International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064

Long Term Administration of *Cannabis sativa* Reduces Food, Water Intake and Body Weight in Mice

V. E. Okon[1], A. O. Obembe[2], V. U. Nna[3], E. E. Osim[4]

Department of Physiology, College of Medical Sciences, University of Calabar, Calabar, Nigeria

Abstract: ***The effects of long-term administration of Cannabis sativa on food, water intake and body weight was studied in mice. Twenty seven albino mice (male and female) were used for the experiment. They were assigned randomly into three groups (control, low dose and high dose) containing nine (9) mice each. Group I (the control group) was given 10ml/kg of normal saline. Group II (The low dose group) was administered 10mg/kg/day of Cannabis sativa; Group III (high dose group) was administered 20mg/kg/day Cannabis sativa. Administration was done orally for a period of 4 weeks during which food and water intake were measured daily. Their body weight was taken every two days. The amount of food taken was weighed, subtracted from original weight and recorded. The results showed that the mean daily food intake were significantly lower (P<0.001) for the Cannabis treated groups compared to control; while mean water intake was significantly lower (P<0.01) and (P<0.001) for low dose and high dose groups respectively compared to control. The Cannabis treated groups also had a significantly lower (P<0.001) body weight than their control. In conclusion, long term administration of Cannabis sativa decreases food, water intake and body weight gain.***

Keywords: body weight, *Cannabis sativa*, food intake, mice, water intake

1. Introduction

Pot, weed, grass, ganja and skunk, are some of the common words used to describe the dried leaves of the plant known as Cannabis. Cannabis is a genus of flowering plant that includes three putative species; *Cannabis sativa, Cannabis indica, Cannabis ruderalis* [1]. Each specie has its own unique characteristics, though for the purpose of this research, we will be more concerned with the specie, *Cannabis sativa* due to its psychoactive effect as compared to others.

Cannabis sativa is an annual herbaceous plant in the Cannabaceae family. It has long been used for religious and medicinal purposes, and as a recreational drug (due to its ''psychoactive'', or mind-altering effects). Some therapeutic uses of *Cannabis sativa* include; treatment of spasticity, movement disorders, asthma and glaucoma. It is also used in the treatment of allergies, inflammation and infection [2]. Marijuana is used in the treatment of cancer [3], multiple sclerosis, menstrual pain and chronic pain [4]. It reduces nausea and is used as a muscle relaxant [5,6].

Although it has positive effects, *Cannabis sativa* has been documented in several studies to have a link with symptoms of schizophrenia [7]. Cannabis has also been known to increase focus and concentration. This may be the reason why students use it during their studies. It has also been said to increase one's level of excitement and sleep [6].

More than 61 chemicals called cannabinoids have been identified as specific to the Cannabis plant. Its constituent, tetrahydrocannabinol (THC) is the main psychoactive cannabinoid, most responsible for the 'high' associated with marijuana use [8]. The pharmacological actions of THC result from its partial agonist activity at the cannabinoid receptor CB1, located mainly in the central nervous system [8]. The psychoactive effects of THC have been said to be primarily mediated by its activation of the CB1 G-protein coupled receptors, which results in decrease of the second messenger molecules cAMP through inhibition of adenylate cyclase [9].

Research into the effects of *Cannabis sativa* on the different systems including the nervous system have been investigated but there is still paucity of information as regards its effect on food intake, water intake, and body weight. This study will validate scientifically whether or not *Cannabis sativa* affects food intake, water intake and body weight hoping that it will contribute immensely to the body of knowledge. The results obtained could also explain their observed effects on the health of users.

2. Materials and Methods

2.1 Preparation of *Cannabis sativa* Extract

The leaves of the plant were dried to evaporate its water content and blended using a manual blender into snuff-like particles, and its weight taken. A solution of 80% ethanol and 20% of distilled water was prepared. The particles were then added into the solution and kept overnight (18 hours). At the expiration of 18 hours, the mixture was filtered using Whatman's No. 1 filter paper into a conical flask. The filtrate obtained was dried using Astell Hearson oven at 45^0C. After all the water content in the filtrate had evaporated, the extract was scrapped off and put into an air tight container.

