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# Anti Inflammatory Activity of Moringa Oeifera

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## I. INTRODUCTION

In India the sources of medicinal plants have been used as medicines since the days of historic Vedic glory. Several medicinal plants and herbs form part of our diet as spices, vegetables and fruits.

Plants are being used in traditional medicine since history of mankind.[1]The knowledge of these medicinal plants has accrued in the course of many centuries leading to medicinal systems in India such as Ayurveda, Unani and Siddha.

It is anticipated that herbal drugs used globally were discovered following leads from local medicine. According to WHO reports that about 25% of modern medicines have been derived from plants which were first used traditionally. Many synthetic analogues are built on models of compounds isolated from plants. Most of the modern medicines in India are derived from natural products. An advanced research effort to describe the advantage of traditional system of medicine with respect to the safety and efficacy could result in a better use of these corresponding systems of medicine which is the need of time to address the issues. [2]

The use of rudimentary drugs and herbal formulations has a important role in new drug discoveries so it is important to justify their acceptability in modern system of medicine. On the other hand the major problems faced by the herbal drug industryis non availability of rigid quality control profile for herbal material and their formulations due to which thereis a need for studies in animals and humans to assess the safety and efficacy of herbs or plant extracts which are claimed to have a very good therapeutic potential. [3 4 5 6 7]

Research studies evaluating the safety, efficacy and appropriateness of the benefits of "*Moringa oleifera*" include an expanding list of promising medicinal and nutritional uses. Its English name is "Drumstick and the local name in Marathi is Shevaga " Although it may yet be too early to provide a significant number of claims about the precise benefits derived from Moringa oleifera, the breadth of current research appears to shed considerable light on many of the potential applications for products containing the primary ingredient of this plant.

Thus far, some of these applications include: neurotransmission, coagulation, anti-viral and antioxidant effects, use as an antifungal agent, hypoglycemic activity, analgesic and anti - inflammatory, radio protective effects, regulation of thyroid hormone, and hypolipidemic activity use in the folklore medicine. It is anticipated these potential benefits will ultimately translate into alternative modalities for treating a variety of medical conditions using a natural approach to patient care**.** [8]

All the parts of the tree (Moringa oleifera) are used in folk medicine practices for the treatment of various diseases such as UTI, External sores and Ulcers, Diabetes, Cancer, Gastritis, Diarrhea, Liver Diseases etc. The plant is reported to possess Anti-inflammatory, Antioxidant, Antiulcer, Anticancer, And Antihyperlipidaemic and Cardiotonic properties. [9 10 11 12 13] The studies on various extracts of its parts, i.e. coat, pulp and seed , leaves revealed more pronounced results indicating that its activity is widely distributed. [14]

Pain can be defined as , unpleasant sensation, usually evoked by an external or internal noxious stimulus. "Analgesic decrease the pain by acting on the CNS or peripheral pain mechanisms, without altering So analgesic activity means capacity of a substance to neutralize the pain sensation. [15] The environment has provided a vast collection of remedies to cure all ailments of mankind. Since the beginning of human era, along with the food crops, man has cultivated herbs for his medicinal needs. The knowledge of dr inquisitive nature, so that today we possess many effective means of ensuring health-care. In the past, almost all the medicines used were from plants. Today there

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has accumulated a vast store of knowledge concerning the therapeutic properties of different plants. The opioid analgesics and their derivative have never been surpassed as painkillers in efficacy or patient acceptability despite their Disadvantages. [16] Therefore, man has been on hunt since ages for suitable alternatives to NSAIDs and Opioid analgesics.

In recent decades, many scientific studies using the Extracts of Leaves, Barks, Seeds and Roots of *"Moringa oleifera"* are being carried out to confirm many potential uses. However very few studies have been done on the Leaf Extracts

Taking this background into consideration we conducted the study to investigate the presence of Phytochemical Constituents and to evaluate the Analgesic Activity of Ethanolic Leaf Extract of Moringa oleifera.

Inflammation is the natural response by a living tissue to various kinds of injury. Cyclooxygenase (COX) is the key enzymes in the synthesis of Prostaglandins, Prostacyclin and Thromboxane which are involved in Inflammation, Pain and Platelet Aggregation. [17] Steroidal and non-steroidal anti-inflammatory drugs (SAIDs and NSAIDs, respectively) are currently the most widely used drugs in the treatment of acute inflammatory disorders,though despite their Renal and Gastric negative secondary effects .[18] These drugs block COX-1 and COX-2 enzyme activity. COX enzymes assist with Prostaglandin Production. NSAIDs, Steroidal Anti-Inflammatory drugs are being used till now, As a result long termuses of these drugs cause adverse side effects and damage human biological system such as liver, gastrointestinal tract, etc on long term use. As a result of adverse side effects can lead to complications, like gastric lesions, cardiovascular, renal failure [19] and gastrointestinal damage in long term.[20]There is a need for the new safe, potent, nontoxic anti-inflammatory drug. In the present review an attempt has been made to investigate the anti-inflammatory activity of *"Moringa Oleifera"* Leaf extract.

Diabetes Mellitus (DM) is a metabolic disorder with significant morbidity and mortality. Diabetic patients present symptoms of chronic hyperglycemia along with glucose tolerance impairment. [21] There is oxidative stress concordantly which occurs with hyperglycemia and causes pathogenesis in many organs, leading to complications such as vasculopathies , neuropathies, nephropathies and ophthalmopathies . The diabetic patients require currently used drugs to control their blood glucose level and to improve blood glucose tolerance .[22] Recently, the use of herbal products has gained more interest for remedy of diabetes and other ailments. In the present review an attempt has been made to investigate the hypoglycemic activity of *"Moringa Oleifera"* Leaf Extract.

