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Effects of Separate and Combined Chronic Ingestion of Codeine and Tramadol on Self Grooming Behavior of Male and Female Albino Rats

Shyngle Kolawole Balogun*, Peter Oluwafemi Famakinde, Deborah Yetunde Adebayo, Godwin Atue

Department of Psychology, University of Ibadan, Ibadan, Nigeria

Email address:
shyngle61@yahoo.com (S. K. Balogun)

*Corresponding author

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Abstract: Rodent self-grooming comprises behaviors devoted to caring of the body surface; presentations that have apparent stereotyped and recurring characteristics which makes rodent grooming a appropriate translational tool for studying the effects of substance abuse in humans. Two opioids, codeine and tramadol, both used for the relief of mild to moderately severe pain but overtime has been abused by people to relieve emotional pain were considered in this study. 54 male and female albino rats (24 females and 30 males) with weight ranging from 120g-180g rats were assigned to three experimental groups (codeine, tramadol and combined group) and one control group. In the study, 6 rats were assigned per group. Rats in the codeine group were orally administered 8mg/kg of codeine while rats in the tramadol group were administered with 20mg/kg of tramadol. Rats in the combined group were administered both 8mg/kg of codeine and 10mg/kg of tramadol. Female rats exposed to chronic intake of Tramadol only (Mean =3.14) were found to significantly displayed more body licking grooming behavior compared to female rats administered Codeine only (Mean = 1.33), combination of Codeine and Tramadol (mean = .67) and the control (mean =1.79) ($p < .001$). Whereas, male rats in the control (mean = 4.23) significantly displayed more body licking grooming behavior compared to male rats administered Codeine only (mean = 3.01), Tramadol only (mean = 3.35), and the combination of Codeine and Tramadol (mean = 2.49) ($p < .05$). Also, female rats exposed to chronic intake of Codeine only (mean = 4.92), significantly displayed more daily face washing grooming behavior compared to female rats administered Tramadol only (mean = 3.33), combination of Codeine and Tramadol (mean = 3.29) and the control group (mean = 4.76) ($p < .001$). Whereas, male rats exposed to chronic intake of Codeine only (mean = 4.92), significantly displayed more daily face washing grooming behavior compared to male rats administered Tramadol only (mean = 3.33), combination of Codeine and Tramadol (mean = 3.29) and the control group (mean = 4.76) ($p < .001$). The findings demonstrated that chronic administration of opioids, codeine and tramadol affected grooming behaviors i.e. face washing and body licking behaviors which are related to possible deterioration of physical appearance and personal grooming habits in humans. Hence, the study suggests that further exploration to unravel the risks related to the consistent consumption of codeine and tramadol on other body systems be considered.

Keywords: Codeine, Self-grooming, Tramadol, Wister Rats

1. Introduction

Self-grooming in animals is an innate behaviour that is involved in hygiene maintenance and other physiologically important processes, including thermoregulation, social communication and de-arousal (1). It is one of the most frequently observed behaviours in rodents and has a patterned, sequential organization. In rodents, typical grooming behaviour shows a general pattern of head-to-toe progression (paw licking – nose/face wash – body wash – tail/genitals wash) (2). Grooming behaviour can serve other functions, such as stimulation of the skin, social interaction,

and arousal, and it can be associated with stress [1].

Self-grooming is remarkably observable in different animals. Even humans engage in self-grooming, and this behaviour shows some similarity to that seen in other animals [2]. Human self-grooming behaviour, however, can become pathological, for example, during stressful conditions or in certain neuropsychiatric disorders. The assessment of rodent self-grooming is potentially useful for translational scientific practice, as unusual rodent self-grooming can be related to human disorders in which abnormal self-grooming is a symptom.

However, animal self-grooming cannot be considered an exact replica of any particular human behaviour. Rather, the broader value of rodent self-grooming is as a representation of complex repetitive, self-directed and sequentially patterned behaviors. Rodent self-grooming is an important behavioral phenotype that can be used to understand the neural basis of complex action patterns in other species, including humans, in both normal and abnormal conditions.

Like all other human behaviour, self-grooming can be affected by substance use and abuse. Substance abuse and addiction are enormous public health concerns that affect society and public policy in multiple arenas, including health care, education, worker productivity, criminal law, and prison systems. The costs of this situation to society are substantial. Animal studies have however been crucial in understanding the biology and patho-physiology of drug addiction and substance abuse. Early demonstrations that drugs could serve as reinforcers maintaining operant behavior in laboratory animals led to the development of a model of human drug abuse [3].

Normally, rodents show increased grooming during both low and high levels of stress. Low levels of stress can increase spontaneous grooming, and it occurs as a transition between other activities [4]; while elevated levels of stress can increase grooming activity as a response to novel environments [5]. Despite the fact that genetic factors appear to play an important role in the regulation of rodent grooming and that various genetic manipulations have been reported to produce robust grooming phenotypes in mice [6, 7], it is agreed that psychoactive substances can be important in the development of these phenotypes [8]. Hence, this study considered the effect of two psychoactive substances that seem quite rampant among youths and adolescents today, codeine and tramadol; both substances are opioids.

Codeine, also known as 3-methylmorphine, is an opiate used to treat pain [9] as a cough medicine, and for diarrhea [10]. It is considered to be a moderate-potency opioid, and it is often suggested for the treatment of pain in the neonatal period, infancy, and childhood. It is typically used to treat mild to moderate degrees of pain. Common adverse effects associated with the use of codeine include drowsiness and constipation. As with all opiates, longer term effects can vary, but can include diminished libido, apathy and memory loss. Some people may also have an allergic reaction to codeine, such as the swelling of skin and rashes.

Tramadol, on the other hand is an opioid-like analgesic used in human and veterinary medicine. Among other reasons, tramadol was chosen because it induces less severe side effects than other opioids [11]. Tramadol is a centrally acting analgesic with both opioid-like and non-opioid-like properties. With its dual mechanism of action (μ-opioid receptor agonist and a monoaminergic mode of action), tramadol provides pain therapy at multiple levels [12]. Researchers have reported that tramadol works on both acute pain (e.g., trauma and renal or biliary colic) and chronic pain (e.g., malignant, nonmalignant and neuropathic) and that it is highly effective in controlling pain caused by urinary stones in rats [13].

