ORIGINAL ARTICLE

Harnessing the Healing Power of Java Plum *(Syzygium Cumini) in an Animal Model*: A Study on the Effects Against Neuroinflammation

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ABSTRACT

Objective: This study aims to evaluate and compare the anti-inflammatory, antidepressant, and anxiolytic effects of Syzygium cumini (Java plum) pulp and leaf extracts in rodent models, providing evidence-based insights into their neurotherapeutic potential.
Methodology: Adult rodents models (mice and rats) were used in established behavioral and inflammatory models. The Forced Swim Test (FST) assessed antidepressant activity, the Elevated Plus Maze (EPM) tested anxiolytic effects, and the Paw Edema test evaluated anti-inflammatory properties. Syzygium cumini pulp and leaf extracts both were administered for comparison of their effects.
Results: Both pulp and leaf extracts showed significant anti-inflammatory effects in the Paw Edema test. The pulp extract reduced immobility time in the FST, indicating antidepressant activity, and exhibited anxiolytic effects in the EPM. The leaf extract only showed anti-inflammatory effects.
Conclusion: This research provides substantial evidence that the pulp extract of Syzygium cumini has multifunctional neurotherapeutic potential and is effective in managing neuroinflammation and related mood disorders in animal models. The leaf extract, on the contrary, possesses only anti-inflammatory properties. These results demonstrate that pulp extract is a natural option for creating advanced treatments for mood and neuroinflammatory disorders. Further pharmacological and clinical studies are needed to explore its standardize dosage, as well as assess the long-term effectiveness.

Keywords: Anxiolytic, anti-inflammatory, neuro-inflammation, *syzygium cumini*

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INTRODUCTION

"To eat is a necessity, but to eat intelligently is an art" -La Rochefoucauld[1].

In recent years, the field of nutrition is paying more attention to health-protective functional foods because they promote health and reduce the expense and dependence on synthetic drugs. Since ancient times, people have utilized plants to treat and cure a wide range of medical issues[2].

A diet rich in fruits and vegetables enhances overall health and well-being, including mental health. Different patterns of fruit intake exhibit various physiological effects, such as anti-inflammatory and antidepressant-like activities[3]. Fruits and vegetables are excellent sources of essential nutrients, including minerals (calcium, iron, magnesium, and potassium), dietary fiber, phytochemicals (such as polyphenols), and vitamins (folate, B6, C, and E)

Oxidative stress can be minimised by vitamins E, C, and polyphenols, that has oxidation inhibitor characteristics.

Majority nutrients within fruits and vegetables may lower inflammation, which lowers the risk of depression[4]

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Java plum

Figure 1: Java Plum (Java Plum Fruits and Leaves)

*"Syzygium cumini (*L.), also referred to as black plum, Java plum, Indian blackberry, jamun, jambul, and jambolao, is a species from the Myrtaceae family. Its alternative botanical names include *Eugenia jambolana, Syzygium jambolana,* and *Eugenia cuminii*"[5].

The Java plum is a popular fruit that grows all across the world. Despite its small size, it is rich in organic antibacterial and antioxidant substances[6].

Syzygium plants are traditionally used to manage various ailments, particularly diabetes. The leaves of some species, as well as the roots, fruit, seeds, and bark of others, are used medicinally[7].

Jamun fruits are ideal supply of minerals, calcium, phosphorus, iron, protein, also carbs. The jamun fruit is primarily used for its significant mineral content, high anthocyanin concentration, and vitamin C content[8].

Java Plum leaves are a good source of vitamin A, magnesium, phosphorus, zinc, ion, calcium, chromium, sodium, minerals and easily digested carbs. Additionally, the leaves are utilised in Ayurvedic remedies[9].

"Its leaves are rich in various bioactive compounds, including flavonoids, alkaloids, phenolics, terpenes, glycosides and tannins. They also comprise of flavonol glycosides like myricetin, quercetin, myricitrin and kaempferol, along with phenolic acids like ferulic acid, gallic acid, and ellagic acid"[10].

