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Research Article

Histological Impact of Aqueous Extract of Neem Leaves (Azadirachta Indica) on the Portal Triad of Adult Albino Rats

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ABSTRACT
Introduction: Neem is a common ingredient of most herbal medicines used throughout the world as a house hold cure for hypertension and diabetes along-with different skin disorders.
Objective: To evaluate the effects of aqueous extract of neem leaves on the light microscopic features of portal triad in hepatic lobules of adult albino rats.
Material & methods: Rats in groups B and C received 40 mg/kg and 100 mg/kg of aqueous Neem extract via orogastric tube for 20 days, while group A rats were given simply distilled water (20 ml/kg). All of the rats were sacrificed at the conclusion of the experiment, and their livers were removed for histopathological analysis.
Statistical Analysis: All the data obtained was analyzed by using SPSS V 26. Comparison for inflammation and congestion in portal triad among groups was performed by using chi-square test. P-value ≤ to 0.05 was taken as significant.
Results: No inflammation seen in the portal triads among control group but it was observed that 13 animals in group B and 10 in group C had inflammation in portal triad.
Conclusion: It was concluded that hepatocytes of adult albino rats were found to be significantly harmed by high dosages of aqueous neem leaf extract.

Keywords: Neem, Albino Rat, Hepato-cellular Architecture and Portal Triad Congestion.

INTRODUCTION

The most valuable medicinal plant found in the subcontinent is neem. It grows on deep sandy soils in tropical and subtropical regions of Sri Lanka, India, and Burma.[1,2] Its white blossoms give way to clusters of tiny, bloated fruits that resemble olives. With spreading branches that resemble a crown, its intricate leaf pattern is similar to that of walnuts.[3] It exhibits a broad spectrum of temperature adaption. It can withstand freezing temperatures between 0°C and 4°C and thrive in hot temperatures up to 44°C.[4]

Although the plant's leaves have been used extensively for restorative and corrective reasons, literature has demonstrated that every single portion of the plant has therapeutic qualities and is commercially available.[5,6] It is a frequent component of the majority of herbal medications used worldwide as a home remedy for diabetes, hypertension, and various skin conditions, making it a part of India's traditional medical system.[4]

In herbal medicine, it is referred described as a "wonder tree" and a "nature's drug store" since it contains approximately 140 bioactive compounds, including proteins.[7] Its various mixtures of "triterpenes" give it a harsh taste. In addition to its amazing bactericidal and fungicidal qualities, it also has the ability to control insect growth.[5] Furthermore, a literature study has shown that Nimbidin, one of the main components of neem leaf aqueous extract, has anti-inflammatory, anti-pyretic, anti-arthritic, hypoglycemic, antiulcer, and anticancer properties.[8,9]

According to one earlier study, increasing the dosage of vepacide raised the levels of the enzymes ALT and AST in the kidneys, lung tissues, and serum, whereas after 45 and 90 days of administration, the levels of these enzymes decreased in the liver tissues of both

male and female rats.[10] However, it has been reported that 200 mg/kg of neem leaves caused inflammation in the liver and testes, among other organs.[11] As the neem is widely utilized by individuals as self-pharmaceutical present study was planned with the aim to evaluate the effect of aqueous neem extract at different doses on liver tissue of albino rats. The current study's findings complemented previous research and emphasized the harmful impact on albino rats' livers.

MATERIAL AND METHODS

Three equal groups (n=15) of forty-five albino rats of both sexes were randomly assigned to the following groups: group A (Control), group B (low dosage), and group C (high dosage). Rats in groups B and C received 40 mg/kg and 100 mg/kg of aqueous Neem extract via orogastric tube for 20 days, while group A rats were given simply distilled water (20 ml/kg). Morphine (0.3–0.5 mg/kg) and sodium penta-barbitol (45 mg/kg) were given intraperitoneally to all rats in-order to sedate.[12,13] All of the rats were sacrificed at the conclusion of the experiment, and their livers were removed for histopathological analysis. The liver was weighed, then cleaned with regular saline to get rid of the blood and preserved in tissue bottles with the proper labels for 48 hours using 10% formalin. Liver paraffin tissue blocks were created when tissue processing was completed. A rotary microtome was used to cut tissue sections in increments of 5 micrometers.

Statistical Analysis: All the data obtained was analyzed by using SPSSv 26. Parameter like inflammation and congestion in portal triad was described as frequencies and percentage. Comparison among groups was performed by applying chi-square. Parameter like weight of liver was described by using mean ± S.D. P-value ≤ to 0.05 was taken as significant.

RESULTS

Relative tissue weight index was found to be 4.66±0.45 for group A while for other groups was shown in table-1 mean ± SD.

Table-1: Weight of Liver among Groups after Neem Extract Administration

Group	RTWI			
	Mean	SD	Minimum	Maximum
Group A	4.66	± 0.45	4.27	6.12
Group B	3.63	± 0.27	3.21	4.21
Group C	3.63	± 0.35	3.22	4.58

Histological appearance of portal triad has been shown in figure-1(Group-A) and fig-2 and table-2 involving (Group– B& C). No inflammation seen in the portal triads among control group but it was observed other treatment groups.