Codeine and tramadol, both opioids, mimic the action of endogenous opioid peptides in the body by interacting with opioid receptor subtypes. Multimodal analgesia, which is the combination of analgesic agents, has been said to offer important benefits in the management of both acute and chronic pain. The mixture of different analgesic agents can achieve improved efficacy and/or tolerability and safety compared to equianalgesic doses of the individual drugs. Combining different agents also enhances efficacy in complex pain conditions involving multiple causes [14].

Although these opioids have true positive use, abusers often get dependent on them because it enhances sexual drive/prolong ejaculation, gives extra energy for manual workers, euphoria (tramadol can produce euphoria comparable to heroin even at a single dose of 75mg), staying alert for long hours especially for commercial vehicle drivers and their mate(s) & students making them dazed and easily drift to deep restful sleep, among other things.

Considering the background mentioned above, the purpose of this study was to examine the independent and combined/interactive effects of codeine and tramadol in the grooming behaviour of male and female rats.

2. Methods

Research Design

The design for this study is the experimental-control group randomized subject design; participants were randomly assigned to four groups based on their weights, 8mg/ kg and 20mg/kg respectively. The independent variables are codeine, tramadol, combination of both which was administered, while the dependent variable is self-grooming behavior (face washing & body licking). The rats were divided into four groups; the first group was administered codeine, the second group was administered tramadol, the third group was administered the combination of codeine and tramadol and the fourth group which was the control group was administered saline. All groups were matched on gender.

Setting

The experiment took place at the animal science laboratory in the department of Animal Science, Faculty of Agriculture, University of Ibadan. The laboratory is situated on the last floor, which is the fourth floor of the animal science building, the laboratory consist of four (4) sinks, metal cages, measuring cylinders, slabs, small feed and water containers, a

few tables and chairs. The laboratory is much well ventilated and averagely spaced, though there was no provision of water and electricity.

Subjects

The subjects of the study were 54 albino rats, 24 females and 30 males with weight ranging from 120g-180g, purchased from the department of physiology, university of Ibadan. They had neither laboratory experience nor previous drug history. The animals were housed in RB3 plastic cages (North Kent Plastic Cages Ltd. With metal grill and plastic tray underneath it). They were later divided into experimental and control groups. There were 18 rats in the experimental group (6 rats for codeine group, 6 rats for tramadol group and 6 rats in combined group) and 6 rats in the control group. The rats were housed in the laboratory under normal day and night condition with access to unlimited food and water during the period they were meant to be acclimatized to the laboratory.

Subjects were left in this housing arrangement for three weeks to acclimatize them to the laboratory environment. For easy identification, the subjects were numbered with markers. Small one ring identifies number one, two rings for number two, three rings for number three, four rings for number four, a large single ring for number five and number six had one large ring with another small ring.

Equipment

The following materials were used in conducting the experiment:

1) Four North Kent Plastic Cages (38 x 25 x 18cm)
2) A big observational cage
3) Weighing Balance
4) Distilled Water
5) Codeine (cough syrup)
6) Tramadol
7) Tunnel and Measuring cylinder used in measuring and diluting the solution
8) Oral canola
9) Blue, red and black marker
10) Paper type
11) Disposable syringes
12) Recording sheet
13) Stop watch
14) Detergent and disinfectant
15) Hand gloves and facial masks.
16) Laboratory

Procedure

Twenty-four (24) female albino rats were housed in cages at the laboratory. At first, they were acclimatized for a period of 3 weeks before the commencement of the experiment. During this period, food and water were freely available without any form of deprivation. Rats that were to be in the experimental group as well as the control group were randomly selected. Four groups were used in the course of the experiment. The codeine group, tramadol group and the combined group served as the experimental group with 6 rats each and the control group had 6 rats a well.

The study took 28 days in which the rats in the experimental group were exposed to treatment, that is, they were orally given codeine and tramadol with the use of oral cannular throughout the period of the experiment while the control group were treated with placebo (distilled water).

On the test days, the rats were weighed first before administration of drugs because the volume of codeine, tramadol and water given to the rats depend on the body weight of the rats. Rats in the codeine group were orally given 8mg/kg of codeine while rats in the tramadol group were treated with 20mg/kg of tramadol. Rats in the combined group took both 8mg/kg of codeine and 10mg/kg of tramadol. After the treatment of the rats, recording of data started 30 minutes after all the groups were treated

Self grooming behavior was determined by putting individual rats in the observation cage for five minutes and recording the number of times the rat washed its face and licked its body.

At each day of the experiment, the following operations were rammed out.

1) Weighing of each rat
2) Removal of water and containers from cages
3) Oral administration of codeine, tramadol and water in experimental and control groups respectively
4) Giving the treated rats food and water
5) Observation of self grooming behavior

Drug Preparation

Codeine preparation

Cough syrup with 220mg of codeine was used for the experiment. Since the drug was already in liquid form, it was not diluted; rather, the weights of the rats determined the amount of the syrup to administer. 8mg/kg was the dosage used for the experiment.

Tramadol preparation

Each 50mg capsule of tramadol hcl was dissolved in 5ml of distilled water and so as to avoid wastage and drug potency, only the volume needed for short periods of time were prepared. 20mg/kg was the dosage used for the experiment.

Statistical Analysis

For the test sessions, the analyses compared responses averaged over blocks of three trials. Randomized Block Analysis of Variance (ANOVA), were used to assess differences based on between group and within subject factors. Post hoc comparisons were performed using the Least Significant Difference test. In all cases, the significance level was set at $p \leq .05$.

3. Results

Hypothesis I

There will be a significant difference in body licking behavior among male and female rats ingested with different drugs. This hypothesis was tested using the Randomized Block ANOVA and the result presented in tables 1 and 2.

