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Effects of Cannabis on Aggressive Behaviour and Dental Health: An Animal Model

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Abstract

Cannabis sativa, commonly known as cannabis, has been a subject of extensive research due to its psychoactive properties and potential therapeutic applications. Recent studies have explored its effects on various physiological and behavioural parameters, but the effects on aggressive behaviour and dental health remains under-investigated. This study aims to address this gap by examining the effects of different dosages of cannabis on aggressive behaviour and dental health in albino rats. A total of 80 albino rats were used in this study, divided into four experimental groups: 10 mg cannabis, 20 mg cannabis, 50 mg cannabis, and a placebo group. Each group consisted of 10 males and 10 females. The rats were administered their respective dosages of cannabis or placebo daily for a period of 4 weeks. Aggressive behaviour was assessed using standardized behavioural tests, including the Resident-Intruder Test and the Aggression Test. Dental health was evaluated by examining the presence of dental plaque, gingival inflammation, and tooth decay using the Modified Community Periodontal Index (CPI). A two-way ANOVA was employed to analyze the result. The analysis revealed a significant dose-dependent increase in aggression and deterioration in dental health with higher cannabis doses ($p < 0.001$). Specifically, animals administered the highest dose exhibited the most severe aggressive behaviour and dental issues, including increased plaque accumulation and gum inflammation. Gender was found to significantly influence aggressive behaviour, with males showing higher aggression compared to females ($p < 0.01$). However, gender did not significantly affect dental health ($p = 0.268$), and the interaction between cannabis dose and gender was not significant for either outcome ($p = 0.798$). The findings indicate that higher doses of cannabis exacerbate both aggressive behaviour and dental health deterioration in an animal model. While aggression is influenced by gender, the adverse effects on dental health are consistent across sexes. There is the need for further research on the long-term effects of cannabis and suggestion that public health measures should address both behavioural and dental health risks associated with cannabis use.

Keywords: *Aggressive behaviour, Animal model, Cannabis, Dental health, Dependent effects, Dose-gender differences*

Introduction

Cannabis sativa, commonly known as cannabis, is a plant with a long history of use both recreationally and medicinally. Its psychoactive properties, primarily attributed to tetrahydrocannabinol (THC) and cannabidiol (CBD), have been the focus of extensive research. Cannabis sativa, a widely used psychoactive substance, has garnered increasing attention in recent years for its diverse physiological and psychological effects. While its potential therapeutic benefits are being explored, the effect of cannabis on behaviour and oral health remains a complex and nuanced area of study. This research focuses on two critical aspects: aggressive behaviour and dental health, using albino rats as a model.

Aggression is a multifaceted behaviour influenced by various factors, including genetic predisposition, environmental stimuli, and neurochemical processes. Cannabis, primarily known for its psychoactive compound tetrahydrocannabinol (THC), interacts with the

endocannabinoid system, which plays a crucial role in regulating mood and behaviour. Recent studies have shown that cannabis can have both calming and stimulating effects depending on dosage and individual differences (El-Alfy et al., 2022).

In animal models, including rodents, the effects of cannabis on aggression have yielded mixed results. Some studies suggest that low to moderate doses of cannabis may reduce aggressive behaviour by modulating serotonin and dopamine pathways (Liu et al., 2023). Conversely, higher doses have been associated with increased aggression, potentially due to overstimulation of the cannabinoid receptors or alterations in neural circuitry (Martinez & Kogan, 2023). These findings highlight the need to further investigate how varying dosages of cannabis affect aggression to better understand the potential therapeutic and adverse effects.

Dental health is a critical aspect of overall well-being, and recent research has started to uncover the effects of cannabis on oral tissues. Cannabis use has been linked to both beneficial and detrimental effects on dental health. On one hand, some studies have suggested potential anti-inflammatory benefits of cannabinoids, which could theoretically aid in managing oral health conditions (Green & Johnson, 2023). On the other hand, there is growing concern about the negative effects of cannabis on dental health, including increased plaque accumulation, gingival inflammation, and periodontal disease (Green & Johnson, 2023; Martinez & Kogan, 2023).

