Research article

The effects of smoking Haschich on blood parameters in young people from the Beni Mellal region Morocco

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Abstract: Objective: The objective of this work is to evaluate the effects of smoking hashish on some blood parameters (Red blood cells, Hemoglobins, Hematocrits, MCV, MCH, MCHC, White blood cells, Urea, Creatinine, Cholesterol, Triglycerides, Liver Aminotransferases) among young people from the Beni Mellal region, Morocco. **Methods:** Blood samples are collected from 30 male, fasting, voluntary and anonymous individuals in three groups; 10 non-smokers (controls), 10 moderate chronic smokers (5 joints/day (5 j/d) or less for a period not exceeding 3 years) and 10 intense chronic smokers (15 joints/day or more for a period equal to or greater than 5 years). **Results:** The results obtained show that with the duration and number of joints consumed, a decrease in the level of HB, RBCs, HT, platelets, urea, cholesterol, triglycerides, SGOT and SGPT while there is an increase in MCH, MCHC, eosinophils and creatinine. **Conclusion**: These results could be explained by the impact of the active ingredients in the joints, including THC in cannabis and the components of smoked cigarettes in conjunction with cannabis resin on consumer nutrition.

Keywords: blood parameters; Beni Mellal region; smoking hashish; young people; joint; tetrahydrocannabinol

Abbreviations: MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; HB: Hemoglobin; RBC: Red blood cells; HCT: Hematocrit; SGOT: (serum) Glutamic oxaloacetic transaminase; SGPT: Serum glutamic-pyruvic transaminase; THC: Tetrahydrocannabinol

1. Introduction

Hemp plant (cannabis sativa) is very popular worldwide [1]. A herbaceous plant, all parts of the plant are covered with hairs, glandular or not; only glandular hairs secrete the cannabis resin. They are more numerous on female feet, especially on leaves and flowering tops. The secretion of the resin is maximum between the flowering period and the complete maturity of the seeds [2].

In Morocco, Lebanon and Afghanistan, hashish is made by compressing this resin obtained after sieving, the resin contains tetrahydrocannabinol (THC), active ingredient isolated in 1964 which is the origin of psychoactive effects appreciated and sought by cannabis users [3].

In Morocco cannabis is consumed in the form of a joint, which is a hand-rolled cigarette with cigarette paper containing tobacco (nicotine) and cannabis resin (THC), these are the biologically active components in these plants [4].

Tobacco (the most widely used by smokers) is the leading cause of preventable death [5], The exact toxic components of cigarette smoke and the mechanisms involved in cardiovascular dysfunction associated with smoking are largely unknown, but smoking increases inflammation (Many studies have shown that Cigarette smoking causes about a 20% to 25% increase in the peripheral blood leukocyte count), thrombosis and oxidation of LDL cholesterol. It is a risk factor for coronary artery disease, vascular disease and brain atherosclerosis [6].

It is estimated that smoking is responsible for 71% of lung cancers, 42% of chronic respiratory diseases and nearly 10% of cardiovascular diseases [7].

Smoking marijuana may cause dizziness, tachycardia, transient and disoriented muscle rigidity [8], It has been reported to significantly affect blood chemistry and may also affect neural functions [9].

The use of tobacco or cannabis increases the risk of adverse health effects. It multiplies the risk of death from lung cancer, coronary heart disease, chronic obstructive pulmonary disease (COPD), and a third of all cancers (U.S. Department of Health and Human Services [USDHHS] [10].

A panel of experts appointed by The National Academies of Sciences, Engineering, and Medicine found significant evidence to support their conclusion that smoking cannabis raises the risk of motor vehicle accidents, episodes of chronic bronchitis, low-weight births and schizophrenia (National Academies of Sciences, Engineering, and Medicine [NASEM]) [11].

Cannabis use can also impair individuals' cognition and redouble the risk of addiction to drugs, including tobacco (NASEM, 2017). Although researchers suspect that smoking tobacco and cannabis in combination increases the risk of harmful health effects in a cumulative or synergistic manner, there is a lack of significant evidence to draw definitive conclusions [12].

