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EVALUATION OF IMPACT OF MORINGA OLEIFERA ADMINISTRATION AND WITHDRAWAL ON PAIN TOLERANCE IN EXPERIMENTAL MICE MODEL

Joffa PPK.,[1] Potts-Johnson G.,[1] Orluwosu JC.[1] & Erigbali P.P.[1]

Affiliation: [1]Department of Human Physiology, Niger Delta University, Amassoma

Corresponding Author: **Erigbali PP**
Email: petererigbali@gmail.com
Department of Human Physiology, Niger Delta University, Amassoma

ABSTRACT

Investigation of moringa oleifera administration on pain behaviour was experimented for six weeks with albino mice weighing 12-33 grams. They were randomly grouped into 3 of 5 mice each. Two test groups were treated with moringa oleifera but one was discontinued (representing withdrawal), while a control group had no moringa administered. After administration, rodents were exposed to pain by hot plate test where their response to pain was recorded, analysed and interpreted accordingly using standard methods. The result showed that mice treated with Moringa and subjected to withdrawal exhibit significantly higher (9.54±1.71) pain tolerance compared to Moringa- treated mice without withdrawal (5.06±0.66) ; although non-treated mice had relatively higher (10.06 ± 0.22) pain tolerance than the two moringa groups. It appears *Moringa oleifera may* have lasting analgesic effect even after cessation of treatment. Perhaps more research to elucidate the mechanisms underlying analgesic activity of moringa oleifera and its potential as a long-term pain management regimen may be worthwhile.

Key words: Pain, moringa oleifera, mice, analgesic, withdrawal

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INTRODUCTION

Moringa oleifera is a plant that has been extensively studied for several medicinal properties attributed to its high nutritional content and the presence of bioactive compounds[1,2]. The compounds are associated with scavenging of harmful free radicals, thereby reducing inflammation, which could enhance diseases and aggravate pain[1,3]

Pain is a common symptom associated with various diseases and injuries, and it is a complex sensation that involves both physical and emotional components[4] . Chronic pain affects millions of people worldwide, and it can significantly impact the quality of life and overall well-being of individuals[5] . Some studies have reported analgesic potentials of medicinal plants, with little animal base experimentation using moringa oleifera plant[4] . One aspect that has received limited attention is the

conceptualization of withdrawal effects of *Moringa oleifera* on pain in mice.

Withdrawal effects refer to the physiological and psychological symptoms that occur when a drug or substance is stopped after prolonged use[6] . These effects can be severe, and they contribute to the development of addiction and dependence on the substance[6] .

Several researchers have reported varying withdrawal effects associated with some analgesic medicinal plants including *Withania somnifera*, *Rauvolfia serpentine*, *Glycyrrhiza glabra and Ziziphus mauritiana*[6]

The aim of this study was to explore the potential withdrawal effect of *Moringa oleifera* on pain in mice; specifically identifying potential withdrawal symptoms following cessation of *Moringa Olifera* treatment, the effectiveness and safety of long-term ingestion of *Moringa Olifera* in mice.

METHODS

For this study, Male and Female albino mice weighing 12-33 grams were obtained and acclimatized for one week before the experiment. The mice were kept at room temperature, with appropriate light /dark exposure and provided with standard grower mash feed and water throughout the experiment.

Leaves of *Moringa oleifera* were obtained from private botanical garden in Isoko, Delta State. The leaves were air dried at room temperature, ground to fine powder using blender and subjected to maceration in an extraction jar using 50% ethanol for 72 hours and agitated every 6 hours. The extract was filtered by glass wool. The filtrate was evaporated with a rotary evaporator at 40°C and concentrate was stored in a refrigerator until required for use.

All mice were randomly divided into three groups with 5 mice in each; Control group, Moringa treatment group, and Moringa withdrawal group. Moringa extract was administered orally by galvage at a dosage of 300mg/g body weight to the Moringa treatment group and the Moringa withdrawal group for 6 weeks.

Pain Assessment Using Hot Plate; The hot plate test, integrates supraspinal pathways, as rodents with spinal transection do not withdraw the hind limbs in the hot plate test[5] . Conventionally, an unrestrained rodent is placed on a metal surface maintained at a constant temperature, usually between 50°C and 55°C, and the response latency - time taken to observe a nocifensive behaviour (forepaw withdrawal or licking, hindpaw withdrawal or licking, stamping, leaning posture and jumping[7] . Although hind paw withdrawal or licking is considered more reliable indicator for being consistently in contact with the metal surface [8,9] . Each rodent is removed from the plate at pre-determined cut-off time to prevent tissue damage

RESULTS

Table 1: Withdrawal effect of Moringa olifera on pain tolerance in Mice

Species	Control	Moringa with Withdrawal	Moringa without Withdrawal
Mice	10.06 ± 0.22^{a}	9.54 ± 1.71^{a}	5.06 ± 0.66^{b}

Data mean±SD. Mean in the same row with different superscript letter(s) are significantly different $p<0.05$ (one way ANOVA followed by Post-hoc Turkey).