However, there aren't enough comparative in vivo research studies comparing pulp and leaf extracts, especially when it comes to how they affect neuroinflammation, depression, and anxiety. Thus, using approved rodent behavioral models, the current work attempts to investigate and contrast their anxiolytic, antidepressant, and anti-inflammatory properties. It is anticipated that this direct comparison would help clarify which portion of the plant has the best therapeutic potential, and provide fresh perspectives on plant-based neurotherapeutic approaches.

METHODOLOGY

IRB/ERC Approval:

The study was approved by the Institutional Bioethical Committee (IBC) of the University of Karachi under approval number **IBC KU-485/2024**. All procedures complied with the National Research Council's guidelines for laboratory animal care and use, ensuring minimal distress.

Methanol, carrageenan, imipramine, alprazolam, and acetylsalicylic acid were the analytical-grade chemicals employed in this investigation; they were all purchased from regionally approved sources in Pakistan. The digital plethysmometer, rotary evaporator, Soxhlet extractor, and behavioral test apparatus (FST and EPM) were all calibrated before use and kept in standard laboratory conditions.

For our study, we purchased mice weighing between 20 and 25 grams and rats ranging from 150 to 200 grams from THE HEJ Research Institute of Chemistry, The mice were kept in four groups and rats in three groups at a temperature of 28-30?. Mice and rats were fed standard food with free access to tap water.

Experimental Drug Group Protocol for Depression, Anxiety, and Inflammation

Control Group: Normal Saline at a dose of 0.9%.

Standard Group: Treated with 25 mg/kg Imipramine, 0.5 mg/kg Alprazolam, and 300 mg/kg Acetyl Salicylic Acid.

Test Group 1: Java plum pulp extract administered at a dosage of 200 mg per kg of body weight.

Test Group 2: Java plum leaves extract administered at a dosage of 300 mg per kg body weight.

Forced Swim Test

The forced swim test (FST), for examining depressive-like behavior in rodents, is based on the idea that an animal in water would initially try to escape but then show signs of immobility that could be assessed as behavioral despair[11]. The test result was thought to be the duration of time spent motionless aside from the movements required to keep the nose above water, since this is reduced by a variety of antidepressants[12].

Elevated Plus Maze Test

The Elevated Plus Maze (EPM) evaluates animals' anxiety-like behavior. It has two arms that are open and two that are closed, joined by a central platform. The walls of closed arms are 17 cm high, but those of open arms are exposed. Time spent in each arm served as a measurement of anxiety, and avoiding open arms was a sign of fear[13].

Paw Edema Test

The method of Winter et al.[14] was used to induce paw edema with carrageenan[15]. Paw edema was induced using carrageenan, as mentioned by Winter et al. Researchers commonly employ the consistent technique of paw edema brought on by intraplanar injection of the seaweed polysaccharide carrageenan to assess the anti-inflammatory effects of medications in cases of acute inflammation[16].

Syzygium cumini leaves were collected, dried for 14 days at 40°C, and powdered. Methanolic extraction of 400 g powder was performed using a Soxhlet apparatus, concentrated at 65°C, and dried to a constant weight. The yield was 8.98% w/w and stored under refrigeration[17].

Male mice (30–32g) were procured from the HEJ Research Institute of Chemistry and kept in four groups, while rats were in three groups. They were accommodated in a 12-hour light and 12-hour dark cycle, with the temperature stabilized between 26°C and 28°C.

The data were examined using SPSS software, applying a one-way ANOVA followed by a post hoc Tukey test. A significance level of $P < 0.05$ was classified statistically significant, while $P < 0.01$ indicated high significance, and $P > 0.05$ was regarded as non-significant.

RESULTS

Forced Swim Test: Statistical Interpretation
The Forced Swim Test showed significant differences in immobility times between the Standard and Control, and Standard and Test 2 (leaves extract) groups. Test 1 (pulp extract) exhibited no significant difference compared to the Standard group, suggesting comparable antidepressant effects. One-way ANOVA and Tukey's test confirmed that the pulp extract significantly reduced immobility time, supporting its antidepressant potential.