Its weight was determined and recorded. The National Drug and Law Enforcement Agency in Cross River State approved the carrying out of the experiment.

2.2 Animal Care

Twenty seven adult albino mice were housed singly in metabolic cages under standard laboratory conditions in

Physiology Department, University Of Calabar, Calabar with room temperature of 25 ± 2^0C, and where they could observe the dark/light cycle throughout the duration of the experiment. They were fed with normal rat chow and given water freely for one week to allow for acclimatization before commencing the experiment.

2.3 Animal Treatment

Twenty seven albino mice were randomly separated into 3 groups. Group I (the control group) was given 10 ml/kg of normal saline. Group II (The low dose group) was administered 10 mg/kg/day of *Cannabis sativa;* Group III (high dose group) was administered 20 mg/kg/day *Cannabis sativa.* Oral route of administration using an oropharyngeal cannula inserted into a 1ml syringe with detachable needle was used. A small bead was attached to the end of the cannula to avoid injuring the animal's mouth during the process of administration. This was done for a period of 28 days.

2.4 Ethical Approval

All authors hereby declare that "Principles of laboratory animal care" were followed. All experiments have been examined and approved by the appropriate ethics committee.

2.5 Measurement of Food and Water Intake

Each mouse in its metabolic cage was provided with water and food (normal rat chow) in two separate small cups throughout the duration of the experiment. Each day, the leftover food was taken and weighed using a sensitive weighing balance, after which the result was subtracted from the amount that was put for the mice the previous day. This gave the amount of food eaten (food intake) by the animal. This was done for all three groups. For water intake, a 10ml syringe was used to measure the amount of water given to the animals in order to ascertain the amount ingested by the animal by the next day. The amount left was subtracted from the actual amount to give the water intake.

2.6 Measurement of Body Weight

This was done using a sensitive weighing balance. Every 2 days before the animals were cleaned and new feed put into their cups, the weight of each animal was taken by placing an empty small bowl on the weighing balance. Thereafter, the mouse was held by its tail and placed inside the bowl to avoid restraining the animal's movement while recording its weight. Its weight was then taken and recorded.

2.7 Statistical Analysis

Statistical analysis was completed using SPSS for Windows. For all the parameters, the dependant variables were analyzed using ANOVA for repeated measures. Post hoc comparisons were made using the Student-Newman-Keuls design among high dose, low dose administered *Cannabis sativa* and the control groups.

3. Results

3.1 *Comparison of daily food intake among high dose (HD), low dose (LD) Cannabis sativa fed mice, and control*

The daily food intake in the treated mice was each significantly lower (P< 0.001) than control. (Fig. 1)

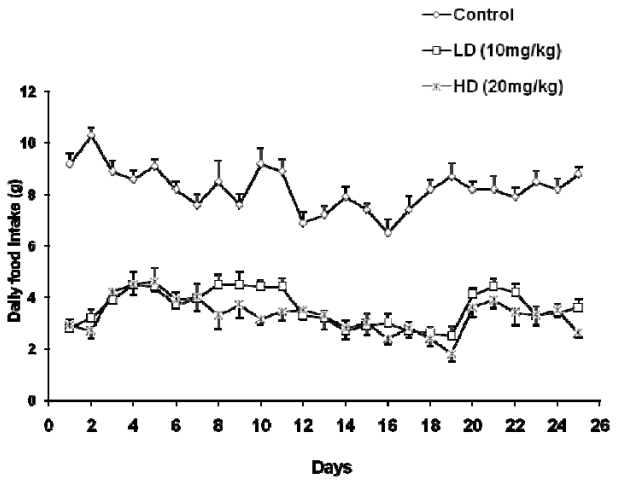

Figure 1: Comparison of daily food intake in the mice following long term administration of *Cannabis sativa*. Values are mean ± SEM, n = 9.

3.2 Comparison of mean food intake for high dose (HD), low dose (LD) *Cannabis sativa*-fed mice, and control

Results for mean food intake showed that mean food intake for LD (3.61±0.14g) and HD (3.31±0.14g) were significantly (P<0.001) lower compared to the control (8.24 ± 0.17g) (Fig 2).