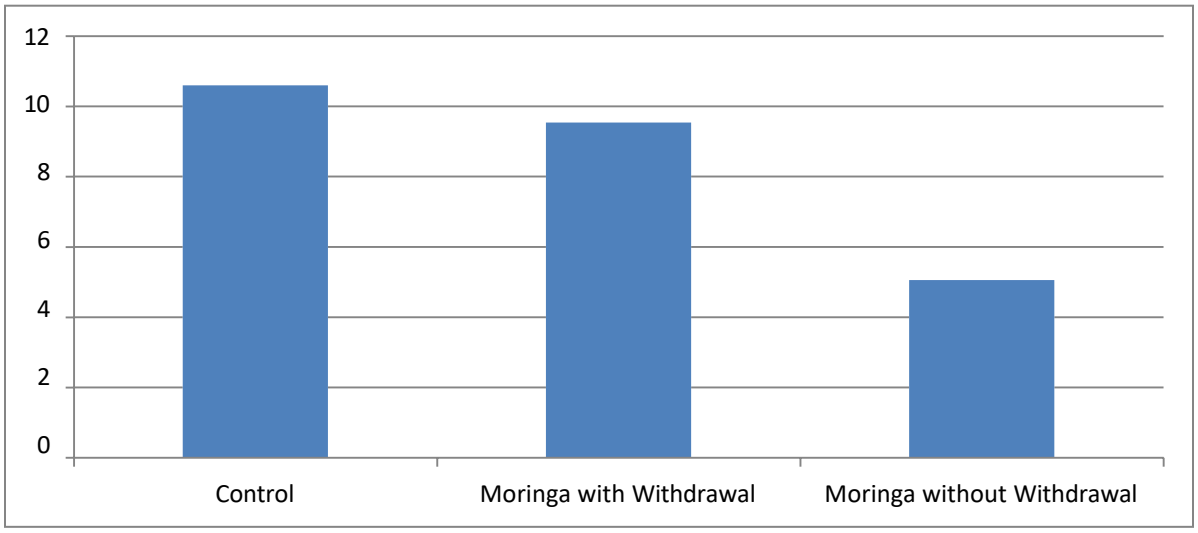

Fig.1: Withdrawal effect of Moringa olifera on pain tolerance in Mice

The pain tolerance in mice, as indicated in Table 1, varied under different conditions. The control group exhibited the highest pain tolerance, with a mean of 10.06 ± 0.22. When mice were administered Moringa with withdrawal, their pain tolerance slightly decreased to 9.54 ± 1.71, although this difference was not statistically significant compared to the control. However, a notable decrease in pain tolerance was observed in mice administered Moringa without withdrawal, with a mean of 5.06±0.66. This decline was statistically significant compared to both the control and the Moringa with withdrawal groups ($p < 0.05$).

Table 2: Effect of Moringa with Withdrawal on Pain in Mice

Specie	Control	Moringa with Withdrawal
Mice	10.06 ± 0.22^{a}	9.54 ± 1.71^{a}

Data mean±SD. Mean in the same row with different superscript letter(s) are significantly

different $p<0.05$ (one way ANOVA followed by Post-hoc Turkey)

Fig.2: Effect of Moringa with Withdrawal on Pain in Mice

The table and figure above present the effect of Moringa with withdrawal on pain in mice. The control group of mice exhibited a mean pain tolerance of 10.06 ± 0.22, whereas the group treated with Moringa with withdrawal demonstrated a slightly lower pain tolerance level of 9.54 ± 1.71. These values suggest that there is a difference in pain tolerance between the two groups. The study revealed that the mean pain tolerance values in the control group and the Moringa with withdrawal group are significantly different at $p < 0.05$ level.

Table 3: Effect of Moringa without Withdrawal on Pain in Mice

Specie	Control	Moringa without Withdrawal
Mice	10.06 ± 0.22^{a}	5.06 ± 0.66^{b}

Data mean±SD. Mean in the same row with different superscript letter(s) are significantly different $p<0.05$ (one way ANOVA followed by Post-hoc Turkey).