Table 1. *Summary Randomized Block ANOVA table showing the influence exposure to chronic intake of psychoactive drugs (Codeine & Tramadol) on body licking grooming behavior among female Wister rats.*

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial η^2
Block	144.733	2	72.367	13.664	.000	.013
Treatment	1648.446	3	549.482	103.751	.000	.134
Error	10645.247	2010	5.296			
Corrected Total	12438.427	2015				

The result from Table 1 shows that exposure to chronic intake of psychoactive drugs (Codeine & Tramadol) significantly affect the body licking grooming behavior among female Wister rats F (3, 2015) = 103.75, $p < 0.001$, η^2=.134. The result demonstrated that body licking behaviour increased by 13.4% with exposure to chronic intake of psychoactive drugs (Codeine & Tramadol) compared to the control group. Further analysis on the mean differences was carried out with descriptive statistics and Tukey post hoc multiple comparison Test and the result presented in Table 2.

Table 2. *Summary of descriptive statistics and Tukey post hoc comparison analysis showing the mean difference between female rats exposed to chronic intake of psychoactive drugs (Codeine & Tramadol) and those exposed to Normal saline.*

	Mean	S.E.M	1	2	3	4
Codeine	1.335	.103	-	.67*	.45*	1.80*
Combined	.669	.103		-	1.12*	2.47*
Control	1.790	.103			-	1.35*
Tramadol	3.139	.103				-

*. The mean difference is significant at the .05 level.

From the analysis, mean differences showed that female rats exposed to chronic intake of Tramadol only ($\bar{x} = 3.14$), significantly displayed more body licking grooming behavior compared to female rats ingested with Codeine only ($\bar{x} = 1.33$), combination of Codeine and Tramadol ($\bar{x}$ =.67) and the control ($\bar{x} = 1.79$) (p<.001). The mean differences were significant. Based on this, hypothesis states that there will be a significant difference in body licking behavior among females rats ingested with different drugs is thus accepted.

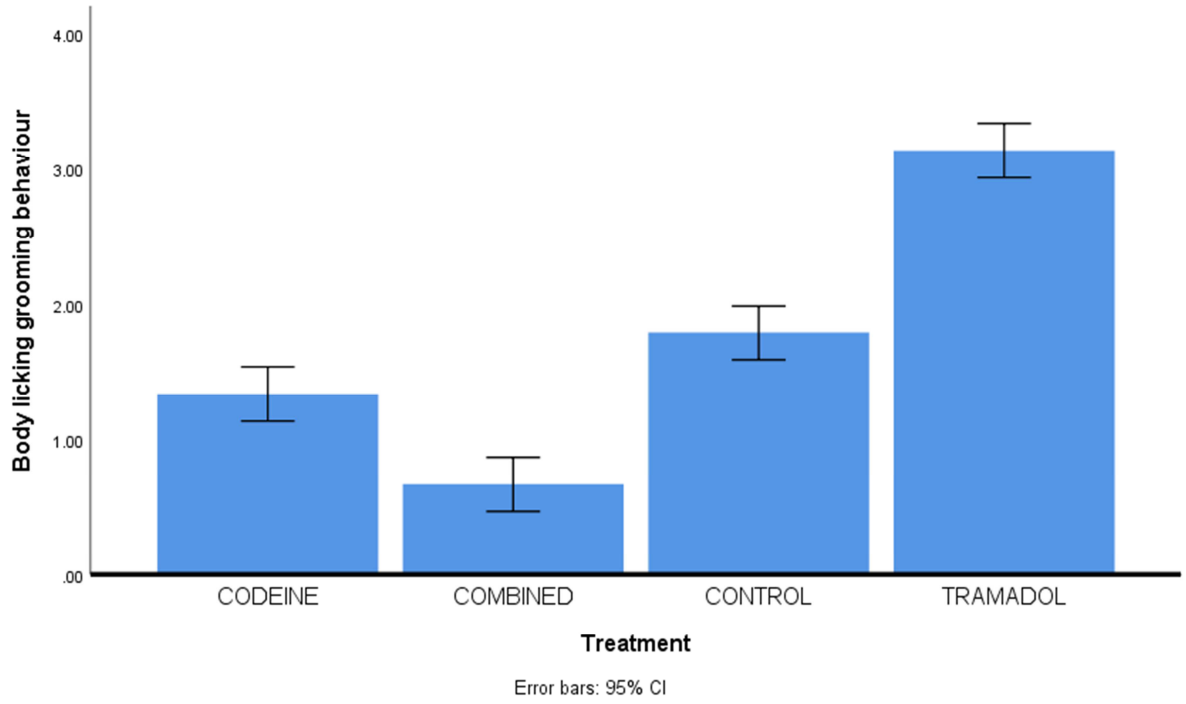

Figure 1. *Line graph showing the effect Chronic intake of psychoactive drugs (Codeine & Tramadol) on body licking behavior among Wister rats.*

The line graph shows that the exposure to chronic intake of psychoactive drugs demonstrated that tramadol induced more body licking grooming behavior compared to the control group. However, codeine and its combination with tramadol influenced lower rates body licking grooming behavior.