In this work we will study the effects of smoking joints (Tobacco + resin) on some blood parameters in young people (20–34 years) in the region of Beni Mellal, Morocco. Hypothesis: smoking joints may cause changes in blood parameters: Red blood cells (RBC), hematocrit (HCT), Hemoglobin (HG), MCV, MCH, MCHC, Platelets, White Blood Cell (WBC), Urea, Creatine, Cholesterol, Triglycerides, Aminotransferases (SGOT, SGPT).

2.   Materials and methods

2.1. Study participants and data collection

The recruitment of participants was carried out in cafes in Morocco. A total of ten cafes were chosen at random. For participant's selection, we used a convenience sampling which consists of selecting participants based on their availability and willingness to participate.

The inclusion criteria for this study were as follows: Male individuals; Age over 18 years, legal age for taking blood samples without parental permission; physically and mentally able to provide all data required for the study and willing to participate in the study.

We excluded female subjects from this study because the menstrual cycle and contraception may impact blood parameters [13]. We also excluded Individuals who were willing to provide data but refused to give a blood sample.

The participation was voluntary and anonymous. Participants were informed about the study objective and they also read carefully and signed a consent form. All data were confidential and protected at all stages of the study.

A total of 30 subjects were included in our study (a control group consisting of 10 individuals who do not use and are not exposed to any psychoactive; 10 individuals who smoke daily between 2 and 5 joints/day "5 j/d" and 10 individuals who smoke daily between 15 and 22 joints/day "15 j/d" for a period greater than or equal to the last 62 months).

It should be mentioned that as it is illegal in Morocco to possess and use hashish, recruiting participants was difficult. Furthermore, even if they agree to participate, the majority of them refuse to take a blood sample, which adds an additional difficulty to recruitment.

For data collection, we conducted a face-to-face interview using a questionnaire which included socio-demographic information, data on health, lifestyle and history narcotic use.

For blood parameters, 5 ml blood sample was taken from each individual on an empty stomach.

2.2. Ethics approval of research

To lead this investigation, written approval was obtained from the Sultan Moulay Slimane University. All the experiments were carried out according to the ICH GCP guidelines and the institutional ethical committee with the approval number of FST/LGB/2016/28-FEB./2017-DEC.2019. For the questionnaire, informed written consent was obtained from all participants after explaining the purpose of the study, the importance of their contribution and their right to refuse participation. The data are anonymized and free of personally identifiable information.

2.3. Limitations

To the best of our knowledge, this is the first study of its kind conducted in Morocco to examine the effects of smoking Haschich on blood parameters in Moroccan young people. However, it has some limitations that should be taken into account when interpreting the results. Firstly, the small sample size in this study due to recruitment difficulties makes it difficult to draw solid conclusions. In this regard, it should be mentioned that the law in Morocco punishes the use and possession of

hashish, which makes it difficult to recruit participants. In addition, even if they agree to participate, the majority of them refuse to take a blood sample, which adds an additional difficulty to recruitment. So, targeting people in addiction centers can be a solution to recruit a large sample.

Secondly, the sampling method used in the selection of participants could affect the results and may not allow the results of this study to be extended to the entire smoking Haschish population in Morocco. Finally, we did not determine the eating habits and physical activity of the target population, which may also affect the blood parameters and therefore the results.

2.4. Samples

5 ml of blood is collected from each individual on an empty stomach. The blood test was carried out in a medical analysis laboratory that complies with ISO 15189.

Each individual undergoes a height and weight measurement, and completes a questionnaire that collects socio-economic, health, lifestyle, narcotic use data.

2.5. Blood sample testing

(1) Red blood cells, Hemoglobins, Hematocrits, platelets, White blood cells, Neutrophils, eosinophils, basophils, lymphocytes and monocytes: Automated technique on laser diffraction automaton. (Sysmex XN 550)
(2) Urea: Enzymatic method with urease. (Indiko 20i)
(3) Creatinine: Kinetic method according to the Jaffe method. (Indiko 20i)
(4) Cholesterol Total: Enzymatic colorimetric technique (CHOD-PAP) (cholesterol-oxidase-peroxidase). (Indiko 20i)
(5) Triglycerides: Enzymatic technique with glycerol-3- phosphate-oxidase (GPO). (Indiko 20i)
(6) SGOT, SGPT: Kinetic method in U.V according to International Federation of Clinical Chemistry (IFCC). (Indiko 20i)

2.6. Statistical analysis

Data entry and analysis were carried out using statistical software Graph pad prism 7, the Student's T test was used for comparison of qualitative variables, the significance rate was set at 0.05 for all analyses.