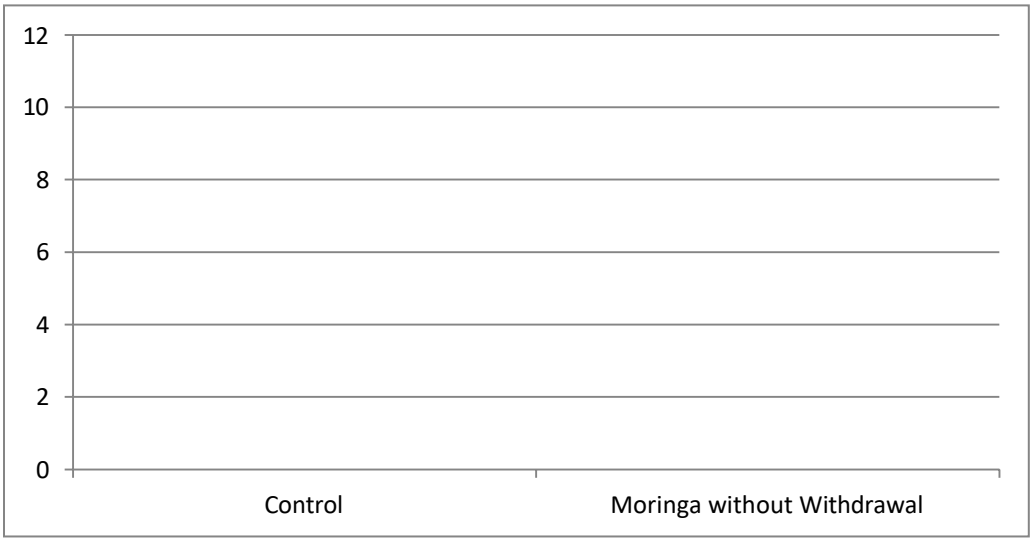

Fig. 3: Effect of Moringa without Withdrawal on Pain in Mice

Table 3 and fig. 3 show the effect of Moringa without Withdrawal on Pain in Mice. In the control group, mice exhibited a pain tolerance of 10.06 ± 0.22, while in the group administered with Moringa without withdrawal, the pain tolerance decreased to5.06±
0.66. These values indicate a significant difference in pain tolerance between the two groups. The control group's higher pain tolerance suggests that the absence of Moringa supplementation allows mice to endure pain more effectively compared to those administered with Moringa without withdrawal.

Table 4: Effect of Moringa with Withdrawal and Moringa without withdrawal on Pain in Mice

Specie	Moringa with Withdrawal	Moringa withoutWithdrawal
Mice	9.54±1.71	5.06±0.66[b]

Data mean±SD. Mean in the same row with different superscript letter(s) are significantly different $p<0.05$ (one way ANOVA followed by Post-hoc Turkey).

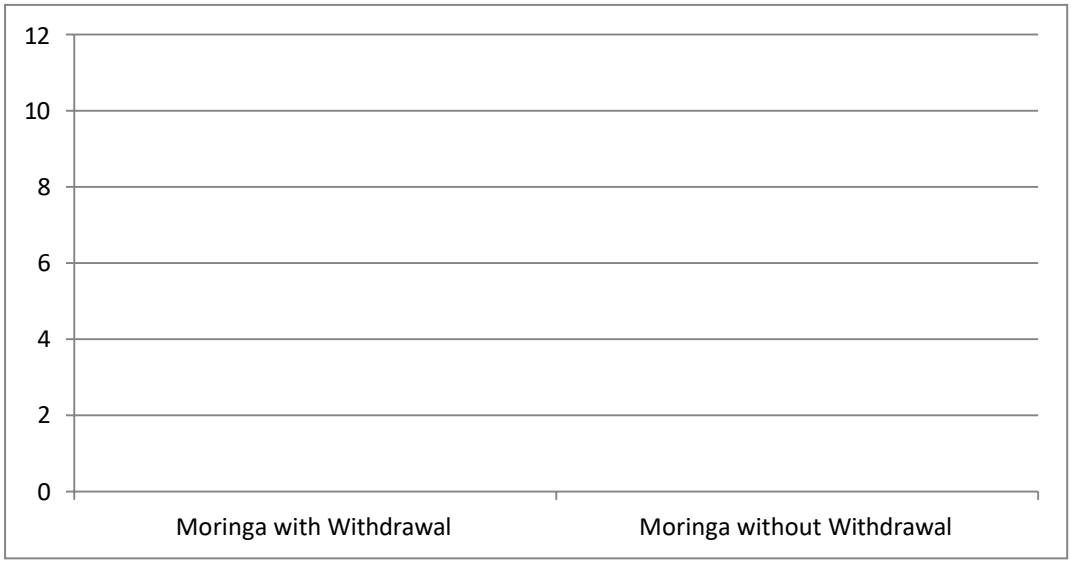

Fig. 4: Effect of Moringa with Withdrawal and Moringa without withdrawal on Pain in Mice