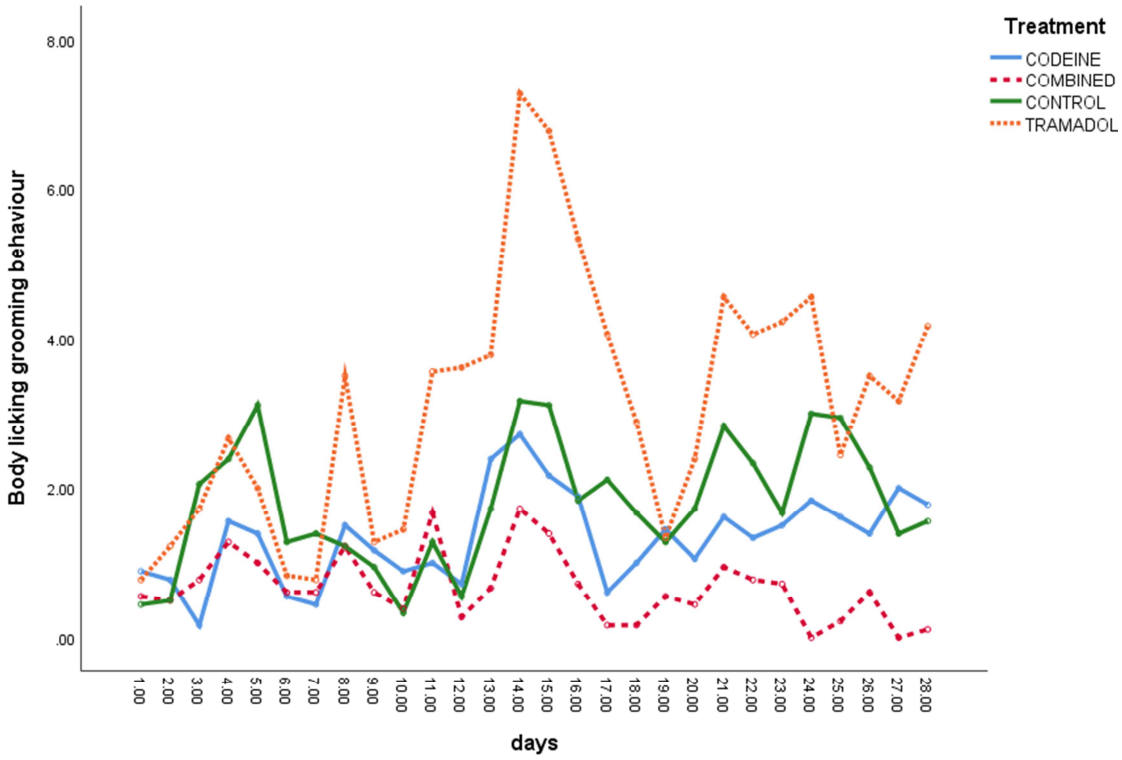

Figure 2. *Interaction graph showing the interaction between time of exposure and treatment to chronic intake of psychoactive drugs on body licking behavior (Codeine& Tramadol) among female Wister rats.*

The line graph shows that longer period of exposure to chronic intake of psychoactive drugs (Codeine& Tramadol) on rats was evident from the 8^{th} – 28^{th} days of the exposure. Rat ingested with Tramadol exhibited more body licking behavior compared to the control group. The rats in the codeine and combination group exhibited significant lower body grooming behavior compared to Wister rats in the control group.

Table 3. *Summary Randomized Block ANOVA table showing the influence exposure to chronic intake of psychoactive drugs (Codeine & Tramadol) on body licking grooming behaviour among male Wister rats.*

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial η^2
Block	22.180	1	22.180	4.555	.033	.007
Treatment	268.969	3	89.656	18.411	.000	.076
Error	3248.017	667	4.870			
Corrected Total	3539.165	671				

The result from Table 3 shows that exposure to chronic intake of psychoactive drugs (Codeine & Tramadol) significantly affect the body licking grooming behavior among male Wister rats [F (3,667) = 18.41, $p < 0.001$, η^2=.08]. The result demonstrated that body licking behaviour decreased by 8% with exposure to chronic intake of psychoactive drugs (Codeine & Tramadol) compared to the control group. Further analysis on the mean differences was carried out with descriptive statistics and LSD post hoc multiple comparison Test and the result presented in Table 4.

Table 4. *Summary of descriptive statistics and LSD post hoc comparison analysis showing the mean difference in body licking behaviour between male rats exposed to chronic intake of psychoactive drugs (Codeine & Tramadol) and those exposed to Normal saline.*

	Mean	S.E.M	1	2	3	4
Codeine	3.01	.170	-	.52*	1.22*	.34
Combined	2.49	.170		-	1.74*	.85*
Control	4.23	.170			-	.88*
Tramadol	3.35	.170				-

*. The mean difference is significant at the .05 level.

From the analysis, mean differences showed that male rats in the control ($\bar{x} = 4.23$) significantly displayed more body licking grooming behavior compared to male rats ingested with Codeine only ($\bar{x} = 3.01$), Tramadol only ($\bar{x} = 3.35$), and the combination

of Codeine and Tramadol ($\bar{x} = 2.49$) (p<.05). The mean differences were significant. Based on this, hypothesis states that there will be a significant difference in body licking behavior among males rats ingested with different drugs is thus accepted.

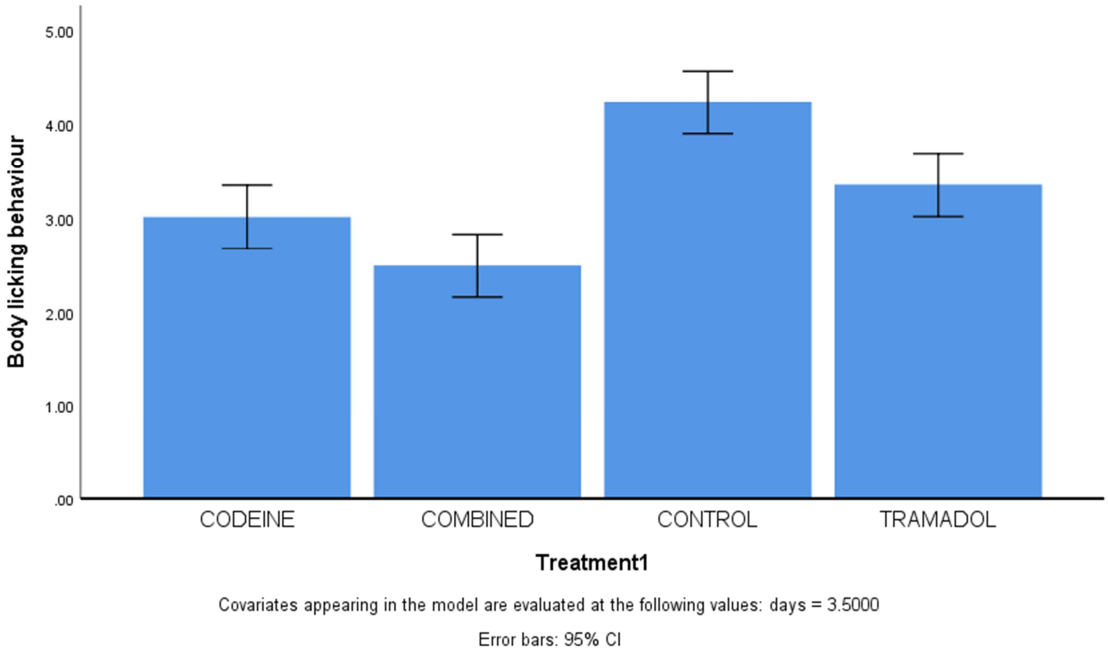

Figure 3. *Bar chart showing the effect Chronic intake of psychoactive drugs (Codeine & Tramadol) on body licking behavior among male Wister rats.*

The line graph shows that the exposure to chronic intake of psychoactive drugs demonstrated that tramadol induced more body licking grooming behavior compared to the control group. However, codeine and its combination with tramadol influenced lower rates body licking grooming behavior.