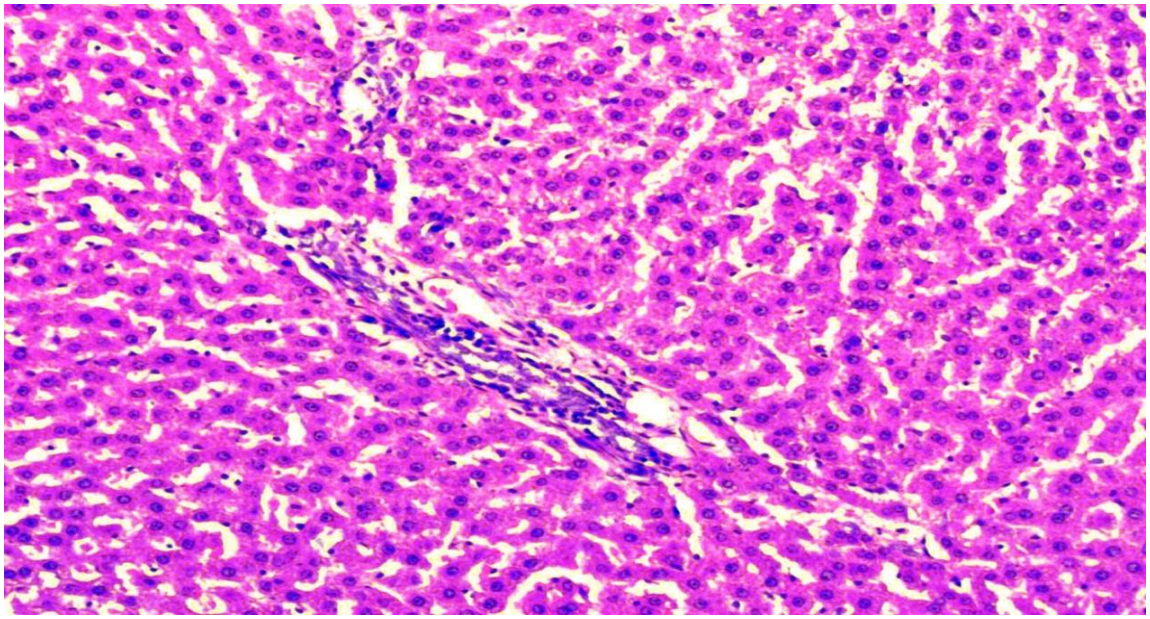

Fig-1: Normal Portal Triad in Control Group

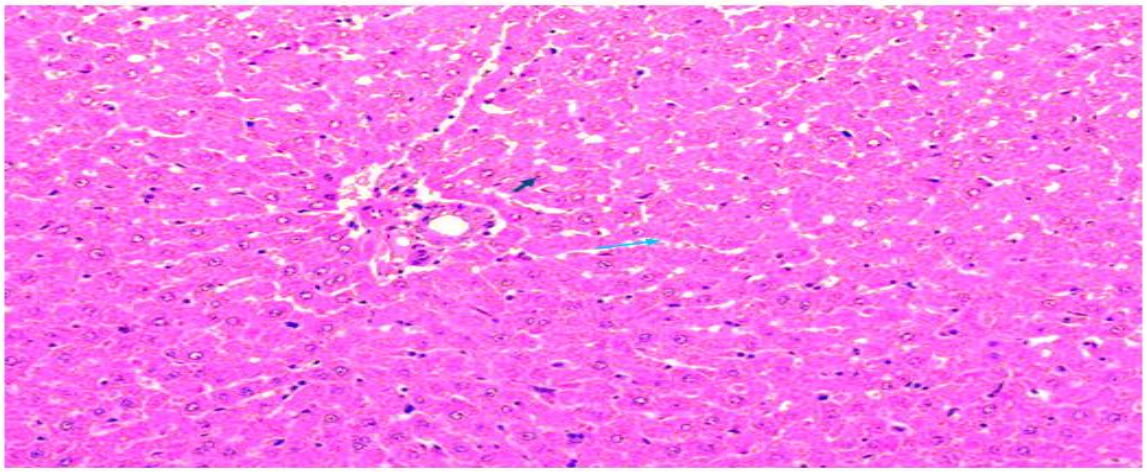

Fig-2: Inflammatory Portal Triad in Experimental Groups

Table-2: Comparison of Inflammation in Portal Triad

Groups	IPT			
	Positive		Negative	
	f	%	f	%
A	0	0	15	100
B	13	86	2	13
C	10	66	5	33
p-value	< 0.001*			

*Statistically significant

Inter group comparison for inflammation of portal triad was shown in table-3. Significant difference was observed when group B and C were compared to control with p-value ≤ 0.01.