3. Results and discussions

We found that almost all subjects (controls and tests) have blood parameter values included in the standards biological Reference Range; Table 1 shows the standards of the blood parameters studied.

Table 1. Standard of blood parameters.

Blood parameters	Biological Reference Range	Units
Red cells	4.2–5.7	M/mm^3
Hemoglobin	14.0–17.0	g/dl
Hematocrit	40–52	%
MCH	28–32	Pg
MCHC	30–35	%
MCV	80–95	μ^3
Platelet count	150000–400000	$/mm^3$
Total leucocyte count	4000–10000	$/mm^3$
Neutrophils	2000–7500	$/mm^3$
Eosinophils	100–400	$/mm^3$
Basophils	0–150	$/mm^3$
Lymphocytes	1500–4000	$/mm^3$
Monocytes	200–800	$/mm^3$
Urea	0.10–0.50	g/l
Creatinine	7–13	Mg/l
Total cholesterol	<2.0	g/l
Triglycerides	<1.50	g/l
SGOT Aminotransferases	<37	UI/l
SGPT Aminotransferases	10.0–40.0	UI/l

Note: MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; MCV: Mean corpuscular volume; SGOT: (serum) Glutamic oxaloacetic transaminase; SGPT: Serum glutamic-pyruvic transaminase.

3.1. Red blood cells (RBC)

We found a very significant decrease in the 15 j/d group (5.046 M/mm^3 ± 0.06654; $P < 0.0001$) compared to the control group (5.658 M/mm^3 ± 0.1033). Also a very significant decrease in the 15 j/d group compared to the 5 j/d group (5.611 M/mm^3 ± 0.049; $P < 0.0001$). While there is no significance of the slight decrease in the 5 j/d group compared to the control group ($P = 0.4715$) (Figure 1a).

3.2. Hemoglobin (HG)

We found a significant decrease in the 15 j/d group (15.16 g/dl ± 0.1291; $P < 0.0015$) compared to the control group (16.42 g/dl ± 0.3116). Also a significant decrease in the 15 j/d group compared

to the 5 j/d group (16.21 g/dl ± 0.2523; P < 0.0016). While there is no significance of the slight decrease in the 5 j/d group compared to the control group (P = 0.6068) (Figure 1b).

3.3. Hematocrit (HCT)

This is the volume occupied by the red blood cells circulating in the blood in %, we found a very significant decrease in the 15 j/d group (44.64% ± 0.3400; P < 0.0004) compared to the control group (48.17% ± 0.7280). Also a very significant decrease in the 15 j/day group compared to the 5 j/day group (48.02% ± 0.5848; P < 0.0001). While there is no significance of the slight decrease in the 5 j/d group compared to the control group (P = 0.8742) (Figure 1c).

3.4. MCH/MCHC

This is the Mean Corpuscular Hemoglobin/Mean Corpuscular Hemoglobin Concentration (amount of hemoglobin contained in red blood cells), we found a significant increase in the 15 j/d group (MHCT, P = 0.04; MCHC, P = 0.03) compared to the control group (Figure 1d, Figure 1e).