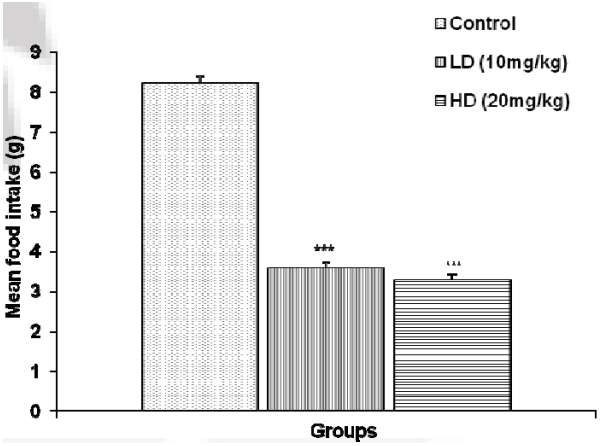

Figure 2: Comparison of mean food intake in *Cannabis sativa* fed mice and control. Values are mean ± SEM, n = 9. ***p<0.001 vs control

3.3 Comparison of daily water intake for high dose (HD), low dose (LD) *Cannabis sativa*-fed mice, and control

Figure 3 shows the daily water intake in the *Cannabis sativa* treated mice was each significantly lower for LD (P< 0.05) and HD (P<0.001) compared to control, though not in all the days as shown by Fig 3.

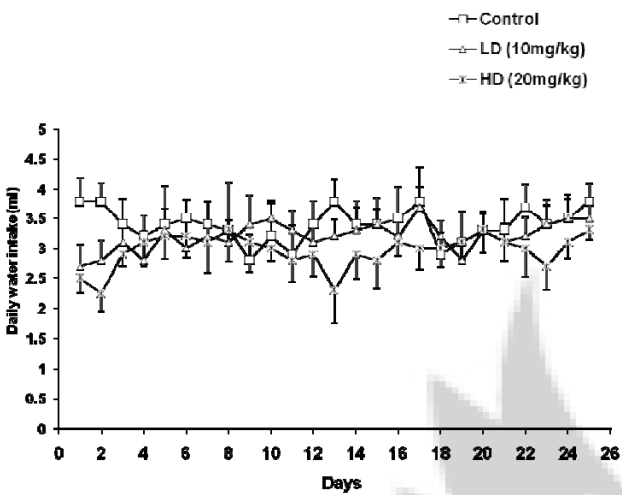

Figure 3: Comparison of daily water intake in the control and *Cannabis sativa* fed mice. Values are mean ± SEM, n = 9

3.4 Comparison of mean water intake for high dose (HD), low dose (LD) *Cannabis sativa* fed mice, and control

The mean water intake values for HD (2.96±0.06ml), and LD (3.20±0.05 ml), were significantly lower for HD (P<0.001) and LD (P<0.05) groups compared to control (3.40±0.06ml). HD was significantly lower (P<0.01) compared to LD groups (Fig.4).

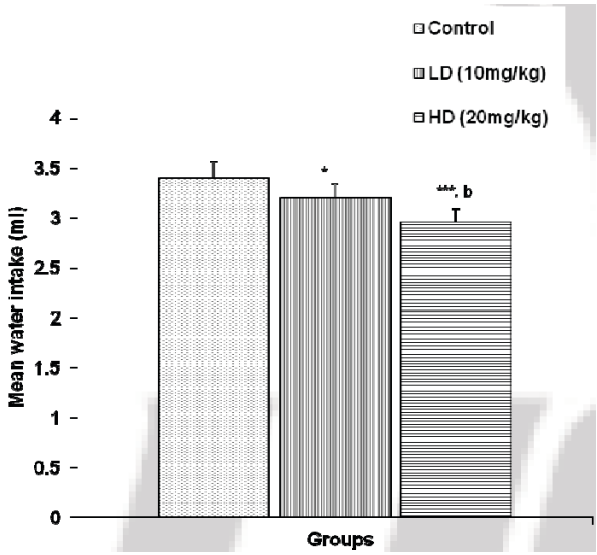

Figure 4: Comparison of mean water intake in *Cannabis sativa* fed mice and control. Values are mean ± SEM, n = 9. *p<0.05, ***p<0.001 vs control; b = p<0.01 vs LD