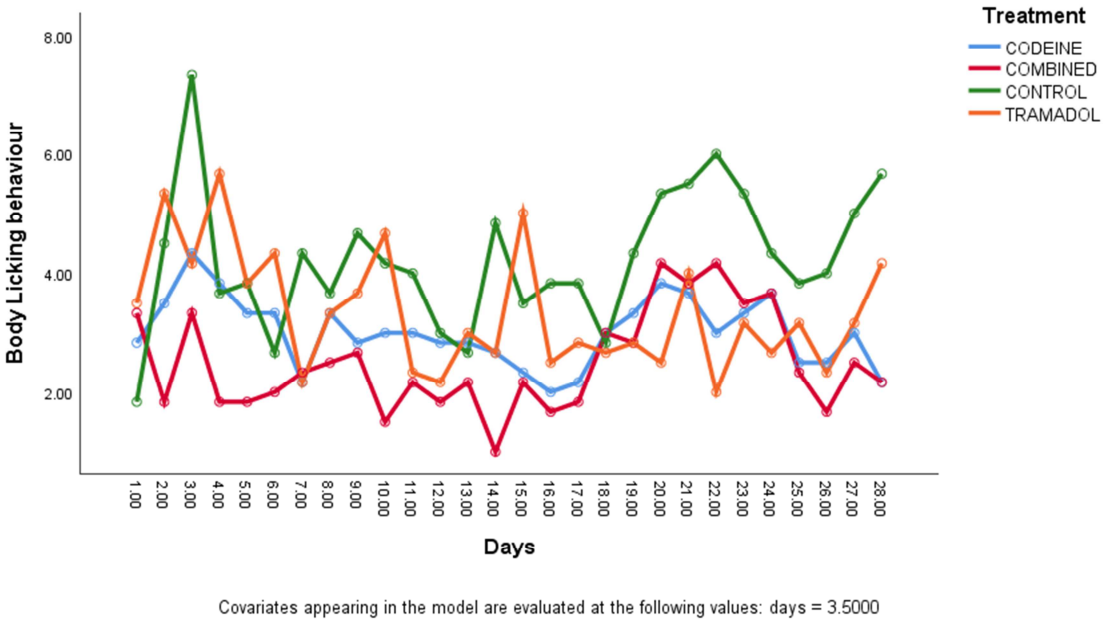

Figure 4. *Interaction graph showing the interaction between time of exposure and treatment to Chronic intake of psychoactive (Codeine & Tramadol) drugs on body licking behavior among male Wister rats.*

The line graph shows that longer period of exposure to chronic intake of psychoactive drugs (Codeine & Tramadol) on rats was evident from the 14^{th} – 28^{th} days of the exposure. Rats in the control group exhibited more body licking behavior compared to rat ingested with Tramadol and codeine. The rats in the codeine and combination group exhibited significant lower body grooming behavior compared to Wister rats in the control group.

Hypothesis II

There will be a significant difference in face washing behavior among female and male rats ingested with different drugs. This hypothesis was tested using the Randomized Block ANOVA and the result presented in Tables 5, 6, 7 and 8.

Table 5. *Summary Randomized Block ANOVA table showing the influence exposure to chronic intake of psychoactive drugs (Codeine & Tramadol) on face washing grooming behavior among female rats.*

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial η^2
Block	2158.385	2	1079.192	114.007	.000	.102
Treatment	1201.815	3	400.605	42.320	.000	.06
Error	19026.633	2010	9.466			
Corrected Total	22386.833	2015				

The result from Table 5 reveals that exposure to chronic intake of psychoactive drugs (Codeine & Tramadol) significantly impacted on the face washing grooming behavior among female Wister rats F (3, 2010) = 42.32, $p < 0.001$, η^2=.06. The result demonstrated that face washing behavior increased by 6% with exposure to chronic intake of psychoactive drugs (Codeine & Tramadol) compared to the control group. Further analysis on the mean differences was carried out with descriptive statistics and Tukey post hoc multiple comparison Test and the result presented in Table 6.

Table 6. *Summary of descriptive statistics and Tukey post hoc comparison analysis showing the mean difference between rats exposed to chronic intake of psychoactive drugs (Codeine & Tramadol) and those not exposed (Control).*

	Mean	S.E.M	1	2	3	4
Codeine	4.942	.145	-	1.65*	.18	1.61*
Combined	3.292	.145		-	1.47*	.05*
Control	4.764	.145			-	1.42*
Tramadol	3.337	.145				-

*. The mean difference is significant at the .05 level.

From the analysis, mean differences showed that female rats exposed to chronic intake of Codeine only ($\bar{x} = 4.92$), significantly displayed more daily face washing grooming behavior compared to female rats ingested with Tramadol only ($\bar{x} = 3.33$), combination of Codeine and Tramadol ($\bar{x} = 3.29$) and the control group ($\bar{x} = 4.76$) (p<.001). The mean differences were significant. Based on this, hypothesis states that there will be a significant difference in face washing behavior among female rats ingested with different drugs is thus accepted.