MCV: This is the Mean Corpuscular Volume, our results show a significant increase in the 15 j/d group compared to the control group (P = 0.0133) and in the 5 j/d group compared to the control group (P = 0.0477) (Figure 1f).
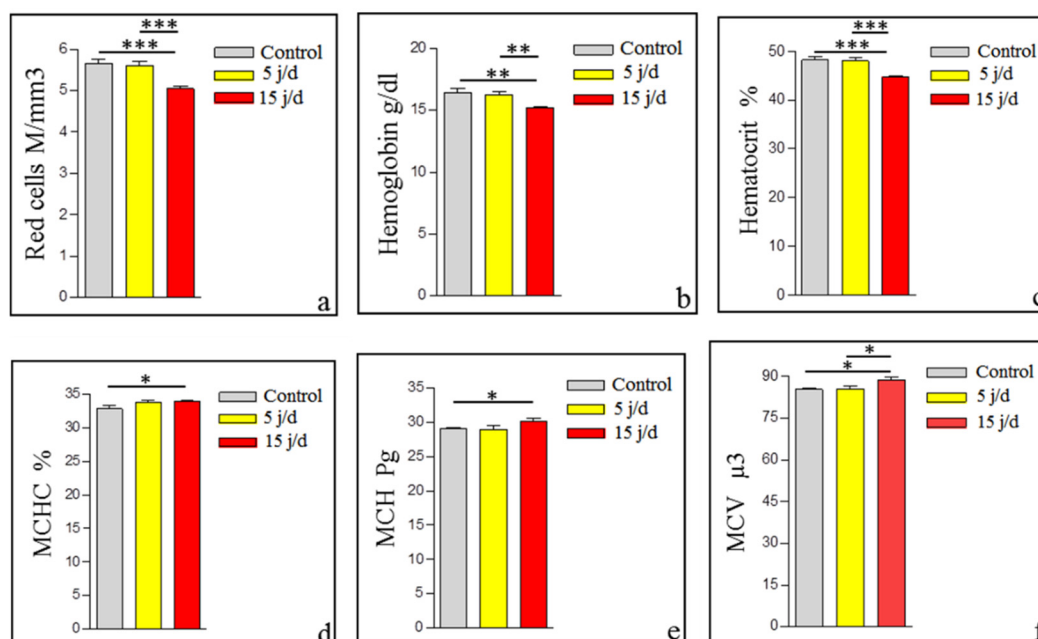

Figure 1. Comparison of means of Red cells, Hemoglobin, Hematocrit, MCH, MCHC and MCV between tests and controls. Value are expressed as mean ± SEM, n = 10, T test. Aserisks indicate the level of significance (*P < 0.05; **P < 0.01; ***P < 0.001).

Our work shows that there is a gradual decrease in the rate of RBC, HG, HCT starting from the control group to the 15 j/d group, this decrease becomes significant with the duration and the quantity of joints consumed, this is consistent with previous studies; Indeed, smoking 4 to 8 Indian

hemp per day shows a non-significant decrease in red blood cells, hemoglobin in tests compared to controls [14] while Irfan Ahmad wani [15], shows that this difference becomes significant in individuals who use 10 or more joints for 15 years and suggests that the use of cannabis Sativa may improve the ability of blood to transport oxygen, but the mechanism of action is not well known, whereas Karimi et al. [16] explains this decrease by the fact that THC has important long-term toxicological implications, which can affect the bone marrow and disrupt the maturation of monocytes and erythrocytes. On the other hand, Amna H [17] explains these results by malnutrition of smokers who could be suffering from anemia. It could be classified into three groups: Microcytic (MCV below normal range), Normocytic (MCV in normal range) and Macrocytic (MCV above normal range) [18].

It can be deduced that the use of cannabis could significantly lower the rates of RBC, HG, HCT and raise the rates of MCH, MCHC and MCV; this is closely related to the number of daily joints and the duration of use, therefore smokers may be affected by anemia [19] (macrocytic anemia) due to malnutrition or poor intestinal absorption of iron and vitamins B6, B9 (deficiency of these elements).

