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BRIEF COMMUNICATION

Changes of HDL-Lipid Composition as Related to Δ^9-THC Action

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KALOFOUTIS, A., A. DIONYSSIOU-ASTERIOU, C. MARAVELIAS AND A. KOUTSELINIS. *Changes of HDL-lipid composition as related to Δ^9-THC action.* PHARMACOL BIOCHEM BEHAV 22(2) 343–345, 1985.—An attempt was made to investigate the possible action of Δ^9-THC on HDL-Lipid composition. Significant changes were observed in the serum total lipids, triglycerides and HDL subfractions after hashish smoking. The results are discussed in relation to the possible alterations of some enzymatic mechanisms regulating lipid metabolism in hashish users.

HDL-lipid composition Δ^9-THC Human studies

DURING the recent years, high-density lipoproteins (HDL) have drawn the interest of many researchers, mainly due to the findings that HDL are inversely related to coronary artery disease. Thus, environmental factors, diet [10], exercise [15], alcohol consumption [2], cigarette smoking [5], have been studied and have been correlated with HDL levels.

Certain pharmacologic agents are among the factors that seem to influence the composition of the levels of HDL [6,12]. It is a well known fact that the active ingredients of cannabinoids have been associated with changes in cell membrane lipids [8,9]. Mainly, the action of Δ^9-THC has been associated with the lipoprotein components of cell membrane because of the lipophilic nature of this hashish ingredient.

In the present study an attempt was made to investigate the HDL composition in chronic hashish smokers under known experimental conditions.

METHOD

Twelve volunteers (age 42 to 56 years), heavy hashish smokers as well as twelve healthy subjects (age 44 to 54 years), were used in these experiments.

Each of the hashish users was allowed to smoke 20 g of 3.6% in Δ^9-THC pure resin by nargile pipe for a period not exceeding 15 min. At the same time, and under the same conditions, each of the control subjects smoked about 20 g of pure tobacco by pipe.

In all cases blood samples were drawn before and 30–60 min after smoking, when the highest concentration of the drug in the blood is noted [11]. All samples were centrifuged at 90 g (MSE Mistral 6L) for 10 min at 4°C. The serum cholesterol and serum triglycerides were measured by Autoanalyzer (Gilford System 203 Gilford Instr. Lab. Inc. Oberlin, OH). Magnesium chloride and dextran sulfate were used to precipitate all low-density and very-low-density lipoporteins in order to determine the HDL-cholesterol and HDL-triglycerides following the method of Yamaguchi [18]. The estimation of these two parameters was also made by Autoanalyzer. The LDL-cholesterol concentration was calculated using the formula: $C_{LDL.}=C_{serum} - C_{HDL.}-(TG/5)$ [4].

RESULTS

The results obtained in this study are presented in Tables 1 and 2. Table 1 shows a remarkable increase in the concentration of total lipids ($p<0.001$) and a decrease in the fraction of serum triglycerides ($p<0.001$) in individuals after smoking hashish. Moreover, no significant change was observed in the cholesterol level of the same subjects. Table 1 also shows that no statistically significant differences exist in the same observed parameters of the control group before and after smoking tobacco.

Table 2 demonstrates that there is a statistically significant decrease in the HDL-cholesterol level ($p<0.05$) and a very significant increase in the HDL-triglycerides level ($p<0.001$) of the hashish users whereas, no statistically significant change was observed in the LDL-cholesterol of the same group. Concerning the same parameters of the control group no statistically significant changes were observed.

DISCUSSION

Hashish compounds have been shown to have a broad spectrum of action on cell functions and structure and there-

TABLE 1

SERUM LIPIDS CONCENTRATION IN HEAVY HASHISH USERS AND CONTROLS

	Controls (n=12)			Hashish Users (n=12)		
Lipid Class	Before	*p*	After	Before	*p*	After
Total lipids	691 ± 49	N.S.	714 ± 48	737 ± 52	0.001	892 ± 55
Cholesterol	212 ± 42	N.S.	219 ± 40	219 ± 21	N.S.	214 ± 20
Triglycerides	127 ± 24	N.S.	132 ± 26	218 ± 42	0.001	174 ± 40

All concentrations are expressed in mg/dl and represent mean ± S.D. of observed values.

TABLE 2

CONCENTRATIONS OF SERUM HDL-LIPID COMPOSITION IN HEAVY HASHISH USERS AND CONTROLS

	Controls (n=12)			Hashish Users (n=12)		
	Before	*p*	After	Before	*p*	After
HLD-Cholesterol	46 ± 9	N.S.	44 ± 8	41 ± 10	0.05	39 ± 7
HDL-Triglycerides	22 ± 6	N.S.	23 ± 7	44 ± 4	0.001	49 ± 4
LDL-Cholesterol	140 ± 9	N.S.	147 ± 8	137 ± 9	N.S.	142 ± 8

All concentrations are expressed in mg/dl and represent mean ± S.D. of observed values.

fore they may affect the metabolism of the cell's macromolecules. Recent research data [1,7] demonstrate that administration of hashish active ingredients, especially Δ^9-THC, induce membrane lipid reorganization.

The results obtained by the present study reflect upon the biochemical action of hashish active ingredients and particularly that of Δ^9-THC on serum lipid concentration and HDL composition. An explanation for the low level of serum triglycerides observed, may be connected with the possible effect of the hashish active ingredients on the functions of the liver. This effect could be expressed as a low ability of hepatic cells to produce adequate amounts of triglycerides.

The marked increase observed in the HDL-triglycerides could be explained as a direct action of Δ^9-THC on the enzymes regulating the metabolic pathways of lipoproteins species, especially due to the alteration of the activity of Lecithin Cholesterol Acyltransferase (LCAT) and Lipoprotein lipase (LPL) in heavy hashish users. It has been suggested [13] that this increase in HDL-triglycerides may be associated with the reduced ability of the HDL molecule to pick up tissue cholesterol. Thus, through this mechanism the reduced after-smoking value of HDL-cholesterol could also be explained.

The statistically significant differences observed in the triglycerides and the HDL-triglycerides before-smoking values of the control group and the hashish smokers could be considered as the chronic effects of hashish smoking in general. A possible explanation for these increased values may be due to the type of diet of the chronic hashish smokers which is very high in carbohydrates or the chronic effects of the hashish active ingredients on these observed parameters.

The results of the present study clearly indicate disturbances in the HDL-lipid composition among heavy hashish users. These observations warrant further research to elucidate the mechanism and the possible effect of hashish compounds on the enzymes refulating lipid metabolism.

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