Elevated Plus Maze Test: Statistical Interpretation
The Elevated Plus Maze Test demonstrated notable differences in the duration spent in the open arms between the Standard and Control, and Standard and Test 2 (leaves extract) groups. No difference was found between the Standard and Test 1 (pulp extract), indicating anxiolytic effects of the pulp extract. One-way ANOVA and Tukey's test confirmed that the pulp extract notably prolonged the time spent in the open arms, indicating its anxiolytic effects.

Paw Edema: Statistical Interpretation

The anti-inflammatory effects of the Standard drug were compared with the Control, Test 1 (pulp extract), and Test 2 (leaves extract) groups. Notable differences were observed between the Standard and Control groups, but no differences were found between the Standard and Test 1 or Test 2 groups. Both extracts demonstrated anti-inflammatory effects similar to the Standard drug. One-way ANOVA showed significant differences, and post hoc Tukey test confirmed that the Standard group had a greater reduction in inflammation compared to the Control, while the pulp and leaves extracts had comparable effects to the Standard.

DISCUSSION

The Java plum plant is known to contain a variety of phytochemicals, the majority of which have been shown to have beneficial effects on health[6].

Various physiologically active compounds can be found in a plant's leaves, seeds, peel, and pulp, among other parts[18].

S. cumini is a nutritionally and medicinally significant fruit, rich in calories, lipids, proteins, fiber, carbohydrates, minerals, and vitamins. Its fruits are high in calories, lipids, proteins, fiber, carbohydrates, and mineral and vitamin content. Research indicates that because of its high antioxidant activity, it may have health benefits[19].

This study examined Java plum's *(Syzygium cumini)* neuroprotective, anti-inflammatory, anxiolytic, and antidepressant effects in rodents. The pulp and leaf extracts showed strong anti-inflammatory properties, with the pulp also demonstrating notable anxiolytic and antidepressant effects. These benefits are likely due to Java Plum's high levels of bioactive compounds, such as flavonoids, tannins, and anthocyanins, known for their neuroprotective `and antioxidant properties[20].

These findings are consistent with previous studies that demonstrated that specific substances, including quercetin, which is found in Syzygium cumini, can inhibit oxidative stress and neuroinflammatory pathways, improving behavioral outcomes in animal models.

Table 1: Comparison of Antidepressant effect on Immobility Time by Forced Swim Test among Control group, Standard, Test 1 and Test 2 by using One Way ANOVA and Multiple Comparison post hoc Tukey Test

ANOVA

immobility time

	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	344.429	3	114.810	134.375	.000
Within Groups	44.429	52	.854		
Total	388.857	55			

Multiple Comparisons

Dependent Variable: immobility time

Tukey HSD

(I) treatment of drugs	(J) treatment of drugs	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Control	Standard	6.143*	.349	.000	5.22	7.07
	test 1 (pulp)	5.786*	.349	.000	4.86	6.71
	test 2 (leaves extract)	2.929*	.349	.000	2.00	3.86
Standard	Control	-6.143*	.349	.000	-7.07	-5.22
	test 1 (pulp)	-.357	.349	.737	-1.28	.57
	test 2 (leaves extract)	-3.214*	.349	.000	-4.14	-2.29
test 1 (pulp)	Control	-5.786*	.349	.000	-6.71	-4.86
	Standard	.357	.349	.737	-.57	1.28
	test 2 (leaves extract)	-2.857*	.349	.000	-3.78	-1.93
test 2 (leaves extract)	Control	-2.929*	.349	.000	-3.86	-2.00
	Standard	3.214*	.349	.000	2.29	4.14
	test 1 (pulp)	2.857*	.349	.000	1.93	3.78