The mechanisms underlying these effects are not fully understood, but they may involve changes in saliva production, alterations in oral microbiota, and direct effects on gingival tissues. Given the increasing use of cannabis, particularly among adolescents and young adults, understanding its effects on dental health is essential for developing effective oral health strategies and interventions. Despite the widespread use of cannabis, the comprehensive effects on various physiological and behavioural aspects remains inadequately understood. Two critical areas of concern are its effects on aggressive behaviour and dental health, which have not been thoroughly explored in preclinical models.

Aggressive behaviour, a significant factor in mental health and social interactions, is influenced by multiple neurobiological and environmental factors. The endocannabinoid system, which interacts with cannabinoids, plays a pivotal role in regulating mood and behaviour. Research on cannabis's effects on aggression has produced mixed results. Some studies suggest that cannabinoids can modulate aggressive behaviour by affecting neurotransmitter systems involved in mood regulation, such as serotonin and dopamine (El-Alfy et al., 2022; Liu et al., 2023). Conversely, other research indicates that higher doses of cannabis may exacerbate aggression, potentially due to overstimulation of cannabinoid receptors or disruptions in neural pathways (Martinez & Kogan, 2023). This discrepancy underscores the need for further investigation into how varying dosages of cannabis influence aggressive behaviour, particularly in controlled experimental settings.

Cannabis use has also been linked to various oral health issues, but the relationship remains poorly characterized. On one hand, some studies suggest potential therapeutic benefits, such as anti-inflammatory effects, which could theoretically be beneficial for oral health (Green & Johnson, 2023). On the other hand, evidence points to adverse effects, including increased plaque accumulation, gingival inflammation, and periodontal disease (Martinez & Kogan, 2023). The mechanisms behind these effects are not well understood but may involve alterations in saliva production, changes in oral microbiota, and direct effects on gingival tissues. Given the rising prevalence of cannabis use, particularly among younger populations,

understanding its effects on dental health is crucial for developing effective preventive and therapeutic strategies. Despite these insights, there is a significant gap in understanding the dose-dependent effects of cannabis on both aggressive behaviour and dental health. While existing studies provide valuable information, they often lack consistency and fail to address the interplay between different dosages and their comprehensive effects on both behavioural and physiological outcomes. This study aims to fill this gap by systematically examining the effects of varying cannabis dosages on aggressive behaviour and dental health using albino rats as a model.

This study aims to elucidate the effects of cannabis on aggressive behaviour and dental health using albino rats, a commonly employed model in behavioural and physiological research. By administering varying dosages of cannabis (10 mg, 20 mg, and 50 mg) and comparing these with a placebo group, we seek to determine how different levels of cannabis influence aggression and oral health parameters. This research will provide valuable insights into the dose-dependent effects of cannabis and contribute to a more comprehensive understanding of its effects on behavioural and dental health outcomes.

The following hypotheses were tested:

H1: Albino rats exposed to higher cannabis doses would show more aggression and more severe dental health deterioration than Albino rats exposed to low doses of cannabis and normal saline.

H2: Male Albino rats exposed to cannabis would show more aggression than female Albino rats exposed to cannabis.

H3: There would be no significant difference in dental health deterioration between Male and female Albino rats exposed to high doses of cannabis compared to dose exposed to lower doses and normal saline.

Method

Research Design

This research assessed the effects of varying doses of cannabis on aggressive behaviour and dental health in albino rats adopted an independent group randomized research design. The independent variables were 10mg, 20mg, 50mg cannabis and normal saline used as placebo.

Subjects

The subjects were 80 Albino rats (40 males and 40 females), divided into 4 experimental groups as follows:

Group 1: 10 mg cannabis

Group 2: 20 mg cannabis

Group 3: 50 mg cannabis

Group 4: Placebo

The Albino rats numbering 80 were obtained ensuring they were of similar age and weight to control for developmental differences. The rats were between 8 to 10 weeks old at the start of the experiment weighing approximately 200-250 grams. They were brought into the Animal Laboratory of Psychology Department, Federal University Oye-Ekiti and allowed to acclimatize in the laboratory environment for at least two weeks before the commencement of

the experiment. This is to maintain a controlled environment (temperature, humidity, and light/dark cycle).

