WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

To Investigate the Anti-Inflammatory Activity of the Leaves Extract of Lactuca Canadensis.Linn in Experimental Animal

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A B S T R A C T

Background: Inflammation is a defensive response mechanism of the body against the harmful stimuli. This process not only removes the injurious stimuli but also helps in initiating the wound healing process of the tissue.Objective: The objective of the present work is to study the effect of Leaves extract of Lactuca canadensis linn. in croton oil induced inflammatory model in order to find out a new herbal medicine for the treatment of Inflammation. Methods: The phytochemical screening revealed that alkaloids, Terpenes, flavonoids, carbohydrates were present in Leaves extract of Lactuca Canadensis Linn.. Injection of Diclofenac Sodium (1ml/kg) used as standard drug. A dose of 0.1ml of croton oil was injected into subplantar surface of the left hind paw. The volumes of injected paws were measured before and 0,1,2,3,4,5 hrs after croton oil challenge using vernier caliper. Result: The result of anti-inflammatory activity for Croton oil induced Rat paw edema of the herbal aqueous Leaves extract of Lactuca canadensis Linn. revealed promising activity by reducing the paw volume in comparison of the control group. The aqueous extract has shown significant ($P < 0.05$) inhibition of paw oedema, 33.11% and 44.4% on 5th hour at the doses of 200 and 400 mg/kg, respectively.Conclusion: The results of present study demonstrate that aqueous extract of the leaves possess significant ($P < 0.05$) anti-inflammatory potential.

Keywords: Inflammation, Croton Oil, Aqueous Extract, Lactuca Canadensis Linn., Paw Edema, Herbal Medicine.

1.INTRODUCTION:

One of the key components of supplementary medicine is herbal medicine. Drugs made from herbs have been used for a long time to treat and prevent illnesses, including inflammation. Because the usage of herbal medicines and phytonutrients or nutraceuticals continues to grow quickly around the world, many people are now using them as part of their daily lives[1-3] Three-quarters of people, according to the World Health Organization (WHO), rely on conventional and herbal treatments for daily healthcare. Due to their less negative effects than synthetic pharmaceuticals, herbal medications are currently more popular. Many medicinal plants are available that have anti-inflammatory effects; some of them have been utilized since ancient times, while others are more recent[4-7]

According to WHO, nearly 75-80% of world population still depends on herbal medicines. Active constituents from plant sources directly used as therapeutic agent and phytoconstituents are also served as lead molecule for the synthesis of various drugs[8-11] Folk medicine and their use against diseases in different cultures is a vast traditional knowledge; which is based on the necessities, instinct, observation, trial and error and long experience of ancient/tribal people[12-14] Ayurveda, literally meaning the "science of life and longevity" in ancient Sanskrit, is the one of the oldest healing system of India, based on lifestyle diet and herbs Natural products with anti-inflammatory activity have long been used as a folk remedy for inflammatory conditions such as fevers, pain, migraine and arthritis. As the inflammatory basis of disease becomes clear, anti-inflammatory food and food products become of greater interest. Inflammation is a defensive response mechanism of the body against the harmful stimuli. This process not only removes the injurious stimuli but also helps in initiating the wound healing process of the tissue[15-17]

The term inflammation takes its roots from the Latin word “inflammare” (to burn) Inflammation is a dynamic process that is elicited in response to mechanical injuries, burns, microbial infections, and other noxious stimuli that may threaten the well-being of the host. To elaborate it further it is an

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essential immune response that enables survival during infection or injury and maintains tissue homeostasis under a variety of noxious conditions. Inflammation comes at the cost of a transient decline in tissue function, which can in turn contribute to the pathogenesis of diseases of altered homeostasis. The Romans described the characteristics of this response almost 2000 years ago. These symptoms came to be known as the four cardinal signs of inflammation: pain (dolar), heat(calor), redness (rubor), and swelling(tumor). This process involves changes in blood flow, increased vascular permeability, destruction of tissues via the activation and migration of leucocytes with synthesis of reactive oxygen derivatives (oxidative burst), and the synthesis of local inflammatory mediators, such as prostaglandins (PGs), leukotrienes, and platelet-activating factors induced by phospholipase A2, cyclooxygenases (COXs), and lipoxygenases. Arachidonic acid is a key biological intermediate that is converted in to a large number of eicosanoids with potent biological activities. . The two major pathways of arachidonic acid metabolism are the COX pathway, which results in the formation of both PGs and thromboxanes, and the 5-lipoxygenase pathway, which is responsible for the formation of leukotrienes and 5S-hydroxy-6E, 8Z, 11Z, 14Z-eicosatetraenoic acid (5-HETE)[18-21]