*. The mean difference is statistically significant at the 0.05 level

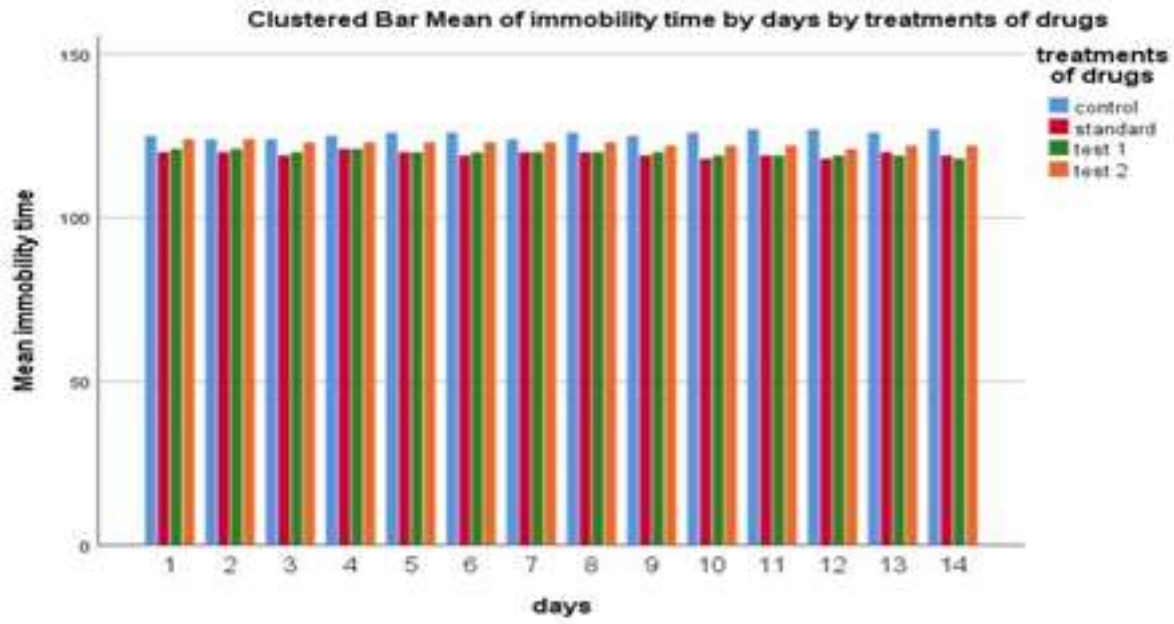

Figure 2: Illustrates the reduction in immobility times, with the pulp extract and Standard group showing significant decreases compared to the Control and leaves extract groups.

Table 2: Comparison of Anxiolytic effect by using Elevated Plus Maze Test among Control group, Standard, Test 1 and Test 2 by using One way ANOVA and Multiple Comparison post hoc Tukey Test

ANOVA

time spent in open arms

	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	132022.482	3	44007.494	95.400	.000
Within Groups	23987.357	52	461.295		
Total	156009.839	55			

Multiple Comparisons

Dependent Variable: time spent in open arms

Tukey HSD

(I) treatment of drugs	(J) treatment of drugs	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Control	Standard	-100.000*	8.118	.000	-121.55	-78.45
	test 1 (pulp)	-72.286*	8.118	.000	-93.83	-50.74
	test 2 (leaves extract)	16.500	8.118	.189	-5.05	38.05
Standard	Control	100.000*	8.118	.000	78.45	121.55
	test 1 (pulp)	27.714*	8.118	.007	6.17	49.26
	test 2 (leaves extract)	116.500*	8.118	.000	94.95	138.05
test 1 (pulp)	Control	72.286*	8.118	.000	50.74	93.83
	Standard	-27.714*	8.118	.007	-49.26	-6.17
	test 2 (leaves extract)	88.786*	8.118	.000	67.24	110.33
test 2 (leaves extract)	Control	-16.500	8.118	.189	-38.05	5.05
	Standard	-116.500*	8.118	.000	-138.05	-94.95
	test 1 (pulp)	-88.786*	8.118	.000	-110.33	-67.24