Heart diseases have been implicated as leading causes of death in all racial and ethnic groups. The elevation of serum total cholesterol and low density lipoprotein (LDL)cholesterol has been reported as a primary risk factor for cardiovascular disease.

Hyperlipidemia and reduced high-density lipoproteins (HDL-C) along with several risk factors such as life style, genetic factors & metabolic disorders have been implicated for the rise of the diseases. Oxidative modification of human low density lipoprotein may play an important role in atherosclerosis.[23] Hence Hypolipidemic Drugs are extensively used as prophylactic agents to prevent such atherosclerosis induced disorders but these hypolipidemic drugs are not free from adverse effects. Pancreatitis and rhabdomylosis due to HMGCoA reductase inhibitors have been reported like Atorvastatin is a well known sideeffect. [24].

A number of plants and herbs are being been used for the treatment of various cardiovascular diseases by the folklore. Use of the various medicinal plants for treatment of various diseases can be attributed to their phytochemical constituents and dates back since history . [25]. There has been an increase in the use of medicinal plants has been observed in metropolitan areas of developed countries . The advantages of herbal medicines reported are effectiveness, safety, affordability and acceptability.[26] Therefore our aim of the present investigation was , to evaluate the Hypolipidemic Effect of Ethanolic Extract of Moringa Oleifera Leaf as very few studies have been done .

Liver is the most important organ, which plays important role in regulating various physiological processes in the body. It performs various vital functions, like metabolism, secretion and storage. It is capable to detoxicate toxic substances and synthesize useful substances. Therefore, hepatoprotective agents having protective action on liver against

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hepatotoxic agents is of importance to be studied.

Liver diseases are mainly linked to the exposure of body to toxic chemicals, excess ingestion of alcohol, infections and various autoimmune disorders. Most of the hepatotoxic chemicals damage liver cells occur mainly by inducing lipid per oxidation and other oxidative damages. Currently drug therapy includes modern system of medicine, medicinal preparations in Ayurveda, the Indian systems of medicine, which are recommended for management of liver disorders. Natural remedies from medicinal plants are considered to be effective and safe alternative treatments for hepatotoxicity.[27]

The consumption of variety of herbs and vegetables by man is believed to contribute significantly to the improvement of human health in terms of prevention and cure of disease because plants have long served as a useful and rational source of therapeutic agents.

The liver is an organ having much importance, as it plays an essential role in the metabolism of various compounds entering the body. Conventional drugs used in the treatment of liver diseases are often inadequate and thus, it is therefore necessary to search for alternative drugs for the treatment of liver disease having better efficacy and safety.[1] Thus this study was undertaken to investigate the Hepatoprotective Nature of *"Moringa oleifera"* on induction of Hepatotoxicity by Carbon Tetrachloride (CCl4) known to cause Liver damage in Albino Wistar Rats.

The major aim of the present study is therefore to investigate the ameliorating potentials of the leaves extract of this plant on carbon tetrachloride (CCl4 ) mediated liver damage in Albino Wistar Rats .

Anxiety affects substantial part of the total population of the world in this new era and has become a very important area of research in psychopharmacology during this decade. Interest in alternative medicine and plant-derived medications that affect the s growing. Anxiety is a important presenting symptom of many psychiatric disorders and a foreseeable component of many medical and surgical conditions. Indeed, it is a universal human emotion, closely allied with appropriate fear and often serving psycho biologically adaptive purposes. A most important clinical generalization is that

commonly associated with depression, especially with panic disorder, Agrophobia, obsessive, Compulsive Disorder. [28]

Currently different therapeutic regimens are employed to treat anxiety and depressive disorders; but their clinical uses are limited by their side effects such as psychomotor impairment, potentiation of other central depressant drugs and dependence liability. In the current context it is implies that there is a need for new therapeutics for management of neurological disorders by use of medicinal plant research .some previous studies have shown effectiveness of different herbs in various animal models in management of neurological disorders.[29]

However, no systematic study on anti inflammatory activity has been reported in the literature. Therefore in the present investigation, we screened the Ethanolic Leaf Extracts of Moringa Oleifera" for Anti-Inflammatory activity in different experimental models in Albino Wistar Rats.

The present study therefore attempts to prove scientifically the traditional claim that Possess the Anti-Inflammatory Activity. The aim of our research is find out new drug preparation from "*Moringa Oleifera*" Which are proposed to be potent and nontoxic agents and possess the various activities. Normally herbal drugs are free from side effects /adverse effects and these are low cost medicines which will be beneficial for the people of our country.