3.5 Comparison of daily body weight for high dose (HD), low dose (LD) *Cannabis sativa* fed mice, and control

Figure 5 shows the daily body weight in the *Cannabis sativa* treated mice was each significantly lower for LD (P<0.001) and HD (P<0.001) compared to control. The graph shows that there was no significant difference in body weight change among the control and Cannabis - treated mice groups from the beginning of the experiment up to day 18. After day 18, the Cannabis - treated groups showed weight loss (P<0.001) when compared to control at the end of the experiment on day 28 (Fig 5).

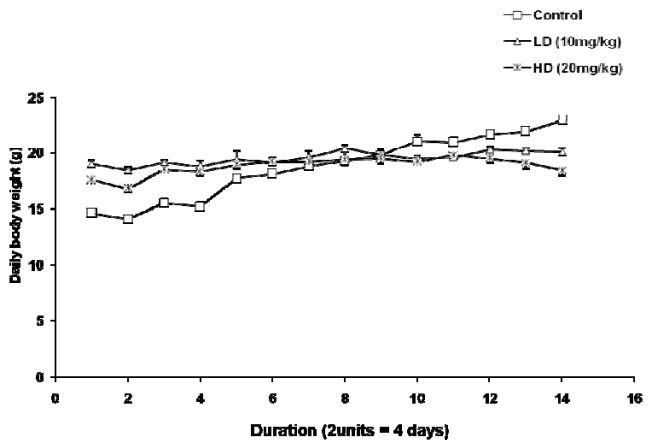

Figure 5: Comparison of daily body weight of the control and *Cannabis sativa* fed mice. Values are mean ± SEM, n = 9

3.6 Comparison of mean body weight change for high dose (HD), low dose (LD) *Cannabis sativa* fed mice, and control

Figure 6 shows the mean body weight change values of HD (18.81±0.22g), LD (19.52±0.16g) and control (18.71±0.79g). The final body weight shows a significant decrease for HD (P<0.05) compared to control. However, there was no significant difference between LD and control.

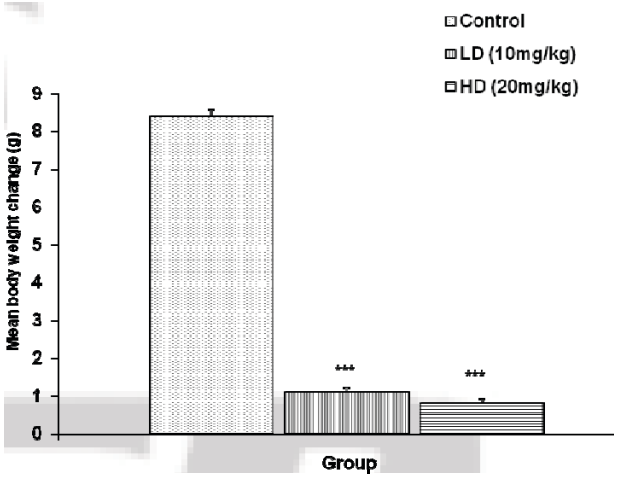

Figure 6: Comparison of mean body weight change in *Cannabis sativa* fed mice and control. Values are mean ± SEM, n = 9. ***p<0.001 vs control

4. Discussion

This study was done in order to investigate the effects of long term administration of *Cannabis sativa* (marijuana) on food intake, water intake, and body weight. The results of mean food and water intake showed that low and high dose *Cannabis sativa* significantly reduced food and water intake compared to their control. This finding contradicts a study done by Bonsor [10] that Cannabis increases food enjoyment and interest in food, known as "the munchies". The reduction in food and water intake could be as a result of the effect of tetrahydrocannabivarin (THCV), a non-psychoactive constituent of *Cannabis sativa.* THCV is believed to oppose the effects of tetrahydrocannabinol

(THC) [11] which increases appetite [12]. It does this by blocking CB1 receptors [13]. CB1 receptors are highly expressed in hypothalamic areas and involved in food intake control and increasing feeding behavior [8].