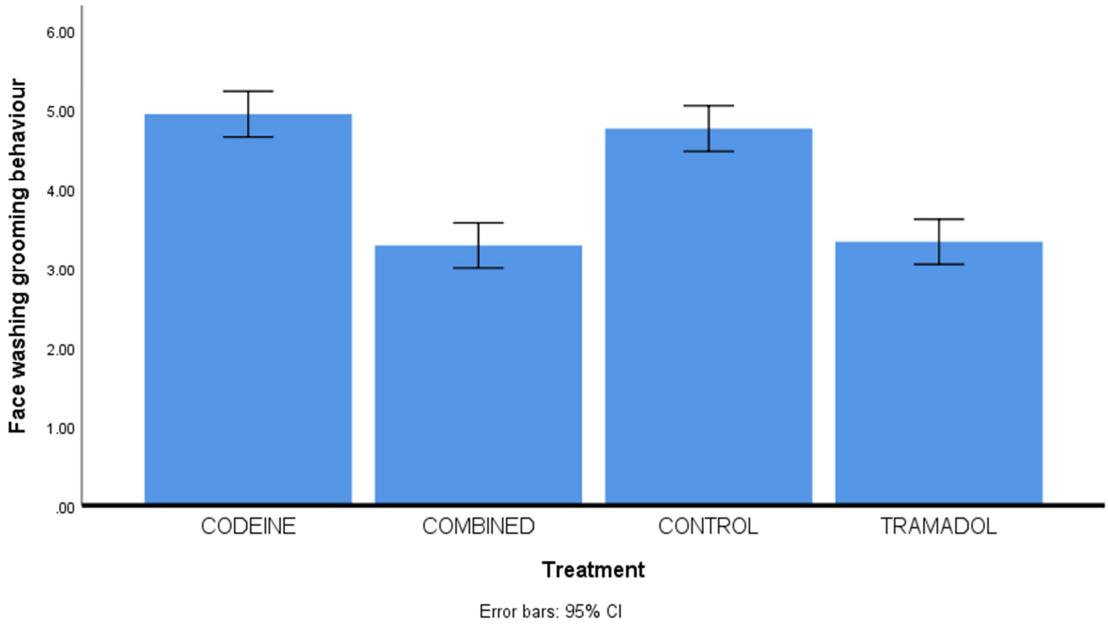

Figure 5. *Line graph showing the effect of Chronic intake of psychoactive drugs (Codeine & Tramadol) on face washing behavior among Wister rats.*

The line graph shows that the exposure to chronic intake of psychoactive drugs demonstrated that codeine induced more face washing grooming behavior compared to the control group. However, tramadol and its combination with codeine influenced lower rates of face washing grooming behavior.

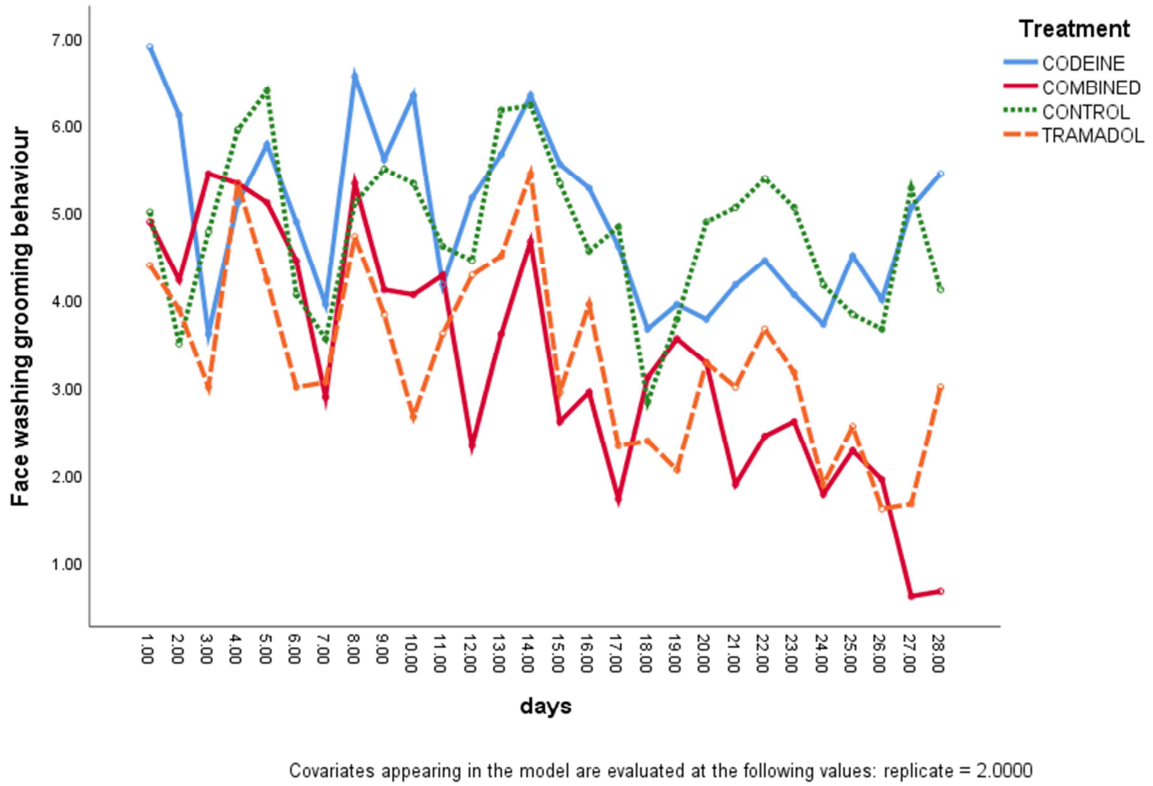

Figure 6. *Interaction graph showing the interaction between time of exposure and treatment to Chronic intake of psychoactive drugs on face washing behavior (Codeine & Tramadol) among Wister rats.*

The line graph shows that longer period of exposure to chronic intake of psychoactive drugs (Codeine & Tramadol) on rats was evident from the 5^{th} – 28^{th} days of the exposure. Rat ingested with codeine exhibited more face washing behavior compared to the control group. The rats in the Tramadol and combination group exhibited significant lower body grooming behavior compared to Wister rats in the control group.

Table 7. *Summary Randomized Block ANOVA table showing the influence exposure to chronic intake of psychoactive drugs (Codeine & Tramadol) on face washing grooming behaviour among male Wister rats.*

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial η^2
Block	.247	1	.247	.124	.725	.000
Treatment	444.101	3	148.034	74.499	.000	.251
Error	1325.360	667	1.987			
Corrected Total	1769.708	671				

The result from Table 7 reveals that exposure to chronic intake of psychoactive drugs (Codeine & Tramadol) significantly impacted on the face washing grooming behavior among male Wister rats F (3,2010) = 74.49, $p < 0.01$, η^2=.25. The result demonstrated that face washing behaviour decreased by 25% with exposure to chronic intake of psychoactive drugs (Codeine & Tramadol) compared to the control group. Further analysis on the mean differences was carried out with descriptive statistics and LSD post hoc multiple comparison Test and the result presented in Table 8.