## II. INFLAMMATION

### Definition and Classification of Inflammation

The term inflammation is derived from the Latin "inflammare" means to burn. It is a physiological response of living tissues to injury. It is not a disease, but a manifestation of disease. Diseases in which an inflammatory reaction is a major component are classified accordingly with suffix. They are usually named from the organ affected followed by the suffix '-itis'. Thus, acute inflammation of the meninges is called meningitis. But like any rule, it has its own exceptions such as in case of pneumonia, typhoid fever, etc. Inflammation is fundamentally a protective response intended to

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remove the initial cause of cell injury as well as the necrotic cells and tissues due to damage by noxious agent. It achieves its protective function by diluting, destroying, or otherwise neutralizing harmful agents (e.g., microbes or toxins). These events eventually heal and reconstitute the sites of injury. Thus, inflammation is intimately interlaced with repair processes whereby damaged tissue is replaced by the regeneration of parenchymal cells, and/or by filling of any residual defect with fibrous scar tissue. [140]

Cardinal signs of inflammation include, among others, swelling (tumour), redness (rubor), heat (calor), pain (dolor), and loss of function (functeo laesa). Inflammation requires the participation of various types of cells expressing and reacting to diverse mediators along a very precise sequence. [141]

Inflammation is generally classified based on the lesion and histological appearances in acute and chronic inflammation. However, these basic forms of inflammation can overlap, and many factors modify their course and histological appearance.

Acute inflammation, in the initial phase is transient series of tissue reactions to injury, of of very short duration, lasting from a few minutes to few days, and is characterized by fluid and plasma protein exudation with predominantly neutrophilic leukocyte accumulation. It is associated with increased vascular permeability, capillary infiltration and emigration of leukocytes. The classical symptoms of redness, heat, edema and pain are associated with acute inflammation. [142]

Chronic inflammation is of longer duration (days to years) due to the persistence of the initiating stimulus, interference of the normal healing process, repeated bouts of acute inflammation or low-grade smoldering due to continued production of immune response mediators. It is typified by influx of lymphocytes and macrophages with associatedvascular proliferation and scarring . [143]

**2.2 Process of inflammation**

Inflammatory process has two phases: acute and chronic. Acute and chronic inflammations are known to be complicated processes induced by several different classes of chemical mediators, e.g. prostaglandins, leukotrienes and platelet-activating factor, etc. Anti inflammatory agents exert their effect through a spectrum of different modes of action.

Acute inflammatory response is characterized by an increase in vascular permeability and cellular infiltration leading to oedema formation as a result of extravasation of fluid and proteins and accumulation of leukocytes at the inflammatory site for short time. [144]

Chronic inflammation is the reaction occurring when the acute response is insufficient to eliminate the pro-inflammatory agents. Chronic inflammation comprises of proliferation of fibroblasts and infiltration of neutrophils leading to exudation of fluid. Chronic inflammation also occurs due to the persistence of infection or antigen, recurring tissue injury, or a failure of endogenous anti-inflammatory mechanisms. Chronic (or acute) inflammation is mediated by activating inflammatory or immune cells, among which macrophages play a dominant role in managing many different phenomena including the overproduction of proinflammatory cytokines and inflammatory mediators, generated by activated iNOS and COX-2.[145]

Under inflammatory conditions, immune cells are also stimulated by adhesion molecule activation signals in order to enhance the migration capacity to inflamed tissue and finally to form heterotypic cell clustering between the immune cells, endothelial cells and inflamed cells. Macrophages in the inflammatory reaction initially requires an interaction between surface receptors such as Toll-like receptors (TLR) and stimuli, and subsequent up-regulation of intracellular signaling events mediated by enzymes such as phosphoinositide 3-kinases (PI3K) and mitogen activated protein kinases (MAPKs) as well as transcription factors (e.g., nuclear factor [NF]- and activator protein [AP]-1) . Overall, these events lead macrophages to express pro-inflammatory genes such as inducible NO synthase (iNOS) and cyclooxygenase (COX)-2. Because large amounts of macrophage- derived inflammatory mediators can cause collateral or severe damage such as septic shock, rheumatoid arthritis and arteriosclerosis, the effective blockade of these inflammatory responses is an important therapeutic target. [146-147]

Inflammatory diseases are a major cause of morbidity of the work force throughout the world. These have been called the "King of Human Miseries" Pain

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is an objectionable sensory and emotional incident associated with actual or potential tissue inflammation. Pyrexia or fever is caused as a secondary impact of inflammation. Inflammation, pain and fever are all associated with enhanced production of prostaglandins. Thus, most anti-inflammatory agents are expected to possess analgesic and antipyretic activity.[148]

**2.3 Chemical mediators of Inflammation** [149]

The inflammatory response is a complex and highly regulated sequence of events that start with an initial production of pro-inflammatory mediators that recruit professional inflammatory cells to the site of injury to clear the offending trigger. Macrophages play major roles in the immune and inflammatory responses involved in host defense. Activated macrophages secrete a number of different inflammatory mediators, including tumor necrosis factor-α - (TNF), interleukin 1-β 1β), interleukin-6 (IL- 6), reactive oxygen species (ROS), prostaglandin E2 (PGE2), nitric oxide (NO), etc.

**A] Cyclooxygenase (COX)**[150]

COX is the key enzyme that catalyses the first two steps in the biosynthesis of the prostaglandins (PGs). The COX pathway leads to the generation of prostaglandins and thromboxanes, which mediate the pain and edema associated with inflammation. There are two isoforms of COX: COX-1 and COX-2. COX-1 is detectable, but COX- 2 is not detectable in most normal tissues, however, COX-2 can be induced by many factors such as pro-inflammatory cytokines etc. Studies indicate that COX-2 plays an important role in inflammation. Thus agents that would suppress the activity or protein expression of COX- 2 are likely to be precious medicine for anti-inflammation and pain ease. Thus, decreasing of synthesis and activity of COX-2 can result in anti-inflammatory action both in localized and systemic conditions.