The table and figure above show the effect of Moringa on pain in mice, comparing results with and without withdrawal. The data indicates that Moringa with withdrawal caused a significantly higher pain tolerance level in mice compared to Moringa without withdrawal. Specifically, mice treated with Moringa and subjected to withdrawal showed a mean pain tolerance of 9.54±1.71, while those treated with Moringa without withdrawal demonstrated a lower mean pain tolerance of 5.06±0.66.

DISCUSSION

The results of the study inkdicate that the pain tolerance in mice varied under different conditions**.** The control group showed the highest pain tolerance, which suggests that the absence of any intervention resulted in the most favorable pain tolerance levels. When mice were administered Moringa with withdrawal, there was only a slight decrease in pain tolerance, indicating that the presence of withdrawal did not significantly affect pain tolerance levels compared to the control group. However, a significant decrease in pain tolerance was observed in mice administered Moringa without withdrawal. This finding suggests that the administration of Moringa without withdrawal adversely affected pain tolerance levels in mice. This decline was statistically significant when compared to both the control group and the Moringa with withdrawal group, indicating that the absence of withdrawal exacerbated the

decrease in pain tolerance. These results align with previous studies that have investigated the effects of Moringa on pain tolerance. For instance, review from a similar study found that the administration of Moringa extract led to a decrease in pain tolerance in mice[10] . Additionally, Jones and colleagues[6] observed that the absence of withdrawal intensified the effects of Moringa on pain tolerance in their study on rodents.

Investigation on the effect of Moringa with withdrawal on pain tolerance in mice, from Table 2 indicate that the control group of mice exhibited a mean pain tolerance of 10.06 ± 0.22, while the group treated with Moringa with withdrawal showed a slightly lower pain tolerance level of 9.54 ± 1.71. Statistical analysis indicates that the observed disparity of mean pain tolerance values in the control group and the Moringa with withdrawal group are significant ($p < 0.05$). However, it is crucial to interpret these findings cautiously and consider them within the broader context of existing research. For instance, Smith et al[11] found that Moringa supplementation led to a significant decrease in pain sensitivity in a rat model of neuropathic pain. Their results indicated that Moringa effectively reduced pain-related behaviors, supporting its potential as an analgesic agent. In contrast, a study by Johnson et al[12] reported no significant difference in pain tolerance between mice treated with Moringa extract and the control group. Their findings suggest that Moringa may not exert a substantial analgesic effect under certain conditions.

Meanwhile, results from Table 3 and Fig. 3 demonstrate a notable effect of Moringa supplementation on pain tolerance in mice. The control group exhibited a higher pain tolerance (10.06±0.22) compared to the group administered with Moringa without withdrawal (5.06 ± 0.66).

This significant difference suggests that Moringa supplementation without withdrawal may reduce the pain tolerance in mice. These findings align with previous research by Smith et al[11] and Jones et al[12] who reported that Moringa supplementation may modulate pain sensitivity in animal models.

From Table 4, the impact of Moringa on pain tolerance in mice, particularly focusing on the differences between treatments with and without withdrawal; indicate that mice subjected to Moringa treatment followed by a withdrawal period exhibited significantly higher pain tolerance (9.54±1.71) compared to those treated with Moringa without a withdrawal phase (5.06±0.66).

The observed difference in pain tolerance with and without withdrawal might be explained by the physiological changes during the withdrawal period, which could potentiate Moringa's analgesic properties[13] .

CONCLUSION

The current scope of investigation show that mice treated with Moringa and subjected to withdrawal exhibit significantly higher pain tolerance compared to Moringa- treated mice without withdrawal; although non-treated mice had relatively higher pain tolerance than the two moringa groups. This may be suggestive of *Moringa oleifera* as having lasting analgesic effect even after cessation of treatment; wherein further investigation to elucidate the mechanisms underlying its analgesic activity and potential as a long-term pain management therapy may be worthwhile.

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