Table 8. *Summary of descriptive statistics and LSD post hoc comparison analysis Face washing showing the mean difference between male rats exposed to chronic intake of psychoactive drugs (Codeine & Tramadol) and those not exposed (Control).*

	Mean	S.E.M	1	2	3	4
Codeine	3.39	.109	-	.67*	.45*	1.80*
Combined	2.74	.109		-	1.12*	2.47*
Control	4.96	.109			-	1.35*
Tramadol	3.49	.109				-

*. The mean difference is significant at the .05 level.

From the analysis, mean differences showed that male rats exposed to chronic intake of Codeine only ($\bar{x} = 4.92$), significantly displayed more daily face washing grooming behavior compared to male rats ingested with Tramadol only ($\bar{x} = 3.33$), combination of Codeine and Tramadol ($\bar{x} = 3.29$) and the control group ($\bar{x} = 4.76$) (p<.001).

The mean differences were significant. Based on this, hypothesis states that there will be a significant difference in face washing behavior among males rats ingested with different drugs is thus accepted.

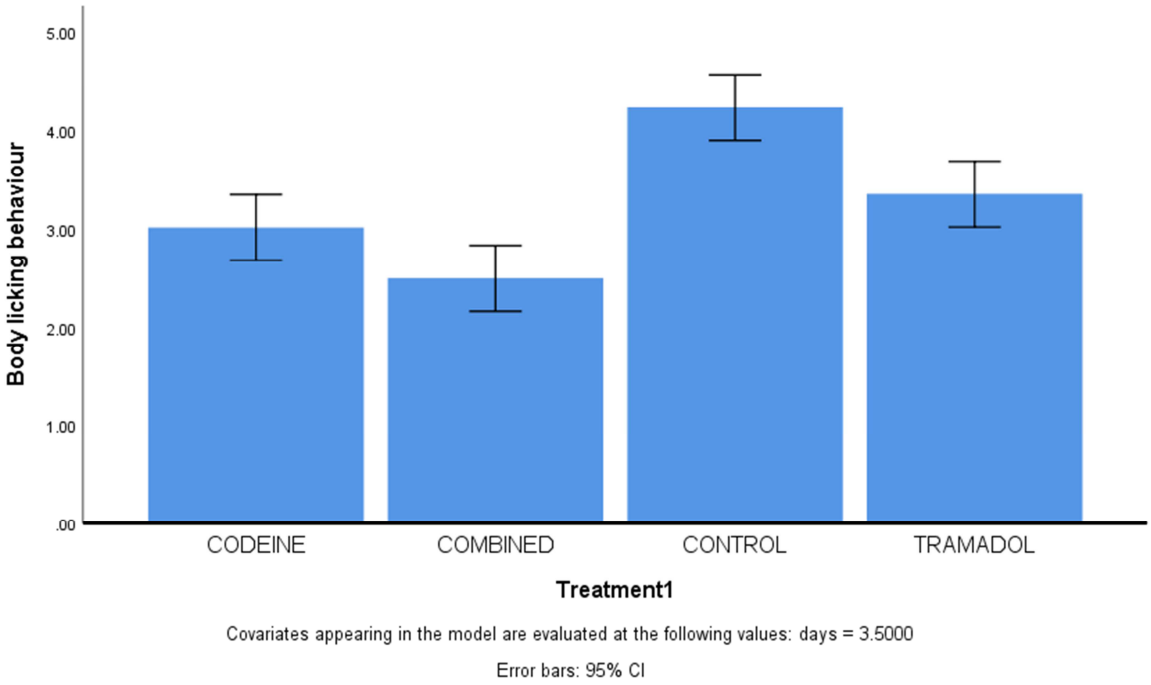

Figure 7. *Line graph showing the effect of Chronic intake of psychoactive drugs (Codeine& Tramadol) on face washing behavior among male Wister rats.*

The line graph shows that the exposure to chronic intake of psychoactive drugs demonstrated that codeine induced more face washing grooming behavior compared to the control group. However, tramadol and its combination with codeine influenced lower rates of face washing grooming behavior.

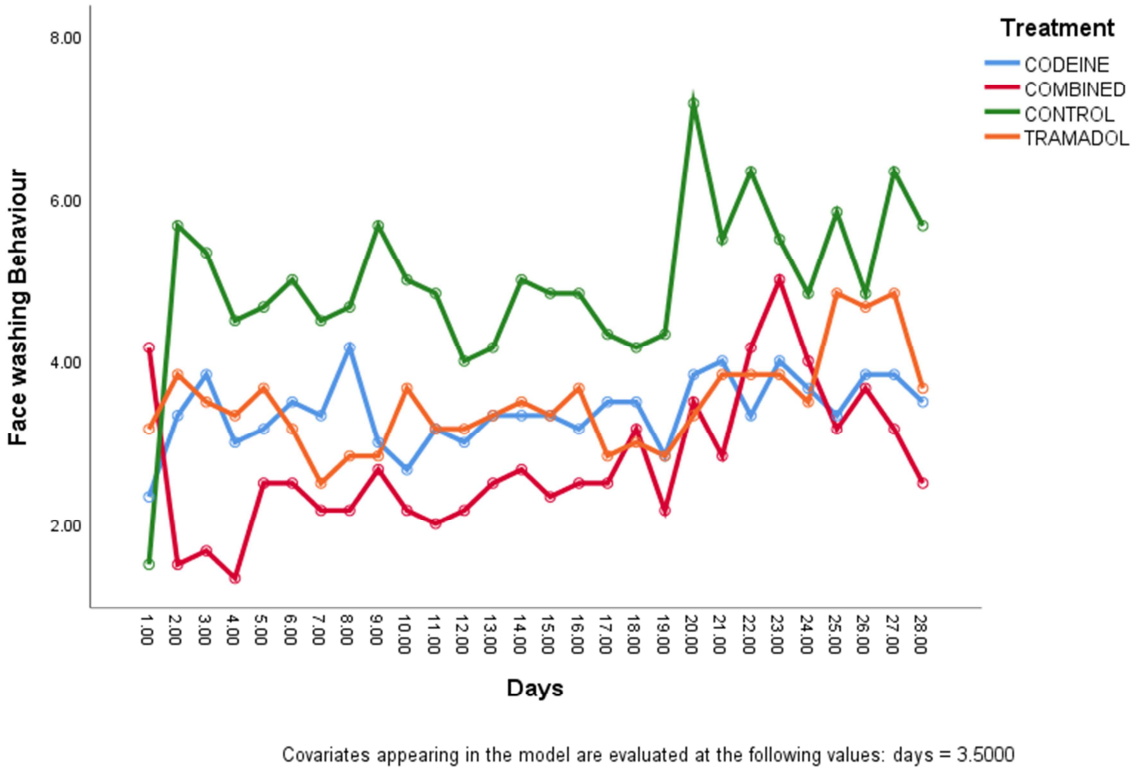

Figure 8. *Interaction graph showing the interaction between time of exposure and treatment to chronic intake of psychoactive drugs on face washing behavior (Codeine & Tramadol) among male Wister rats.*