**B] Arachidonic acid**

The lipoxygenase pathway utilizes arachidonic acid by 5 -lipoxygenase to produce the lipoxygenase products e.g. leucotrienes (LTs) which are also involved in inflammatory reactions as pro-inflammatory mediators. Leukotrienes, i.e. LTC4 and LTD4 cause edema together with increased microvascular permeability.

**C] Thromboxane** [152]

Thromboxane A2 (TXA2) is an arachidonic acid metabolite produced during the catalysis of arachidonic acid by the sequential action of COX and thromboxane synthase (TXS), which is well established as a potent vasoconstrictor. This metabolite participates in various physiological and pathological processes ranging from synaptic transmission to inflammation. Platelets represent the best known cell type to produce TXA2 in response to various stimuli. However, many other cells and tissues are also able to synthesize TXA2.

**D] Leukotrienes** [153]

Leukotrienes (LT) are end products of the metabolism of arachidonic acid by 5 - lipoxygenase. Leukotrienes have physiological roles in innate immune responses and pathological roles in a variety of inflammatory and allergic diseases, such as rheumatoid arthritis, inflammatory bowel disease, psoriasis, allergic rhinitis, but most prominently in bronchial asthma.

**E ] Polyunsaturated fatty acids (PUFA)**[154]

Linoleic acid (LA) and α-linolenic acid (ALA) belong to the n-6 (ω-6) and n-3 (ω-3) series of polyunsaturated fatty acids (PUFA). LA and ALA are precursors for the synthesis of higher unsaturated species: arachidonic acid deriving from LA, and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) deriving from ALA. One possible mechanistic explanation for these anti-inflammatory and antitumorigenic effects may be that an increased consumption of EPA and DHA results in an increased incorporation of these fatty acids into phospholipids at the expense of arachidonic acid. Consequently, they also replace arachidonic acid as a substrate for COX and LO that results in a reduced formation of PGE2, TXA2, LTB4 and LTE4.

**F] Histamine** [155]

Histamine (HA) is a biogenic amine that affects a variety of functions in the human body. It has been known to play a role in inflammation, gastric acid secretion, and neurotransmission

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.Multiple receptors exist for histamine in the mammalian tissues and these have been classified into 4 distinct receptor types (H1, H2, H3, and H4), all of whichare G-protein coupled receptors (GPCRs). Histamine appears to play a complex role in pain modulation. Histamine released from mast cells is an established mediator of acute allergic reactions and chronic inflammation. Histamine and other mediators of inflammation increase the vascular permeability during the process of injury. Chemical - induced vascular permeability (such as seen with acetic acid) causes an immediat e sustained inflammatory reaction that is prolonged over 24 hours.

**G] Nitric oxide (NO)**[156]

It is widely known that nitric oxide (NO), synthesized from L-arginine by nitric oxide synthase (NOS), is involved in diverse physiological processes. An excess in NO production is largely thought of as causing a variety of inflammatory diseases, such as sepsis, psoriasis, arthritis, multiple sclerosis, and systemic lupus erythromatosus.

**2.4 Physiological Role of Inflammation** [157]

Inflammation is an important physiological reaction, which occurs in response to a wide variety of injurious agents (bacterial infection or physical trauma) ultimately aiming to perform the dual function of limiting damage and promoting tissue repair. It has beneficial effects, such as the destruction of invading micro-organisms and the walling-off of an abscess cavity, thus preventing spread of infection. The endogenous biochemical pathways activated during defense reactions can counter-regulate inflammation and promote resolution.

**2.5 Pathological Role of Inflammation** [158]

Although inflammation helps clear infections and, along with repair, makes wound healing possible, both inflammation and repair have considerable potential to cause harm. In many diseases such as arthritis, obesity induced insulin resistance, multiple sclerosis, inflammatory bowel disease, and asthma, the inflammatory process is not appropriately regulated contributing to the pathogenesis of common chronic inflammatory diseases. As a result, significant tissue dysfunction (leading to the generation of the symptoms that typify these diseases), and tissue re-structuring occur (e.g., fibrosis) that can further impair tissue function. Thus, inflammatory responses are the basis of life-threatening anaphylactic reactions to insect bites or drugs, as well as of certain chronic diseases such as rheumatoid arthritis and atherosclerosis. Other harmful examples include inflammationin the peritoneum leading to fibrous bands that cause intestinal obstruction, or pericardial inflammation resulting in dense encasing scar that impairs cardiac function.

**2.6 Management of inflammation**

There are more drugs designed to fight inflammation in the human body than any other single category of drugs. Anti-inflammatory agents stop or disrupt inflammation by suppressing or altering the chemical signals associated with the inflammatory response.

**A] Non-steroidal anti -inflammatory drugs**[159-160]

Non-steroidal anti-inflammatory drugs (NSAIDs) mediate their action by inhibiting both cyclooxygenase (COX-1 and -2) include; Aspirin, Ibuprofen and Indomethacin. Selective COX-2 inhibitors include the Coxibs (e.g., Celecoxib) and Meloxicam. NSAIDs are mainly indicated for mild to moderate pain and rheumatoid arthritis. Other indications include osteoarthritis, soft-tissue injury, renal colic, postoperative pain, and dental procedures. The main mechanism of action of these drugs is believed to be the inhibitionof the COX enzymes (COX-1 and COX- 2) and consecutively the conversion of AA to PGs.

