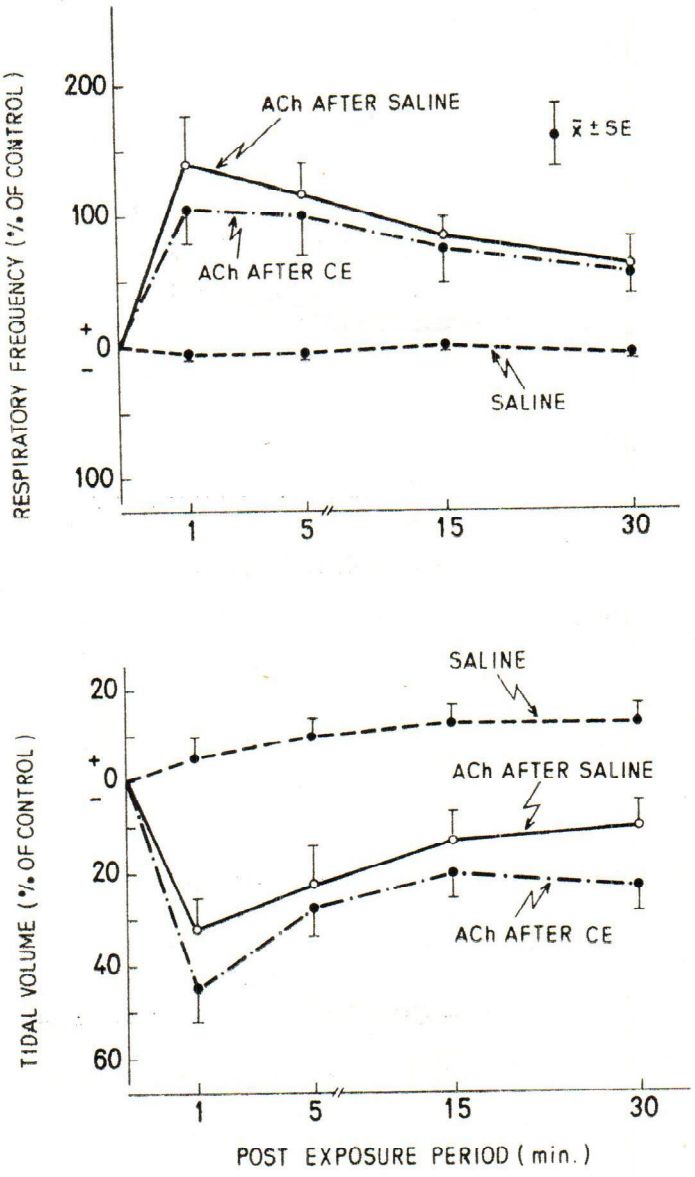

Fig. 3. *Relative mean changes in respiratory frequency (RF) and tidal volume (V_T) as percentages of control values after 20.0 mg/ml ACh inhalation following pretreatment with saline or green coffee dust extract.*

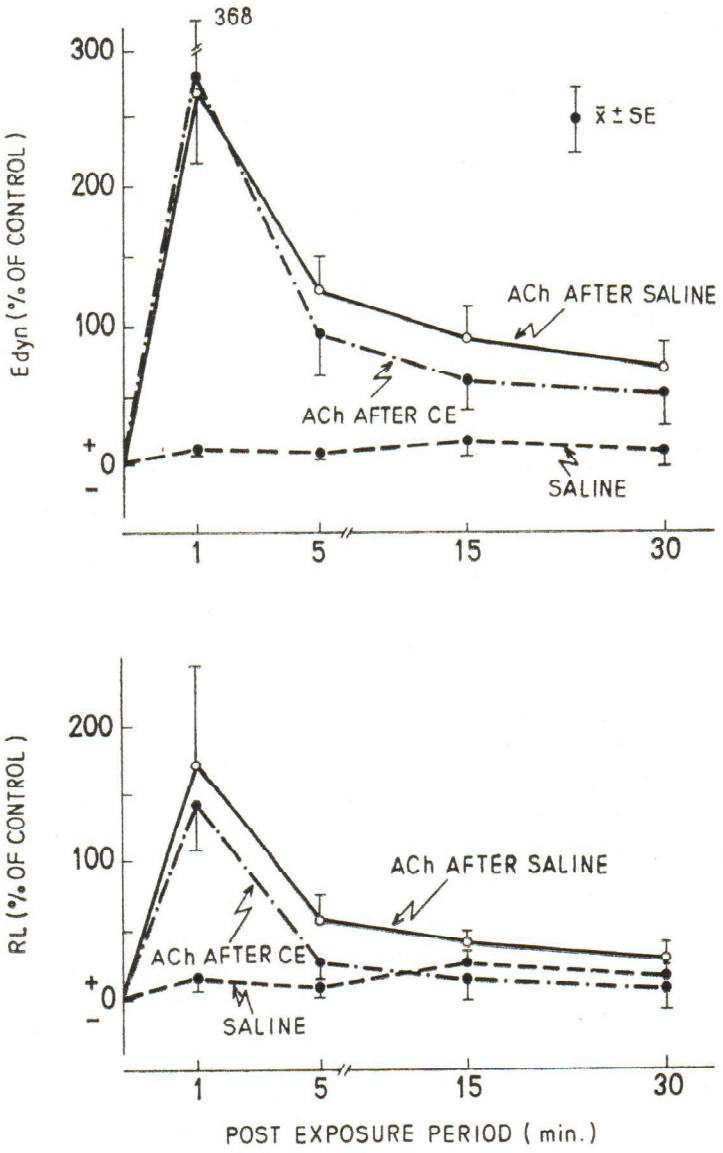

Fig. 4. *Relative mean changes in lung resistance (RL) and dynamic elastance (Edyn) as percentages of control values after 20.0 mg/ml ACh inhalation following pretreatment with saline or green coffee dust extract.*

30 minutes after ACh inhalation. ACh following green coffee dust extract inhalation caused almost no changes of MV; at one minute a slight decrease (2%), and a smaller increase at 30 minutes (8%) in comparison to increase after saline (48% and 35% resp.). Changes in other respiratory parameters following ACh were similar after pretreatment with saline or green coffee dust extract.