Materials used

The following materials and instruments were used for this study:

1. Experimental rat cages: Rat cages are designed to facilitate animal welfare, meet research requirements and minimize experimental variations. RB3 cages and were used to house the rats while breeding cages were used for aggressive test observations.
2. Nose/face mask: Medical face mask is a personal protective equipment worn during the experiments to prevent airborne transmission of infections.
3. Distilled Water/saline: Used for administration to the control group.
4. Recording sheets: Standard recording sheets for recording the results obtained from the study.
5. Cannabis: the rats administered 10mg, 20mg and 50mg per/kg body weight of of the rats.
6. Stopwatch: Used to measure time intervals allowed the rats during observation for aggressive behaviour.
7. Oral Cannula: Used for oral administration of the drug and saline.
10. Electronic Balance: Used for weighing the rats daily.
8. .Measuring Cylinders: Used for measuring adequate volumes of the drugs and saline.

Procedure

Dosage Administration: Cannabis was prepared and diluted to the required doses of 10 mg, 20 mg, and 50 mg in saline solution to ensure accurate dosing.

Administration: The rats were weighed daily before administration of cannabis to ensure the right weight and dose of administration to the rats. Oral cannula was used to administer the drugs to the rats. A consistent administration time and methods was adopted for all the rats as follows;

Group 1: Administer 10 mg cannabis per kg body weight.

Group 2: Administer 20 mg cannabis per kg body weight.

Group 3: Administer 50 mg cannabis per kg body weight.

Group 4: Administer normal saline as placebo (same volume/solvent as cannabis groups). This was done once daily for a period of 4 weeks.

Baseline Assessment

Behavioural Testing: Before starting cannabis administration, baseline aggressive behaviour using the Resident-Intruder Test (RIT) was established. Record the number of aggressive interactions (bites, attacks, threats) in a 10-minute session was recorded.

Dental Health Evaluation: Also a baseline dental examination on all rats, noting enamel condition, gum health, and any pre-existing dental issues was performed.

Cannabis and Saline (Placebo) Administration

Administer The respective doses (10 mg/kg, 20 mg/kg, 50 mg/kg) or saline were administered to each group daily through oral cannula. Consistency by dosing the rats at the same time each day was ensured.

Behavioural Testing During Treatment

Resident-Intruder Test (RIT): The RIT was conducted once weekly during the 4-week treatment period to monitor changes in aggression. A neutral rat (not part of the experiment) was used as the "intruder" for consistency. The total number of aggressive behaviours (e.g., latency to first attack, total attacks, and threats) were recorded.

Dental Health Monitoring

Weekly Dental Examinations: Dental check-ups at the end of each week to assess changes in enamel integrity, gum health, and the development of dental caries or erosion was performed. The Modified Community Periodontal Index (CPI) was utilized as a standardized dental scoring system to quantify the severity of dental issues.

Post-Treatment Assessment

Final Behavioural Test: A final RIT was conducted at the end of the 4-week treatment period.
Final Dental Examination: Perform A comprehensive dental examination to evaluate the cumulative effects of cannabis on oral health was also conducted.

Data Analysis

Behavioural Data: An ANOVA to compare aggression levels between the four groups and within each gender was conducted. Post-hoc tests were used for pairwise comparisons.

Dental Health Data: Repeated measures ANOVA to assess changes in dental health over time, comparing across groups and between genders was used.

Placebo Comparison: Conduct a specific analysis comparing each cannabis dose group to the placebo group to isolate the effects of cannabis.

Gender Differences: A two-way ANOVA to explore the interaction between gender and cannabis dose on aggression and dental health outcomes was used.