**B] Glucocorticoids**[161]

Glucocorticoids (corticosteroids or steroids) are the most effective anti-inflammatory agents available for many inflammatory and immune diseases including, asthma, rheumatoid arthritis, inflammatory bowel disease, and other autoimmune diseases. Glucocorticoids are able to bind with the cortisol receptors and trigger various biological effects. Although there are several mechanisms by which glucocorticoids reduce inflammation, a major one could be to reduce expression of cytokine-induced genes. Glucocorticoids inhibit the expression of proinflammatory cytokines. They also inhibit the generation of inflammatory mediators PGs, TXs, LTs and NO by suppression of gene expression of PLA2, COX-2, and iNOS. Further they alter recruitment and

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activation of inflammatory cells such as, monocytes, macrophages, eosinophils or lymphocytes.

**Models of anti-inflammatory studies in animal models**

here are number of steroidal and non steroidal anti-inflammatory drugs available in the market; and they are having good potential as anti-inflammatory and antipyretic drugs (eg. diclofenac, aspirin, indomethacin, etc.), but they cause undesired, unpleasant and serious adverse side effects on liver and gastrointestinal track. There is a need to develop new and more potent anti-inflammatory drugs with minimum adverse effects. There are a number of animal models used for studying anti-inflammatory activities of medicinal plants. The below mentioned models are used commonly for evaluating the anti-inflammatory and analgesic potential of medicinal plants.

**A] Models for acute inflammation**[166]

1. Agar induced paw edema
2. Arachidonic acid induced paw edema
3. Capsaicin induced ear edema
4. Carrageenan induced paw edema
5. Croton oil induced ear edema
6. Dextran induced paw edema
7. Formaldehyde induced paw edema
8. Egg-albumen induced paw edema
9. Histamine induced paw edema
10. Prostaglandin induced ear edema
11. Serotonin induced paw edema
12. TPA(12-O-tetradecanoylphorbol-
13. 13-acetate) induced ear edema
14. Xylene induced ear edema
15. Zymosan induced peritonitis

**B] Model for chronic inflammation**

1. Cotton pellet induced granuloma
2. Complete Freund's Adjuvant

In comparison of all these models, carrageenan induced rat paw edema is the most commonly used animal model for evaluation of anti-inflammatory property of medicinalplants.

**C] CARREAGEAN**

Carrageenan belongs to a family of gel-forming polysaccharides, obtained by extraction from species of red seaweeds . Carrageenan is derived from a number of seaweeds belonging to class Rhodophyceae. Carrageenan is used in food preparation for its gelling, thickening, and emulsifying properties. It is also used in pharmaceutical applications and experimental medicine this substance is often used for the evaluation of anti-inflammatoryagents.

**Chemical structure** [167]

Carrageenan is a sulfated polygalactan with 15 to 40% of ester-sulfate content and an average relative molecular mass well above 102 kDa. Composition is by alternate units of d-galactose and 3,6-anhydro-galactose (3,6-AG) joined by -1,3 -1,4- glycosidic 35% sulphate groups.

linkage. Carrageenan is divided into various types such as λ, κ, ι, ε, μ, all containing 22 to α and β

**Biological activities** [168]

The antioxidant activity of all carrageenans has been studied. λ- Carrageenan exhibits the highest antioxidant and free radical scavenging activity. Carrageenan from red marine algae is known to be a potent inflammatory agent in rodents and primes mice leucocytes to produce tumour necrosis factor- - lipopolysaccharide.

α (TNF α) in response to bacterial

**Carrageenan-induced paw oedema model** [169]

Carrageenan-induced rat paw oedema is a most widely used test to determine anti-inflammatory activity and comprises of a simple and routine animal model for evaluationof pain at the site of inflammation without any injury or damage to the inflamed paw. Ratpaw oedema has been increasingly used to test new anti-inflammatory drugs as well as to study the mechanisms involved in inflammation. In the literature, there are about many papers reporting the use of rat paw oedema.

A freshly prepared solution of 1 3% carrageenan in saline as an intraplantar injection in doses of 50 –150 µl is commonly used higher concentrations have been used for the modelling of specific pathophysiological conditions . The development of oedema following the injection of carrageenan the rat hind paw there is biphasic response which is achieved due to various mediators of inflammation to produce the inflammatory response.

The initial phase of oedema, which is not inhibited by nonsteroidal anti- inflammatory

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drugs (NSAIDs) such as indomethacin or aspirin, has been attributed to therelease of histamine, 5-hydroxytryptamine (5-HT) and bradykinin. The second accelerating phase of swelling has not only been correlated with the elevated production of prostaglandins, but more recently has been attributed to the induction of inducible cyclooxygenase (COX-2) in the hind paw. It can be blocked by the NSAIDs. Local neutrophil infiltration and activation also contribute to this inflammatory response by producing, among other mediators, oxygen- derived free radicals such as superoxide anion ($O_2$ ) and hydroxyl radicals.

Another important mediator in acute inflammation is nitric oxide (NO) which is produced in pathological conditions by three distinct isoforms of nitric oxide synthase (NOS): endothelial NOS (eNOS), neuronal NOS (nNOS) and inducible NOS (iNOS).

Aim & Objective

**AIMS & OBJECTIVE OF STUDY**

Herbal drugs play a role in the diseases and most of them speed up the natural healing process. Numerous medicinal plants and their formulations are used for various disorders in ethno medical practices as well as traditional systems of medicines in India.