Inflammatory response is divided into innate immunity and adaptive immunity. The innate immune system mounts the initial response to tissue invasion. Vasodilation increased vascular permeability and cellular infiltration due to sepsis, severe trauma,etc are part of the innate immune response. The primary cellular components of the innate immune system are neutrophils, macrophages, dendritic cells, and natural killer (NK) cells. In addition to these cellular components, vasodilators and cytokines also play important roles in innate immunity. The classical cytokine-Secreting cells of the innate immune system are macrophages[22-25]

2.Materials and Methods

The plant extract were purchased from Shivay herbals and health care, Jaipur, Rajasthan.The extract would be subjected to different phytochemical tests for identification of different phytochemical principles. Extract would be studied for presence of important phytochemicals which may be involved in action of plant extract viz. sesquiterpene, alkaloids, flavonoids, tannins, steroids, saponin, carbohydrates etc.

2.1 Preliminary Phytochemical Screening

Phytochemical testing was carried to find out the secondary metabolites because secondary metabolites possess biological activity. The phytochemical screening revealed that alkaloids, Terpenes, flavonoids, carbohydrates were present in Leaves extract of *Lactuca Canadensis Linn.*

2.2 Experimental design Animals

Experiments would be performed in accordance with the committee for the purpose of control and supervision of experimental animals (CPCSEA) guidelines after the approval of the experimental protocol by the institutional animal ethical committee (IAEC). Wistar albino rats of either sex and 8- 10 weeks age would be used for the study,the animal would be housed 14 per cage at temperature (22 ± 3^0C) with 50- 60% of relative humidity under 12h day and night cycle and fed standard rodent chow and water ad libitum.

2.3 Drugs and Chemicals:

Standard drug:Injection of Diclofenac Sodium(1ml/kg) this is an Non steroidal anti-inflammatory drug (NSAID) purchased from Maharashtra Medicals, Gandhi chowk,Akola.

1.4 Other Chemicals

Croton Oil-Inducing Agent ordered online.
Normal Saline

2.5 Treatment Design

Group I Control- Normal Saline (1ml/kg)

Group II 1ml/kg diclofenac sod. Injection as standard reference
Group III Test extract of l*actuca canadensis L.*(100mg/kg)

Group IV Test extract of *lactuca canadensis L.*(200mg/kg)
Group V Test extract of *lactuca canadensis L.*(400mg/kg)

2.6 Evaluation of invivo anti-inflammatory activity

Wistar Rats were fasted for 12 hrs with free access to water before used for the experimentsFive groups of rats of either sexes were used in this experiment and each group was composed of six ratsThe First group as a control, received normal saline solutionThe second group as Standard, Received DiclofenacThe Third, Fourth and fifth group as test, received 100,200 and 400 mg/kg ethanol extract respectively.All the treatments were by oral gavage except standard dose it is given by intraperitonially.A dose of 0.1ml of croton oil was injected into subplantar surface of the left hind paw, 30 minutes after the oral administration of the test substances, the standard and the vehicle.The volumes of injected paws were measured before and 0,1,2,3,4,5 hrs after

croton oil challenge using vernier caliper.Edema was measured and percentage reduction in edema was calculated using the following formula:

$$\% \text{ reduction in edema} = \frac{\text{Mean edema (control)} - \text{Mean edema (drug treated)}}{\text{Mean edema (control)}} \times 100$$

2.7 Statistical Analysis

Data were expressed as mean±SEM; Mean diference between groups were analyzed by one-way ANOVA followed by Dunnet multiple comparison test using Graph pad prism version 5.0 software. $p \leq 0.05$ was considered as statistically signifcant.Data is presented in mean ± SEM. Here * means Significant difference ($p<0.05$) in compare to control group.

3.Results

Table 2: Effect of aqueous Leaves extract of *Lactuca Canadensis L*inn in Croton oil induced Paw edema model using vernier caliper.