*. The mean difference is statistically significant at the 0.05 level

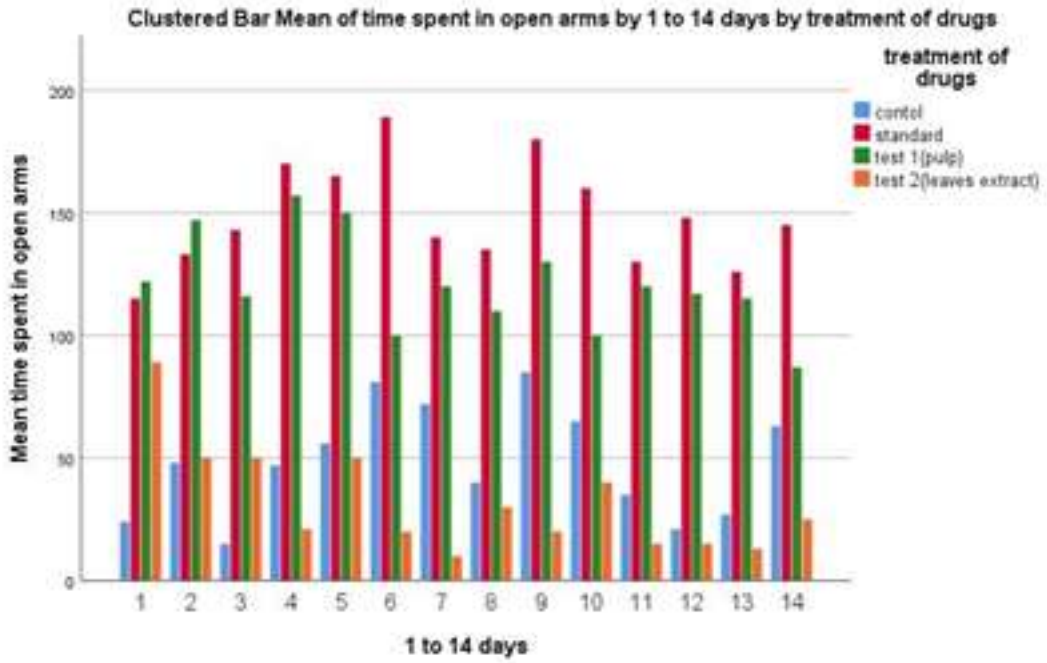

Figure 3: Illustrates the EPM results, emphasizing the increased time duration in the open arms by the pulp and Standard group compared to other groups.

Table 3: Anti-inflammatory effect by using Paw Edema Test among Control group, Standard, Test 1 and Test 2 by using one way ANOVA and Multiple Comparison Post hoc Tukey Test

ANOVA

inflammation reduced

	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	9.345	3	3.115	5.114	.004
Within Groups	31.671	52	.609		
Total	41.016	55			

Multiple Comparisons

Dependent Variable: inflammation reduced

Tukey HSD

(I) treatment of drugs	(J) treatment of drugs	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Control	Standard	1.13786*	.29497	.002	.3550	1.9207
	test 1 (pulp)	.69143	.29497	.101	-.0915	1.4743
	test 2 (leaves extract)	.49357	.29497	.348	-.2893	1.2765
Standard	Control	-1.13786*	.29497	.002	-1.9207	-.3550
	test 1 (pulp)	-.44643	.29497	.437	-1.2293	.3365
	test 2 (leaves extract)	-.64429	.29497	.141	-1.4272	.1386
test 1 (pulp)	Control	-.69143	.29497	.101	-1.4743	.0915
	Standard	.44643	.29497	.437	-.3365	1.2293
	test 2 (leaves extract)	-.19786	.29497	.908	-.9807	.5850
test 2 (leaves extract)	Control	-.49357	.29497	.348	-1.2765	.2893
	Standard	.64429	.29497	.141	-.1386	1.4272
	test 1 (pulp)	.19786	.29497	.908	-.5850	.9807