3.5. White blood cells (WBC)

Total White Blood Cells (WBC): Our study shows that there are no significant differences in the levels of WBC, basophils, neutrophils, lymphocytes and monocytes in the three groups (Figure 2a, b, c, e, f); This is consistent with previous literature; Indeed, Beacofield et al. [20] shows that there are no significant differences between smokers and non-smokers in chest radiography, blood parameters and alveolar debris, as well as Isager and Hagerup [21] found that there are no effects of pipe and cigar on haematological values; also Granville-Grossman [22] and Rang et al. [23] suggest that smoking marijuana does not appear to inflict visible physiological stress on smokers since the neutrophil ratio: lymphocytes does not differ between marijuana smokers and non-smokers and Govan et al. [24] shows that the slight decline in WBC in smokers remains in the normal range, while Brent [25] shows that peripheral blood leukopenia could be caused in rats by a single oral dose 23–30 mg of cannabinoids/kg weight which could complicate the general bronchitis felt in smokers. In addition, the 15 j/d group shows a very significant increase in eosinophils (M = $305.4/mm^3 \pm 58.47$) (Figure 2d) which in addition to blood circulation, they are also found in tissues near external contact points with the environment and in inflammatory infiltrates; they are clearly active in their protection against foreign substances, such as smoke and cannabinoids [26]. This increase in eosinophils may be an individual response, since each has its own sensitivity; this resistance may be related to the nutritional status of the individual, as well as the dose smoked and the effect of chronicity [27]. Brent [25] explains the increase in eosinophilic rates due to the contamination of cannabis plants with spores from a range of fungi, which may cause eosinophilic secondary pneumonia in smokers, 40% of the patients have a history of smoking cigarettes [28].
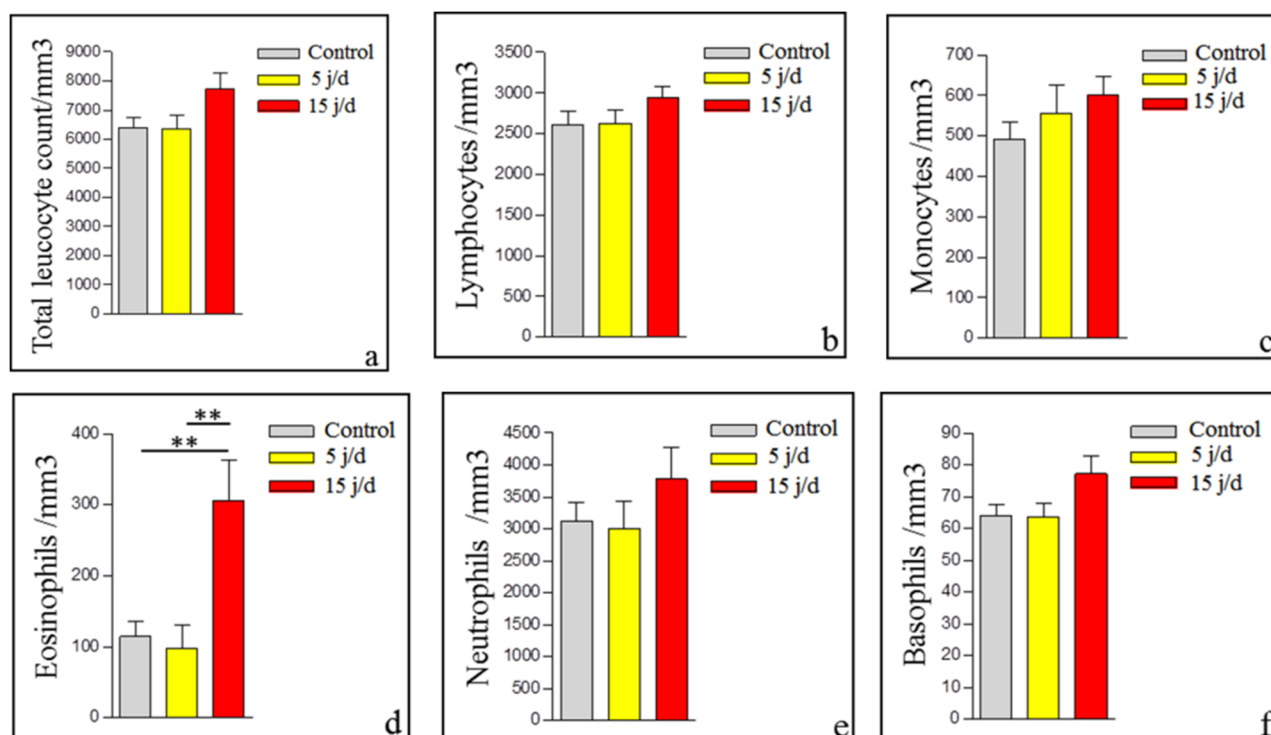
Figure 2. Comparison of means of Total leucocyte count, Neutrophils, Eosinophils, Basophils, Lymphocytes and Monocytes between tests and controls. Value are expressed as mean ± SEM, n = 10, T test. Aserisks indicate the level of significance (*P < 0.05; **P < 0.01; ***P < 0.001).