Since prehistoric days attempts are being made to find out suitable drugs from natural sources for treatment of different diseases. The rational approaches, experiences of folk medicines provide a valuable approach in search for the development of new and useful therapeutic agents. Gradually keeping in pace with the scientific interpretation of drug actions, the causes of the diseases and the development in field of chemistry and technology, intensive efforts are being directed towards the design and the synthesis of new drugs.

The aim of research is to find out new drugs from indigenous plants, which are potent and nontoxic agents. These plants are traditional medicinal plants. Their chemical characters, mode of actions and toxicity studies is yet to be established. Our Present study deals with the study

**To Evaluate The Study Anti-inflammatory, Activity Of *"Moringa Olefera"* Leaf Extracts In Albino *Rats Model For Preventive And Curative Effect"***

Normally herbal drugs are free from side effects /adverse effects and they are low cost medicines which will be beneficial for the people of this country. Keeping this in view we have selected the Moringa Oleifera plant.

The present study**, To Evaluate The Study Anti-inflammatory, Activity Of *"Moringa Olefera"* Leaf Extracts In Albino wistar Rats.** Was undertaken at the Department of pharmacology, AIPS, Sagar with the following objectives:

a) Identification, Collection and Extraction of Moringa oleifera leaf .

b) To evaluate the Anti inflammatory effect of Moringa oleifera leaf extract by the carregenan induced inflammation model.

The research into plants having folklore use as pain relievers and anti-inflammatory agents is definitely a productive and logical research strategy for development of new analgesic and anti-inflammatory drugs .Moringa Oleifera is one such plant whose anti- inflammatory activities have not been yet explored .Only few studies have been done which are as follows .

**Caceres el al** reported anti-inflammatory activity from the hot water infusions of flowers, leaves, roots, seeds and stalks or bark of Moringa oleifera using carrageenan-induced hind pawedema in rats.

**Medhi et al** evaluated anti-inflammatory activity of methanol extract of Moringa oleifera root bark using carrageenan induced paw edema in mice as animal model

**M. Ndiaye el al** evaluated the anti-inflammatory action of an aqueous extract of root of Moringa oleifera in rats using indomethacin (10 mg/kg) as standard drug and oedema was induced in the rat-paw by subcutaneous injection of carragenan. At a dose of 750 mg/kg the Moringa oleifera treatment significantly inhibited the development of oedema at 1, 3 and 5 hours (reduction by 53.5, 44.6 and 51.1% respectively).

**S. G. mahajan et al** investigated anti inflammatory activity from the ethanolic extract of seeds of Moringa oleifera. The extract was pharmacologically evaluatedagainst immune mediated inflammatory responses in toluene di isocyanate (TDI as antigen)- induced asthma in Wistar rats .

**Ammara Saleem et al** 2020 were evaluated nti-arthritic potential of Moringa oleifera (wild type). Different extracts of the plant leaves The plant extracts were assessed for in vitro antioxidant activity by different methods followed by in vitro anti-inflammatory assays such as protein denaturation, membrane stabilization and anti-proteinase activities. The plant extracts were

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further assessed in Wistar rats by formaldehyde induced arthritis model at 150, 300 and 600 mg/kg dosage level. Chemical analysis showed that methanolic and aqueous extracts contained the highest total phenolic and flavonoid contents.

**Mutmainnah Nurul et al** 2020 were Systematic Reviewed of Moringa oleifera's Potential as Antibacterial and AntiInflammatory in the Oral Cavity**.** Moringa plant is a plant that is spread throughout the region in Indonesia and has many benefits. Moringa oleifera L. plant is also known as the "miracle of tree" because almost all parts of the plant, from the leaves, bark, seeds, fruit of moringa to the roots are used by humans, especially as traditional medicine. Moringa has been proven effective as antibacterial and anti-inflammatory, for example in toothpaste, mouthwash, and root canal irrigation from chitosan.

**Yong-Bing Xu et al 2019** were worked on Antioxidant and Anti-Inflammatory Activities of the Crude Extracts of Moringa oleifera from Kenya and Their Correlations with Flavonoids Moringa oleifera Lam. (M. oleifera) is commonly distributed and utilized in tropical and sub-tropical areas. There has been a large number of reports on the antioxidant and anti-inflammatory activity of its leaves, but only a few about its seeds and roots. Hence, in this work we aimed to systematically compare the antioxidant and anti-inflammatory activities of the ethanol crude extracts of leaves, seeds, and roots of M. oleifera from Kenya, and further correlate the differential activities with the chemical constituents from these three parts.

**Asha Jaja-Chimedza et al 2017** were studied to develop, validate and biochemically characterize an isothiocyanate-enriched moringa seed extract (MSE), and to compare the anti- inflammatory effects of MSE-containing moringa isothiocyanate-1 (MIC-1) with a curcuminoid- enriched turmeric extract (CTE), and a material further enriched in its primary phytochemical, curcumin (curcumin-enriched material; CEM). MSE was prepared by incubating ground moringa seeds with water to allow myrosinase-catalyzed enzymatic formation of bioactive MIC-1, the predominant isothiocyanate in moringa seeds. Optimization of the extraction process yielded an extract of 38.9% MIC-1. Phytochemical analysis of MSE revealed the presence of acetylated isothiocyanates, phenolic glycosides unique to moringa, flavonoids, fats and fatty acids, proteins and carbohydrates. MSE showed a reduction in the carrageenan-induced rat paw edema (33% at 500 mg/kg MIC-1) comparable to aspirin (27% at 300 mg/kg), whereas CTE did not have any significant effect.