*. The mean difference is significant at the 0.05 level

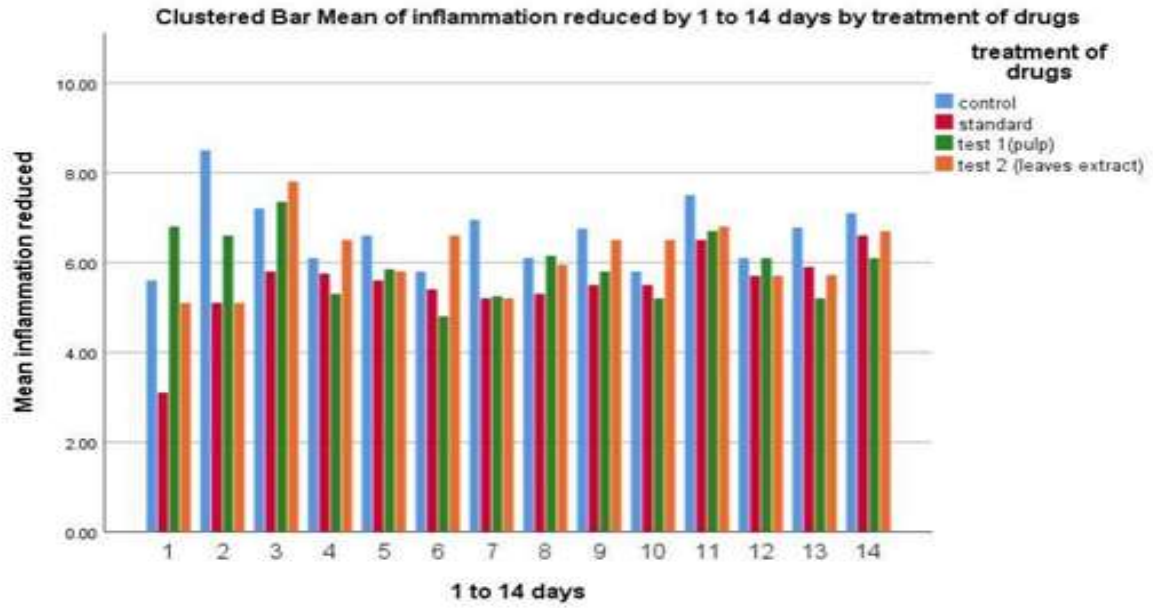

Figure 4: Illustrates the significant reduction in paw edema observed in the Standard, Test 1, and Test 2 groups compared to the Control.

The results highlights Java Plum's neuroprotective and anti-inflammatory effects. Quercetin, a flavonoid in Java Plum, has been shown to suppress neuro-inflammatory pathways and protect against oxidative stress. Additionally, tannins like ellagic acid in Java Plum is recognized for its anti-inflammatory and antioxidant aspects[21]. Java Plum's ability to regulate inflammatory pathways, particularly by inhibiting the NF-kB signaling cascade, may explain its neuroprotective effects. Anthocyanins, strong antioxidants responsible for Java Plum's colour, can suppress pro-inflammatory cytokines like TNF-á, IL-1â, and IL-6, which are boosted in neuro-inflammatory conditions. By inhibiting this pathway, Java Plum may reduce inflammation linked to mood disorders and neurological diseases[22].

Furthermore, although earlier studies examined the characteristics of pulp and leaf extracts separately, this study directly compares both the components using validated in vivo models for inflammation, anxiety, and depression, providing novel insight into their respective therapeutic potential.

The study assessed the anxiolytic and antidepressant effects of Java Plum extracts using the EPM and FST. EPM results showed increased time in open arms, suggesting reduced anxiety, while FST results revealed decreased immobility time, indicating potential antidepressant effects.

CONCLUSION

This study assessed *Syzygium cumini* (Java plum) extracts for their effects on depression, anxiety, and inflammation in rodents. Both pulp and leaf extracts showed anti-inflammatory effects, with the pulp extract also demonstrating anxiolytic and antidepressant properties. The leaf extract exhibited anti-inflammatory activity but lacked notable anxiolytic or antidepressant effects. These findings suggest Java Plum, especially its pulp, could be a potential treatment for mood disorders and neuroinflammation. More research is required to explore its long-term effects and mechanisms.

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