3.6. Platelets

We found a significant decrease in the 15 j/d group (M= 235600/mm^3 ± 10760; P = 0.0109) compared to the control group (267900/mm^3 ± 3737). While there is no significance of the slight decrease in the 5 j/d group compared to the control group (P = 0.2363) (Figure 3), this is consistent with Oseni BS et al. [29], who worked on the human model. Our result can be explained by peripheral thrombocytopenia (destruction of platelets in the circulation) or central thrombocytopenia (insufficiency of production), the dropping in the level of platelets could cause nasal hemorrhages, intestinal affecting intestinal absorption.
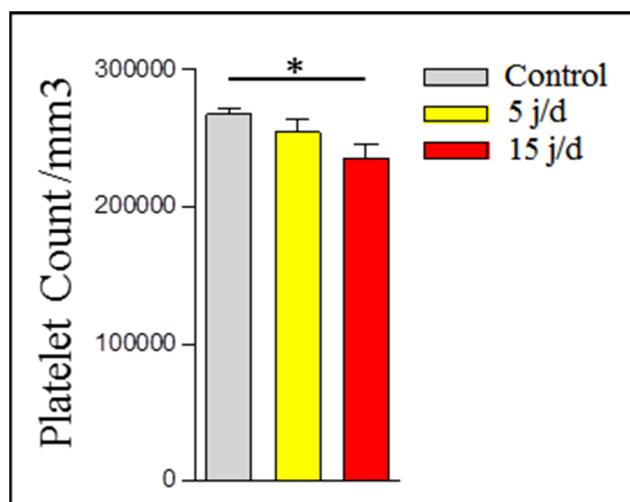
Figure 3. Comparison of means of Platelet Count between tests and controls. Value are expressed as mean ± SEM, n = 10, T test. Aserisks indicate the level of significance (*P < 0.05; **P < 0.01; ***P < 0.001).

3.7. Cholesterol and triglycerides

O Ebuehi's work [9] shows that there is no significant difference in plasma levels of cholesterol, HDL and triglycerides between smokers of cigarettes, marijuana or both and non-smokers, while Waterreus et al. [30] Shows that frequent cannabis use was associated with metabolic risks (increased waist circumference and elevated blood pressure, triglycerides and glucose and low HDL). But the possibility that cannabis use reduces dietary intake through appetite suppression should be considered, this association is consistent with studies that demonstrate reduced weight gain in dietary obese rats fed cannabis extract [31,32] which is consistent with our study, which shows that the duration and quantity of joint consumption reveals significance for triglycerides between the 5 j/d group (M = 1.07 g/l) and the 15 j/d group (M = 0.71 g/l) (Figure 4a), similarly for cholesterol which shows a significant decrease in the 15 j/d group (M = 1.41 g/l) compared to the non-smoking group (M = 1.69 g/l) (Figure 4b). Our result could be explained by the fact that cannabis users neglect their diet. Indeed, cannabis use is associated with low dietary intake among psychosis samples from the first episode [33]; and that each year, increased marijuana use was significantly associated with increased risk of metabolic syndrome and hypertension [34].
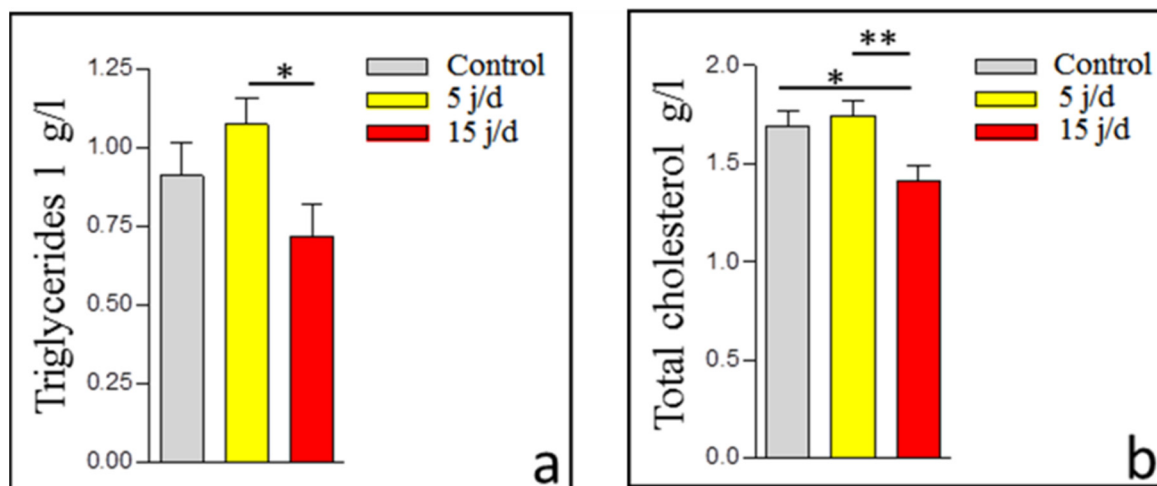
Figure 4. Comparison of means of Total cholesterol and Triglycerides between tests and controls. Value are expressed as mean ± SEM, n = 10, T test. Aserisks indicate the level of significance (*P < 0.05; **P < 0.01; ***P < 0.001).