Table-3: Pw-Comparison of Inflammation in Portal Triad among Groups

Comparison among Groups		Test	p-value
A	B	22.94	< 0.001**
	C	15.00	
B	C	1.68	0.195+

*Statistically significant

Congestion in the Portal Triad:

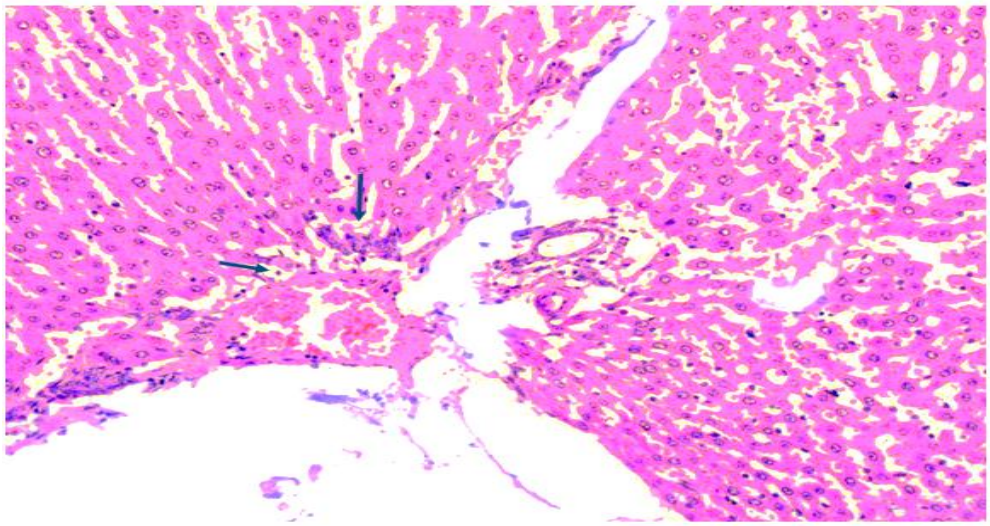

Fig-3: Group-C showing Portal Triad Congestion

The difference among three groups was significant with p-value < 0.001. It was observed that the group B animals did not have any congestion in portal triad while the congestion was present in 14 of the animals of group C while pair wise comparison was shown in table-4.

Table-4: Pw-Comparison of Congestion in Portal Triad among Groups

Comparison among Groups		Test	p-value
A	B		< 0.001**
	C	26.25	
B	C	26.25	0.195+

*Statistically significant

DISCUSSION

Although the plant's leaves have been used extensively for restorative and corrective reasons, literature has demonstrated that every single portion of the plant has therapeutic qualities and is commercially available.[5,6] It is a common ingredient of most herbal medicines used throughout the world as a house hold cure for hypertension and diabetes along-with different skin disorders thus constituting traditional medical system of India.[4] Many individuals in contemporary society ingest raw Neem leaves, and its extract is a typical supplement that is readily available in pharmacies. In a broad range of dosages, it is typically regarded as safer. It has since been established that greater dosages, particularly when used for an extended period of time, are harmful. It has also been well established to have detrimental effects on the liver, kidneys, lungs, and both male and female reproductive organs.

In present study, three groups were made with 15 albino rats in each group. Group-A was control group while Group-B and C received Neem extract at low and higher doses respectively. In contrast to present study, one researcher in his study had four groups and had 20 albino rats in each group and gave erythromycin along-with Neem extract in experimental groups. Thus methodology adopted in present study was different from above mentioned study.[14]

In contrast to control group A, the average body weight of experimental groups B and C in this study demonstrated a progressive decrease in weight and feed intake following neem ingestion. With a p-value <0.001, the difference was significant (table 1). Our findings were consistent with a prior study that shown that albino rats lost weight and had less appetite when given larger dosages of neem extract.[14]

Histological appearance of portal triad has been shown in figure-1(Group-A) and fig-2 involving Group– B& C). No inflammation seen in the portal triads among control group but it was observed that 13 animals in group B and 10 in group C had inflammation in portal triad. Similarly, inflammation in portal triad was observed by other researchers in their study after administration of Neem extract. This may be due to the fact that the inflammation areas lead to increase in blood flow and alterations in calibre of vessels.[13,14] Paradoxically, one previous study showed that Neem extract has anti-inflammatory effect but caused mild congestion of portal triad and sinusoidal spaces.[15]

CONCLUSION

It was concluded that hepatocytes of adult albino rats were found to be significantly harmed by high dosages of aqueous neem leaf extract. Its detrimental effects could be brought on by oxidative stress at the cellular level. Therefore, it is necessary to assess the safer dosage and duration of neem use in the general population.

Authors' Contribution:

SA & MFK: Conceptualization of Project
SA & AS: Data Collection & Write-up
AZ, MU&TL: Literature Search & Proof Reading

Conflicts of Interest: The authors declare that they have no conflict of interest.

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