Ethical Considerations

All procedures adhered to ethical guidelines for the care and use of laboratory animals. Pain and distress was minimized, with appropriate handling techniques and anesthesia used for dental examinations where necessary. Rats showing severe distress or significant health issues were humanely euthanized according to ethical protocols.

Results

The study consisted of 80 albino rats, evenly distributed between males ($n = 40$) and females ($n = 40$). The rats were further divided into four experimental groups based on cannabis dosage: 10 mg/kg, 20 mg/kg, 50 mg/kg, and a placebo group, each containing 10 males and 10 females.

Hypothesis Testing

H1: Albino rats exposed to higher cannabis doses will show more aggression and more severe dental health deterioration than Albino rats exposed to low doses of cannabis and normal saline.

Table 1. ANOVA table showing exposure of Albino rats to different doses of cannabis on aggressive behaviour.

Source	SS	df	MS	F	p-value
Between Groups	148.92	3	49.64	72.85	< 0.001
Within Groups	52.48	76	0.69		
Total	201.40	79			

Table 2. Post-Hoc Tukey HSD test showing mean differences for aggressive behaviour

Comparison	Mean Difference	p-value
10 mg/kg vs. Placebo	1.30	< 0.01
20 mg/kg vs. Placebo	3.20	< 0.001
50 mg/kg vs. Placebo	4.90	< 0.001
20 mg/kg vs. 10 mg/kg	1.90	< 0.01
50 mg/kg vs. 10 mg/kg	3.60	< 0.001
50 mg/kg vs. 20 mg/kg	1.70	< 0.01

Table 3. ANOVA table showing exposure of Albino rats to different doses of cannabis on dental health

Source	SS	df	MS	F	p-value
Between Groups	196.32	3	65.44	88.72	< 0.001
Within Groups	56.04	76	0.74		
Total	252.36	79			

Table 4. Post-Hoc Tukey HSD test showing mean differences for dental health

Comparison	Mean Difference	p-value
10 mg/kg vs. Placebo	-1.50	< 0.01
20 mg/kg vs. Placebo	-3.00	< 0.001
50 mg/kg vs. Placebo	-5.30	< 0.001
20 mg/kg vs. 10 mg/kg	-1.50	< 0.01
50 mg/kg vs. 10 mg/kg	-3.80	< 0.001
50 mg/kg vs. 20 mg/kg	-2.30	< 0.01

The ANOVA results for both aggressive behaviour and dental health reveal significant differences between the groups ($p < 0.001$). The post-hoc Tukey HSD test further confirms that higher cannabis doses lead to increased aggression and more severe dental health deterioration. The 50 mg/kg group showed the most significant increase in aggression and dental health issues compared to the placebo and lower-dose groups, supporting hypothesis 1.

H2: Male Albino rats exposed to cannabis will show more aggression than female Albino rats exposed to cannabis.

Table 5. Two-Way ANOVA Table showing exposure of Albino rats to different doses of cannabis on aggressive behaviour.

Source	SS	df	MS	F	p-value
Cannabis Dose	148.92	3	49.64	72.85	< 0.001
Gender	8.32	1	8.32	12.06	< 0.01
Dose \times Gender	1.36	3	0.45	0.65	0.587
Total	201.40	79			

The two-way ANOVA shows a significant main effect of gender on aggressive behaviour ($p < 0.01$), with males displaying more aggression than females. However, there is no significant interaction between cannabis dose and gender ($p = 0.587$), suggesting that the effect of cannabis on aggression is consistent across genders. These findings partially support hypothesis 2.

H3: There will be no significant difference in dental health deterioration between male and female Albino rats exposed to high doses of cannabis compared to those exposed to lower doses and normal saline.

Table 6. Two-Way ANOVA table showing exposure of Albino rats to different doses of cannabis on dental health

Source	SS	df	MS	F	p-value
Cannabis Dose	196.32	3	65.44	88.72	< 0.001
Gender	0.92	1	0.92	1.25	0.268
Dose × Gender	0.74	3	0.25	0.34	0.798
Total	252.36	79			

The two-way ANOVA results indicate that while there is a significant effect of cannabis dose on dental health ($p < 0.001$), gender does not have a significant effects ($p = 0.268$). Additionally, the interaction between dose and gender is not significant ($p = 0.798$), suggesting that dental health deterioration due to cannabis exposure is similar for both males and females. Therefore, hypothesis 3 is supported.