3.8. Transaminases

Cannabinoids are possible hepatotoxic substances associated with liver morphological and enzymatic alterations [35]. They also intensify alkaline phosphatase (PAL) activity in injected rats and human smokers and this will increase (run up) with increased dose and time but SGOT (Aspartate-Amino-Transferase or [SGOT] = Serum Glutamo Oxaloacetate Transferase) and SGPT (Alanine Aminotransferases [SGPT] GlutamoPyruvate Transferase Serum) increase at the beginning of consumption and will then decrease with time [36]. PTSM is more likely to assess hepatocellular damage than OTMS [15]. In this study, SGOT and SGPT rates decreased significantly among consumers in the group (15 j/d) (Figure 5) this is consistent with previous studies that have shown a significant decrease (or meaningful fall) in these enzymes over time in cannabis smokers compared to controls. Hegde et al. [37,38] reported that cannabinoids such as 9-tetrahydrocannabinol (THC) showed therapeutic potential in the treatment of inflammatory diseases resulting in hepatitis inhibition (significant decrease in liver enzymes and reduction of tissue damage).
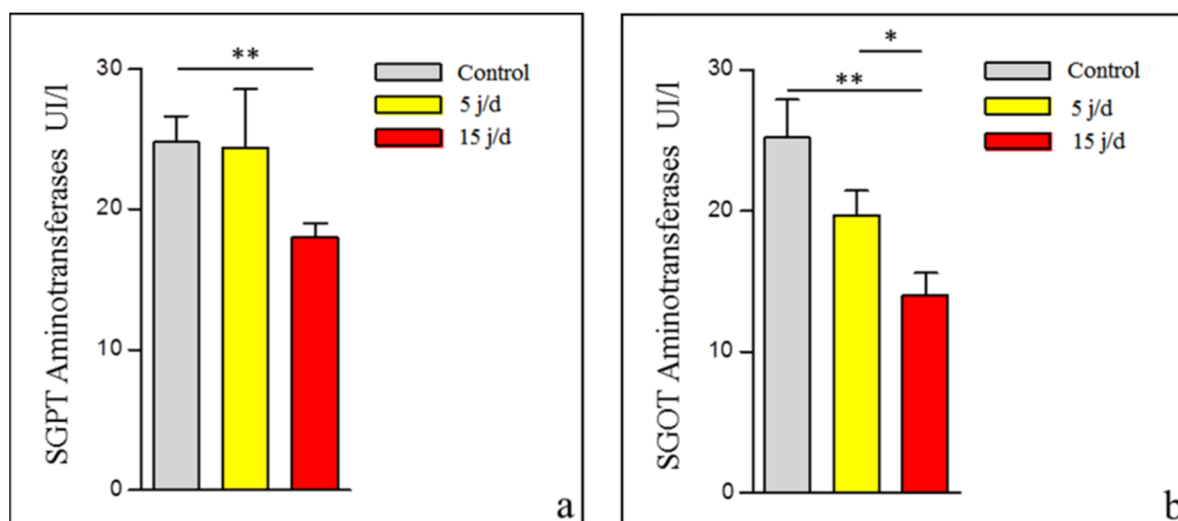
Figure 5. Comparison of means of SGPT and SGOT Aminotransferases between tests and controls. Value are expressed as mean ± SEM, n = 10, T test. Aserisks indicate the level of significance (*P < 0.05; **P < 0.01; ***P < 0.001).