**Munirat Abolore Idris et al 2016** were reviewed on the use of Mornga oleifera seed extract and it application in the environment. It is usually referred to as the miracle tree because of its vast usefulness of its various parts. It is a source of protein, calcium, iron, carotenoids and phytochemicals utilized for several usage in developing countries. The plant parts have been used in various applications such as medicine, cosmetics, food supplements and water purification.

**J. Hartman et al. 2015** reviewed on Moringa oleifera leaves, seeds, bark, roots, sap, and flowers are widely used in traditional medicine, and the leaves and immature seed pods are used as food products in human nutrition. Leaf extracts exhibit the greatest antioxidant activity, and various safety studies in animals involving aqueous leaf extracts indicate a high degree of safety. No adverse effects were reported in association with human studies. Five human studies using powdered whole leaf preparations of M. oleifera have been published, which have demonstrated anti-hyperglycemic (antidiabetic) and anti-dyslipidemic activities. These activities have been confirmed using extracts as well as leaf powders in animal studies. A rapidly growing number of published studies have shown that aqueous, hydroalcohol, or alcohol extracts of M. oleifera leaves possess a wide range of additional biological activities including antioxidant, tissue protective (liver, kidneys, heart, testes, and lungs), analgesic, antiulcer, antihypertensive, radioprotective, and immunomodulatory actions.

**Duero (2014)** studied the antibacterial activity of leaves of Moringa oleifera. Leaves extract was prepared by solvent extraction using ethyl alcohol and water as solvent and antibacterial activity against both the organism in the form of zone of inhibition in the culture media.

**Cacereers et al. (2012)** found preliminary screening of antimicrobial activity of Moringa oleifera. Leaves, root and seeds were tested against bacteria, yeast dermatophytes and helminthes by using disc diffusion methods. The result showed that fresh leaf juice and aquous extracts of seed inhibit the growth of Pseudomonas aeruginosa and Staphylococcus aureus.

The assessment of various plant products according to their traditional uses and medicinal value is established on their therapeutic efficacy which leads to the discovery ofnovel and modern drugs for treating various ailments. This fact

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forms the basis for the
belonging tothe family Moringaceae, is one such plant of medicinal value which is also commonly
known as 'Sahajan' in Hindi , "Shevaga" in Marathi and "Horse radish" in English.[6]

**Geographical distribution**

"*Moringa oleifera*" is a small to medium sized tree, attaining a height of about 10 meters high and is cultivated throughout the plains of Indi is a commonly grown plant species in the areas of India, Pakistan, Bangladesh and Afghanistan. The rapidly-growing tree was utilized by the ancient Romans, Greeks and Egyptians and is now widely cultivated and has become acclimatized in many locations in the tropics. It is a perennial softwood tree having timber of low quality, which since centuries has been used for traditional, medicinal and industrial uses. It is an commonly grown crop in India, Ethiopia, the Philippines and the Sudan, and is now also being grown in West, East and South Africa, Latin America tropical Asia, the Caribbean, Florida and the Pacific Islands. All the parts of the Moringa oleifera tree are utilized and have been consumed by humanssince ancient times.

**Plant morphology**

"*Moringa oleifera*" is a small, rapidly-growing, deciduous tree that growing to height of 10 or 12 meters . It has a fragile branches, which are feathery and foliage of tri-pinnate leaves, the bark is thick, corky.

**Leaves and young shoots**

The Leaves are bipinnate and sometimes tripinnate, 45 cm long, and are arranged alternately and spirally on the twigs. Pinnae and pinnules are opposite; leaflets are 1.2 to
2.0 cm long and 0.6 to 1.0 cm wide, petioles of lateral leaflets are 1.5 to 2.5 mm long, whilethose of terminal ones 3 to 6 mm in length.

**Flowers, fruits and seeds**

The flowers are slender, with hairy stalks in spreading or drooping axillary clusters (panicles) 10 25 cm long. Individual flowers are set in a basal cup (hypanthium) about 3 mm long and approximately 0.7 to 1 cm long and 2 cm broad, with five unequal yellowish-white, thinly veined, spatulate petals, five stamens with five smaller sterile stamens (staminodes), and a pistil composed of a 1 - celled ovary and slender style. The fruits are linear, three-sided pods with nine long ridges, usually 20 to 50 cm long, but can be 1 m or longer, and 2.0 to 2.5 cm broad. The pods, each contains up to 26 seeds which are dark green during their development and take approximately 3 months to mature after flowering.

They turn brown on maturity, and split open longitudinally along the three angles, releasing the dark brown, trigonous seeds. Seeds measure about 1-1.2 cm in diameter, with three whitish papery wings on the angles. Seed weights differ among varieties, ranging from 3,000 to 9,000 seeds per kilogram.

**Figure 1 Figure showing flowers, leaf, seed and fruits of Moringa Oleifera**

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**Scientific classification of moringa oleifera**
**Kingdom:Plantae**
**Division:Magnoliophyta**
**Class:Magnoliopsida**
**Family: Moringaceae**
**Genus: Moringa**
**Species:Oleifera**
**Scientific name:Moringa oleifera Lam**
**Vernacular names**
**English:Horse radish tree, Drum-stick tree**
**Hindi.:Sahijana**
**Marathi:Shevga**
**Sanskrit .:Sobhanjana, Bahola, Sakapatra, Sigru Gujrati .:MidhoSaragvo, Saragavo, Segto, SeylaKannada. :Nugge**
**Tamil:Murungai**
**Telugu: Sajana, Munaga Habitat**:The tropics and subtropics

**PHYTOCHEMISTRY OF MORINGA OLEIFERA LEAF**

Various compounds have been documented in the leaves of Moringa oleifera. The phytochemicals are polyphenol, phenolic acids, flavonoids, alkaloids vitamins, carotenoids, ,isothiocyanates, tannins, glucosinolates, saponins ,oxalates and phytates.