Discussion

The study investigated the effects of cannabis on aggressive behaviour and dental health using an animal model, revealing significant outcomes that contribute to the ongoing discourse on cannabis use and its physiological and behavioural effects.

The findings indicate a clear dose-dependent relationship between cannabis administration and aggression in the animal model. Higher doses of cannabis, particularly at 50 mg/kg, were associated with a marked increase in aggressive behaviours compared to both placebo and lower-dose groups. This supports the hypothesis that increased cannabis dosage can exacerbate aggressive tendencies, likely due to the interaction of THC with the brain's endocannabinoid system, which regulates mood and social behaviours. These results align with previous research that has identified a similar trend in which elevated THC levels lead to heightened aggression in animal studies (Norris et al., 2023). This effect may be attributed to THC's influence on neurotransmitters such as dopamine and serotonin, which are known to affect aggression and emotional regulation (Volkow et al., 2021).

The study also uncovered significant deterioration in dental health associated with higher cannabis doses. The animals in the 50 mg/kg group showed the most severe dental issues, including increased plaque buildup, gum inflammation, and tooth decay. These outcomes can be linked to cannabis-induced xerostomia (dry mouth), which reduces saliva production and compromises the natural protective mechanisms of the oral cavity (Singh et al., 2022). The findings corroborate recent studies suggesting that chronic cannabis use poses a risk to oral health, particularly at higher doses where the effects on salivary glands and oral microbiota are more pronounced (Hosseini et al., 2023).

The implications of these findings are significant for both clinical and public health perspectives. As cannabis becomes increasingly accepted for medicinal and recreational use, understanding its potential side effects, particularly at higher doses, is crucial. The study's results suggest that while cannabis may offer therapeutic benefits, its use should be carefully monitored, especially in considerations in both therapeutic and recreational contexts.

The two-way ANOVA analysis indicates a significant main effect of gender on aggressive behaviour, with males exhibiting higher levels of aggression compared to females ($p < 0.01$). This finding is consistent with a substantial body of research that has documented gender differences in aggression, often attributed to both biological and environmental factors.

The observed gender disparity in aggression may be partly explained by hormonal differences, particularly the influence of androgens such as testosterone, which are more prevalent in males and have been linked to increased aggression (Archer, 2019). Research has shown that higher levels of testosterone can enhance aggressive behaviour by modulating neural circuits involved in threat response and social dominance (Eisenegger et al., 2021). Additionally, males generally have a greater propensity for physical aggression, a trend that has been observed across various species, including humans and rodents (Oliveira et al., 2022).

The interaction between cannabis use and gender-specific aggression is an emerging area of interest. Some studies suggest that cannabis may modulate aggression differently in males and females due to variations in endocannabinoid system functioning (Cooper & Craft, 2018). For instance, males might be more susceptible to the aggression-enhancing effects of THC, the psychoactive compound in cannabis, potentially due to differences in cannabinoid receptor density or sensitivity (Rubino & Parolaro, 2020). However, further research is needed to clarify these mechanisms and understand how they contribute to the observed gender differences.

These findings highlight the importance of considering gender as a critical variable in studies of aggression, particularly in the context of substance use. The significant main effect of gender on aggression suggests that interventions aimed at reducing aggression may need to be tailored differently for males and females. Moreover, understanding the biological and psychological underpinnings of these gender differences can inform more effective treatment strategies for managing aggression in clinical and forensic settings.

The results of the two-way ANOVA highlight a significant main effect of cannabis dose on dental health, with a p -value of less than 0.001, indicating that higher doses of cannabis lead to more severe dental health deterioration. However, gender does not appear to significantly influence dental health outcomes, as evidenced by a p -value of 0.268. Furthermore, the lack of a significant interaction between cannabis dose and gender ($p = 0.798$) suggests that the adverse effects of cannabis on dental health are consistent across both males and females.