3.9. Urea and creatinine

Urea is the main form of nitrogen waste removal from proteins and amino acids. It is synthesized in the liver (which can often boost and lessen synthesis) when amino acids are degraded. It is then secreted in the blood to be excreted by the kidneys in the urine. Urinary urea concentration is a control of protein intake and reflects kidney function when coupled with blood urea [39]. However, uremia may be influenced by dietary protein intake. Therefore, the dosage of blood creatinine is preferred in order to assess renal function [40].

Creatinine is a degradation product of creatine formed during muscle contraction, its concentration in the blood is rather constant and proportional to muscle mass. Since the kidney is the only way to eliminate creatinine, its measurement makes it possible to evaluate the efficiency of the work of the kidney. By measuring its concentration in blood or urine.

THC is mostly eliminated by the intestinal route and only 30% of a dose of THC is excreted by the kidneys [41] which minimizes the possibility of renal alteration due to any consumption of cannabis. Indeed, an assessment via creanemia in a cross-sectional study in 2018 found no significant association between cannabis use and kidney function (the Glomerular filtration rate) [42].

This study shows a significant decrease in urea levels in the 15 j/d group (Figure 6a), while creatinine levels increased very significantly at the beginning of cannabis use (5 j/d group) (Figure 6b), and since the possibility of kidney damage due to any use of cannabis is negligible according to previous literature, these results can be explained by the fact that cannabis use is associated with low dietary intake [33] resulting in decreased uremia and muscle degradation leading to increased creanemia.
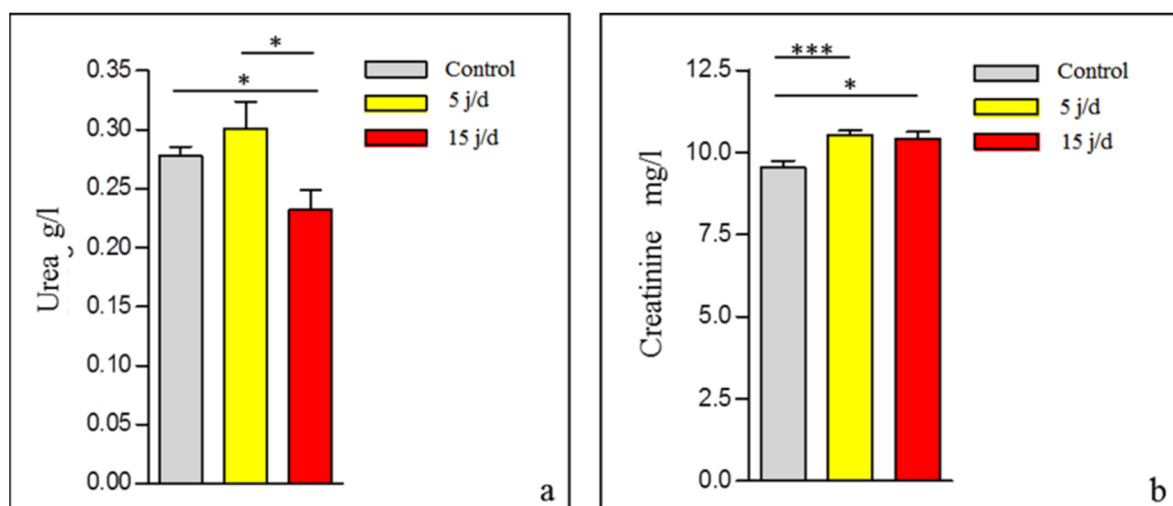
Figure 6. Comparison of means of Urea and Creatinine between tests and controls. Value are expressed as mean ± SEM, n = 10, T test. Aserisks indicate the level of significance (*P < 0.05; **P < 0.01; ***P < 0.001).

4. Conclusions

The present study shows that joint use of cannabis and tobacco leads to a decrease (decline) in blood levels of urea, cholesterol and triglycerides as well as an increase (incline) in creanemia and macrocytic anemia with the duration and number of joints. This could be caused by appetite suppression in consumers, resulting in reduced dietary intake aggravated by poor intestinal absorption, linked to hemorrhages caused by decreased platelet levels. In addition, consumers may still have eosinophilic secondary pneumonia due to chronic respiratory inflammations.

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Conflict of interest

All the authors declare that there are not biomedical financial interests or potential conflicts of interest in writing this manuscript.

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