Groups	Dose / Kg	Change in the Paw thickness (mm) ± SEM					
		0 Hr	1 Hr	2 Hr	3 Hr	4 Hr	5 Hr
Croton oil control	0.1 ml	3.90±0.04	4.91±0.030	5.76±0.061	6.26±0.105	6.16±0.076	5.98±0.065
Standard (Diclofenac)	1 ml	3.01±0.059	3.81±0.17	4.51±0.08	3.90±0.12	3.45±0.089	3.10±0.14
Croton oil + extract	100 mg	3.21±0.152	4.23±0.13	5.15±0.11	5.56±0.08	5.23±0.08	4.75±0.20
Croton oil + extract	200 mg	3.31±0.05	4.12±0.08	5.12±0.08	4.94±0.169	4.57±0.20	4.00±0.18
Croton oil + extract	400 mg	3.25±0.121	4.09±0.104	4.91±0.09	4.45±0.19	3.84±0.179	3.32±0.13

Table 2: % inhibition of Croton oil Induced paw edema in rat

Group	Dose in mg/kg	(%) Percent inhibition				
		1 hr	**2 hr**	**3 hr**	**4 hr**	**5 hr**
Control	Normal Saline Sol.	0.0%	0.0%	0.0%	0.0%	0.0%
Standard	1ml	22.4%	21.7%	37.6%	43.9%	48.16%
Test-1	100	13.84%	10.5%	11.18%	15.0%	20.56%
Test-2	200	16.01%	11.11%	21.08%	25.8%	33.11%
Test-3	400	16.7%	14.7%	28.9%	39.6%	44.4%

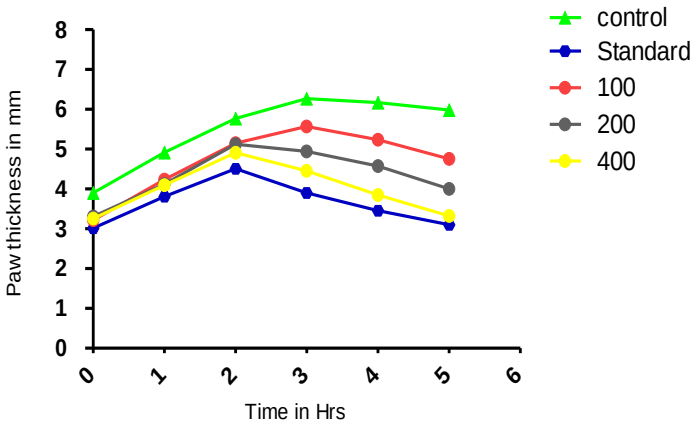

Fig. 1 Anti-nflammator Graph representing Effect of aqueous Leaves extract of *Lactuca Canadensis* Linn. in Croton oil induced Paw edema model using vernier caliper.

The result of anti-inflammatory activity for Croton oil induced Rat paw edema of the herbal aqueous Leaves extract of *Lactuca canadensis Linn.* revealed promising activity by reducing the paw volume in comparison of the control group. But activity of the extract was less than drug Diclofenac treated group. In the inflammatory responses histamine, serotonin, prostaglandin are the major mediator of the inflammation. The anti-inflammatory response of *Lactuca canadensis Linn.* Leaves extract may be because of the inhibition of cyclooxygenase which in turns inhibits prostaglandin biosynthesis that cause anti-inflammatory effect. Further investigations are necessary to determine and characterize the bioactive compounds responsible for the anti-inflammatory activity of the plant. The present study provides the scientific evidence for the anti-inflammatory activity of herbal aqueous Leaves extract of *Lactuca canadensis Linn*. and substantiate the conventional usage for inflammatory disorders.

The results of present study demonstrate that aqueous extract of the leaves possess significant ($P < 0.05$) anti-inflammatory potential.

4.Disscusion

The therapeutic use of herbal medicine increased from past decades due to the side effects of synthetic drugs. In the present study, the aqueous Leaves extract of *Lactuca canadensis Linn*. at a dose of 400 mg/kg significantly decreased the rat paw edema induced by croton oil in all phases, suggesting that the possible mechanism of the anti-inflammatory action of *Lactuca canadensis linn*. could be due to inhibition of release of mediators in all phases. The first phase of inflammation occurs within an hour of croton oil injection and is partly due to the trauma of injection and also due to histamine and serotonin component. All the mediators appear to be dependent upon an intact complement system for their activation and release. Diclofenac (non-steroidal) anti-inflammatory drugs were tested on croton oil induced edema. It was noticed that Diclofenac administration 1 ml/kg respectively showed a significant inhibitory effect starting after 1 and 1.5 hours following croton oil injection.

5.Conclusion

Aqueous Leaves extract of *Lactuca canadensis* L. possess significant anti-inflammatory potential. These findings support the use of the extract in traditional system of medicine for the management of inflammatory conditions.

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