Figures 3 and 4 show relative mean changes in RF, V_T, Edyn and RL, as percentages of control values after 20.0 mg/ml ACh aerosol inhalation following green coffee dust extract and saline inhalation. Responses to ACh following pretreatment with saline or green coffee dust extract were similar in all respiratory parameters, being slightly more pronounced after pretreatment with saline.

DISCUSSION

Our study demonstrated that exposure to coffee extract in dogs caused an increase in RF, MV, RL and Edyn, and a slight decrease in V_T. The changes were greater in comparison to changes following saline inhalation.

Increased RF following inhalation of green coffee dust extract might be due to stimulation of irritant receptors by bronchoconstrictive substances, like histamine. Recently it has been shown that exposure to low concentrations of bronchoactive drugs in dogs is associated with a significant increase in the sensitivity of the bronchomotor system to ACh (10). However, in this study inhalation of green coffee dust extract did not change the sensitivity of bronchial system to aerosolized ACh, suggesting that other factors might be responsible for the effect of green coffee dust extract. Increased RF following inhalation of green coffee dust extract could be due to resorptive effects of coffein which stimulate breathing. Increased respiratory drive associated with elevation of RF may contribute to increase in nonelastic resistance, and partly accounts for increase in Edyn (11).

The increase of bronchial hypersensitivity in coffee workers may be due to the effect of proteolytic enzymes. It was found that exposure of the upper part of the airtract to pronase causes an increase in reactivity of the lower airways to ACh. Pronase aerosol given to the lower part of the airways also might cause bronchopulmonary sensitization to ACh (12). However, our results obtained in dogs did not show the change in airway response to ACh given after exposure of lower airways to aerosol of green coffee dust extract, suggesting that this mechanism is not of significant importance.

In these experiments, there was an increase in RL after administration of green coffee dust extract. The airway caliber in the baseline

state may influence the subsequent response to agents that induce bronchoconstriction. Any decrease in the radius of a narrow airway causes a greater change in airway resistance than does the same decrease in the radius of the normal airway. Some studies have shown that the hyperreactivity of the airways in disease is primarily due to the fact that the airways are narrower in the control state before bronchial provocation (13). Based on these results, the change in the bronchomotor tone cannot explain unexpected findings that inhalation of green coffee dust extract does not change bronchial response to bronchoactive sbstances. If there was any effect, the elevation of bronchomotor tone should rather increase than decrease the airway reactivity to aerosolized ACh.

Different studies have demonstrated increased airway sensitivity after exposure to various agents such as ozone or SO_2 (14, 15). In the present study changes in respiratory parameters caused by acetylcholine were slightly more pronounced in dogs previously exposed to saline than to green coffee dust extract.

Data obtained in epidemiological studies suggest that only a certain number of coffee workers are sensitive to green coffee dust and react by developing occupational asthma or other respiratory symptoms (6, 16). The atopic status as well as the nature and intensity of exposure may play an important role in the development of hypersensitivity (4). Our data obtained in dogs suggest that there is a great variability in sensitivity to green coffee dust extract. The differences in the effect of coffee dust might also depend on the type of green coffee, i. e. on the amount of biologically active substances.

Study of *Žuškin and co-workers* (8, 17) suggested that the effect of coffee dust depends also on solubility of the active agent/s in the dust. Our study with pure green coffee dust water-extract in dogs support the data of *Žuškin and co-workers* (8, 17) suggesting that bronchospasm in coffee workers associated with exposure to this vegetable dust is not due to the pharmacological activity of the water soluble agent in the dust.

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Sažetak

DJELOVANJE VODENOG EKSTRAKTA PRAŠINE SIROVE KAVE NA REAKCIJU DIŠNIH PUTOVA

Ispitivanje djelovanja vodenog ekstrakta prašine sirove kave na reakciju dišnih putova na bronhokonstriktorne agense izvršeno je na 11 anesteziranih mongreal pasa. Inhalacija ekstrakta prašine sirove kave uzrokovala je povećanje respiratorne frekvencije (RF), minutnog volumena (MV), plućnog otpora (RL) i dinamičke elastance (Edyn) te neznatno smanjenje dišnog volumena (V_T). Premda je odgovor na ekstrakt prašine sirove kave bio veći u odnosu na odgovor prema fiziološkoj otopini, razlike nisu bile statistički značajne ($p > 0,05$). Inhalacija ekstrakta prašine sirove kave nije značajno promijenila osjetljivost bronhalnog sistema na inhalirani acetilkolin (ACh). Reakcije na ACh nakon tretiranja fiziološkom otopinom ili ekstraktom prašine sirove kave bile su slične za sve respiratorne parametre. Naše ispitivanje s vodenim ekstraktom prašine sirove kave upućuje na to da bronhospazam radnika u preradi kave nije uzrokovan u vodi topljivim farmakološki aktivnim agensima prisutnim u prašini.

Škola narodnog zdravlja »Andrija Štampar«
Medicinskog fakulteta Sveučilišta u Zagrebu[1]
i Institut za kliničku fiziologiju Medicinskog
fakulteta u Prištini[2]

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