The line graph shows that longer period of exposure to chronic intake of psychoactive drugs (Codeine & Tramadol) on rats was evident from the 5^{th} – 28^{th} days of the exposure. Rat ingested with codeine exhibited more face washing behavior compared to the control group. The rats in the Tramadol and combination group exhibited significant lower body grooming behavior compared to Wister rats in the control group.

4. Discussion

Self-grooming is natural to rats. It is a behavior that is unlearnt and is as natural to rats as blinking and breathing is to man. One of the most obvious functions of self-grooming is hygiene. A major way to recognize a Wister rat that has not been grooming properly is through the neatness of its coat [15].

Face washing, as observed during the experiment is generally carried out more than body licking. Codeine group had the highest face washing behavior. This was higher than the control group by a little margin. Regular face washing is a sign of good health in rats. When it goes above the norm, as rats in the codeine group did, the possible reason for that degree of face washing could be de-arousal and stress reduction.

Codeine is an opiate which is used for relieving pain but chronic use of this drug can cause side effects such as dizziness, constant drowsiness, fever, stomach pain, malnutrition and mild itching [16]. Possibly, the conscious attempt to fight the drowsiness and dizziness could account for the high face washing behavior; an intense struggle to get rid of the discomfort associated with the drug.

Combined (codeine and tramadol) group recorded the lowest rate of face washing behavior as well as body licking behavior. It is important to note that chronic use of codeine could lead to decreased awareness or responsiveness, damage to the lungs, liver and respiratory depression. The side effects of tramadol also include seizure, hyperactivity, euphoria, serotonin syndrome (comprising of symptoms such as high body temperature, agitation, increased reflexes, tremor) respiratory depression, rashes and liver failure [17]. The combined group, from observations in the laboratory, showed physical symptoms such as tiredness or fatigue (shown by the inability to move when placed in the observation box), chromodacryorrhoea (also known as red tears, characterized by red staining around eyes and nose), gasping for breath, shaking and tremors, dirtier body coat (as a result of little grooming), lack of appetite (shown by low intake of feed despite adequate provision).

Low self-grooming in the combined group can be attributed to a number of factors. One of such is decreased responsiveness or awareness which is a side effect of codeine. Also, tramadol and codeine individually can cause damage to organs such as the liver and kidney. Combination of both drugs most likely brought about damages to the body which led to observations such as chromodacryorrhoea (red tears). Red tears is associated with nutritional deficiencies, respiratory diseases, chronic physiological stress, etc in essence, red tears is a definite sign or symptom of illness. However, no matter how sick a rat could be, there is always self-grooming although the frequency might be reduced. For rats in the combined group, the rate of self-grooming is alarmingly low such that it might not just be as a result of these organ failures.

Self-grooming is an unlearnt behavior which is ingrained in the brain. Low self-grooming as recorded in the combined group could be as a result of not just physiological symptoms but also psychopathology. It was observed in the laboratory that a rat (tramadol group) which experienced muscle deterioration (shown by a lack of movement in the right limbs) still groomed itself on a more regular basis than those in the combined group. This is to further explain that bodily deterioration would definitely reduce self-grooming but not as low as the combined group which gives the hint of psychopathology although more research could be done to confirm this.

Tramadol group showed the highest degree of body licking behavior which is also a form of self-grooming. Tramadol group had a mean of 4.942 while the control group had a mean of 4.764. Itching and restlessness are some of the side effects of tramadol which are responsible for the abnormally high body licking behavior. As observed in the laboratory, body licking behavior of rats in the tramadol group were short but constant. Another factor responsible for the high body licking behavior is serotonin syndrome, caused by too much secretion of serotonin in the body. The agitation, increased reflexes and tremor associated with this syndrome distracts the rat from carrying out a full body grooming process. From observation, the rats tend to be very active including trying to climb out of the observation box. Some rats would jump all of a sudden without any external stimuli. In cases where the rats are allowed to mix with other rats, they tend to be aggressive when grooming the other rats by intense biting and scratching.

Self-grooming in albino rats can be interpreted into the grooming behavior of humans which includes bathing, brushing of teeth, wearing clean clothes and other habits that ensure hygiene in man. The result gotten for the codeine group shows that codeine users may not have a problem or great difficulty maintaining hygiene although there might be sluggishness in carrying them out. Tramadol users also might not have issues with hygiene but might be restless about it, that is, carrying out healthy behaviors too often or getting constantly distracted while carrying it out. Chronic users of both codeine and tramadol would most likely not carry out hygiene related activities. This is because of the deep state of unawareness or responsiveness caused by the drugs. Chronic use of both codeine and tramadol would also reduce body grooming as a result of damages done to organs in the body. These damages tend to get the person weak and unable to carry out functions properly.

Other observations made in the laboratory include high mortality (4 out of 6 rats died before the end of the experiment in the combined group), cannibalism (a rat in the tramadol group was found dead and its head was eaten by the

other rats in the group), low appetite (this was observed in all the groups except control with the most significant as the combined group).

5. Conclusion

This research work is suggestive that consumption and administration of codeine and tramadol induce social behavior abnormalities. The findings demonstrated that chronic administration of opioids codeine and tramadol affected grooming behaviors i.e. face washing and body licking behaviors which are related to possible deterioration of physical appearance and personal grooming habits in humans. Further investigations are needed for information to unravel the danger of codeine and tramadol on other body systems.

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