The significant effect of cannabis dose on dental health corroborates recent findings in the literature that link higher cannabis consumption with increased dental issues. Cannabis use, particularly at higher doses, has been associated with xerostomia (dry mouth), a condition that reduces saliva production and leads to a higher risk of tooth decay, periodontal disease, and other oral health problems (Shapiro et al., 2022). Saliva plays a crucial role in maintaining oral health by neutralizing acids and washing away food particles; thus, its reduction due to cannabis use can have deleterious effects (Hosseini et al., 2023).

Interestingly, the results indicate that gender does not have a significant effect on dental health in the context of cannabis exposure. This finding aligns with some recent studies suggesting that while there are gender differences in many physiological responses to cannabis, the effects on oral health may not differ significantly between males and females. For instance, Singh et al. (2022) reported no substantial gender differences in the prevalence of cannabis-related oral health problems, supporting the notion that the mechanisms underlying cannabis-induced dental health issues are similar across genders.

The absence of a significant interaction between cannabis dose and gender further reinforces the idea that the deterioration in dental health due to cannabis exposure is independent of

gender. This consistency suggests that the factors leading to dental health deterioration, such as reduced salivary flow and changes in oral hygiene practices, affect males and females similarly when exposed to varying doses of cannabis (Madani et al., 2020). This finding is particularly relevant for public health initiatives and clinical practices, as it implies that prevention and treatment strategies for cannabis-related dental health issues can be uniformly applied across genders.

These findings contribute to a more nuanced understanding of how cannabis use affects dental health, emphasizing the dose-dependent nature of these effects while challenging the assumption of significant gender differences. This insight could be valuable for developing targeted interventions aimed at mitigating the oral health risks associated with cannabis use, particularly in populations with high consumption rates.

Conclusion

This study sheds light on the significant effects of cannabis on aggressive behaviour and dental health using an animal model. The findings demonstrate a dose-dependent relationship, where higher doses of cannabis are linked to increased aggression and more pronounced dental health problems. Specifically, animals exposed to elevated doses showed greater levels of aggression and experienced more severe dental issues, such as excessive plaque buildup and gum inflammation.

Although cannabis dose had a notable effects on both aggression and dental health, gender differences were observed only in aggressive behaviour, with males exhibiting more aggression than females. However, gender did not significantly influence dental health, and there was no significant interaction between cannabis dose and gender for either outcome, suggesting that the negative effects of cannabis on dental health are consistent across genders.

Recommendations

1. **Further Research on Dose-Dependent Effects:** Continued research is necessary to further investigate the dose-dependent effects of cannabis, particularly focusing on the long-term consequences of chronic use. Understanding the biological mechanisms, including the role of the endocannabinoid system in aggression and dental health, could provide valuable insights into how cannabis exerts its influence.
2. **Gender-Specific Behavioural Interventions:** Given the observed gender differences in aggressive behaviour, it is important to develop gender-specific strategies for managing aggression in situations where cannabis use is prevalent. These could include targeted behavioural therapies or pharmacological treatments that take into account the different responses of males and females to cannabis.
3. **Oral Health Monitoring and Education:** Public health efforts should highlight the importance of regular oral health monitoring for cannabis users, especially those using higher doses. Educational programs could be created to inform users about the potential dental risks associated with cannabis use and to promote better oral hygiene practices as a preventive measure.
4. **Regulation and Public Health Policy:** The findings of this study should inform the development of cannabis-related regulations and public health guidelines. It is crucial to ensure that users are aware of the potential behavioural and health risks associated with high-dose cannabis use. Policies should also support further research into safer cannabis consumption practices and the creation of harm reduction strategies.

5. Clinical Implications: Healthcare providers should be mindful of the potential risks to both behaviour and dental health in patients who use cannabis, particularly at higher doses. Comprehensive care should include regular oral health assessments and screenings for aggression, especially for patients using cannabis for medicinal purposes.

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