The reduced body weight observed in the treated dose groups compared to control further supports these results.

The results of this study differ from previous work by other researchers who discovered that Cannabis increases food intake and body weight and this could be due to the species of cannabis used and the duration of use. Even the environment it is grown (virgin land is said to be more potent) influences chemical content and hereditary determinants [14, 15]. In addition, THC has been found to be largely concentrated around the flowering parts of the female plant. The leaves (which were used in this study) and male plants have less THC [16].

5. Conclusion

Cannabis sativa may lead to decreased food intake, water intake, and body weight gain. If these results are applicable to man, then long term administration of *Cannabis sativa* may be dangerous.

Competing Interests

Authors have declared that no competing interests exist.

References

[1] Elsohly M. *Marijuana and the cannabinoids*. Humana Press. 2008. P.8
[2] Grotenhermen F, Russo E. *Review of therapeutic effects: Cannabis and Cannabinoids- Pharmacology, toxicology, and therapeutic potential.* New York, Haworth Press. 2002:pp.123, 439.
[3] Elsohly MA, Harland JC, Murphy PW, Waller CW. Cannabinoids in glaucoma: a primary screening procedure. *Journal of clinical pharmacology*. 1985:21: 472S-478S.
[4] Noyes R, Brunk SF, Avery AD, Canter AC. The analgesic properties of A-9-tetrahydrocannabinol. *Clinical pharmacology and therapy.* 1975:18: 84-89.
[5] Matsuda LA, Lolait SJ, Brownstein MJ. Structure of a cannabinoid receptor and functional expression of the cloned cDNA. *Nature.* 1990:*346*: 561-564.
[6] Hollister LE. Hunger and appetite after single doses of marihuana, alcohol, and dextroamphetamine. *Clinical Pharmacology on Therapy.* 1971:12*:* 44 – 9.
[7] Hall W, Solowij N. Adverse effects of cannabis. *Lancet*. 1998:352(9140):1611–1616.
[8] Pertwee RG. The pharmacology of cannabinoid receptors and their ligands: An overview. *International Journal of Obesity*. 2006:30: S13–S18.
[9] Elphick MR, Egertova M. The neurobiology and evolution of cannabinoid signaling. *Philosophical transactions of the royal society B: Biological Sciences* 2001:356 (1407): 381–408.
[10] Bonsor K. How Marijuana Works. *European Journal of Pharmacology.* 2007:28:164-75.
[11] Pertwee RG, Thomas A, Stevenson LA. The psychoactive plant cannabinoid, delta-9-tetrahydrocannabinol, is antagonized by delta-8-& delta-9-tetrahydrocannabivarin in mice in vivo. *British Journal Pharmacology*. 2007:150(5):586-94.
[12] Turner CE, Bouwsma OJ, Billets S, Elsohly MA. Constituents of Cannabis sativa: LXVIII – Electron voltage selected ion monitoring study of cannabinoids. *Biological Mass Spectrometry*. 1980:7(6): 247–56.
[13] Grotenhermen F. The Toxicology of Cannabis and Cannabis Prohibition. *Chemistry & Biodiversity*. 2007:4 (8): 1744–69.
[14] Kirkham MB. Cadminim in plants, on polluted soils: Effect of soil factors hyper accumulation and amendment. *Geoderma.* 2006:137(1 – 3); 19–32.
[15] Pate DW. Chemical ecology of cannabis. *Journal of international hemp association.* 1994:2(29); 32–37.
[16] Mahlberg PG, Eun SK. THC(tetrahydrocannabinol) accumulation in glands of cannabis (Cannabaceae). *The hemp report,* 2001: 3(17).

Author Profile

V. E. Okon is a post - graduate student, Department of Physiology, College of Medical Sciences, University of Calabar, Calabar, Nigeria.

A. O. Obembe is a Senior Lecturer, Department of Physiology, College of Medical Sciences, University of Calabar, Calabar, Nigeria.

V. U. Nna is a Graduate Assistant, Department of Physiology, College of Medical Sciences, University of Calabar, Calabar, Nigeria.

E. E. Osim is a Professor of Physiology, College of Medical Sciences, University of Calabar, Calabar, Nigeria.