**Uses of Moringa**

**1] Medicinal uses of Moringa**

Multiple uses have been found of various parts of the Moringa Oleifera plant. The high quality protein present in the leaves has led to its widespread use by physicians, healers, nutritionists to treat malnutrition and other illnesses. The seeds of Moringa are considered to have antipyretic action but are slightly acrid and bitter [91] and also reported to have antimicrobial activity. The plant also contains numerous phytochemicals, having other medicinal properties. Current studies demonstrate that isothiocyanates present in Moringa Oleifera have antitumor activity against cancers of the lung, breast, skin, oesphagus, and pancreas [92-93] and this family contains fairly unique group of glycoside compounds called glucosinolates and isothiocyanates. Small proteins/ peptides were isolated from the leaves of Moringa oleifera which are known to have antifungal and antibacterial activity [94]. The leaves are emetic in nature and their juice with black pepper is used to treat headache in folklore. The wrapping of leaves is helpful in reducing glandular swelling. The leaves possess anthelmintic properties, aphrodisiacs, treat hallucination, cough and asthma.

Decoction of dried leaves is used externally for treatment of rheumatism, and also for wound healing. Also the leaves made in to a paste with salt are used to treat edema .[95] Leaves are also used in scurvy and catarrhal affection. The leaves are known to possess anti-inflammatory, anthelmintic, properties. The crushed leaves are taken in the form of a tablet preparation to relieve stomach pain in menstruation by women in north western region of Karnataka. A paste of the leaves is applied externally to promote healing of wounds. The juice extracted from leaves has a strong antibacterial and antimicrobial properties [95] . All parts of the tree are considered to possess medicinal properties and used in treatment of Ascites, rheumatism, and venomous bites and as cardiac and circulatory stimulants.

The root is known to posess laxative, expectorant, diuretic activity and also used for treating inflammations, throat pain, bronchitis, piles, urinary discharges, and obstinate asthama. [96] Root bark is useful in heart complaints, eye diseases, fevers, inflammation, dyspepsia.[97] The root and barks are known to possess abortifacient properties. The flowers are used in conditions of inflammations and muscles diseases, the fruit is used in flklore to treat biliousness pain, leucoderma and tumour.[98] Oil is also useful in treatment in letrous ulcers and used as external aplications for rheumatism. [99]

**Other uses**

**1] Moringa as food**[100-101]
**2] Moringa as animal feed and plant growth enhancer**[102] **3] Moringa seeds as water purifying agent**[103-104]

**PLAN OF WORK**

**Part 1:**

- To collect the plant material selected for study *Moringa oleifera* (leaf ).
- Authenticate the selected plant.
- Extraction of selected plant using ethanol as a solvent.

**Part 2:**

- Acute toxicity study of extracts.

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**Part 3:**

- A Study of Antinflammatory, Activity Of Moringa Oleifera Ethanolic Leaf Extracts.
- Rats Models for the Study-
- Carrageenan induced inflammation

**Part 4:**
Statistical analysis of the resultant data.

**Part 5:**
Result, Discussion and conclusion.

All the procedures were performed in accordance with the Institutional Animal Ethics Committee (IAEC) constituted as per the direction of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Under Ministry of Animal Welfare Division, Government of India, New Delhi, India.

**Experimental Animals**

Male Albino Wistar Rats weighing 150-200g were used for the present study. The animals were maintained under controlled conditions of temperature (23 ± 2C), humidity (50 ± 5%) and 12-hour light-dark cycles. All the animals were acclimatized for seven days before the study. The animals were randomized into experimental and control groups and housed individually in sanitized polypropylene cages containing sterile paddy husk as bedding. They had free access to standard pellets as basal diet and water. Animals were habituated to laboratory conditions for 48 hours prior to experimental protocol to minimize if any of nonspecific stress. The present study was conducted at Dept. of Pharmacology, AIPS Sagar (MP). Studies conducted were approved by the Institutional Animal Ethical Committee (IAEC) (No - 1777/PO/Ere /S/1 4/CPCSEA).

**MATERIALS:**

A) **Chemicals:-**

**Table 1 Chemicals used for study of Moringa Oleifera**

| **Chemicals** | **Manufacturer** |
|---|---|
| ALLOXAN MONOHYDRATE | OZONE CHEMICALS, MUMBAI |
| ETHANOL | DIPA CHEMICALS, AURANGABAD |
| PETROLEUM ETHER | DIPA CHEMICALS, AURANGABAD |
| CARBON TETRACHLORIDE | GUJARAT ALKALIES AND CHEMICALS LIMITED |
| CARREGENAN | SIGMA CHEMICAL COMPANY, U.S.A. |
| CHOLESTEROL DIET PELLETS | M/S RAYANS BIOTECHNOLOGIES PVT.LTD., HYDERABAD. |

**DRUGS**

**Table 2 Drugs Used In Study of Moringa Oleifera**

| **DRUG** | **MANUFACTURER** | **BRAND** |
|---|---|---|
| INDOMETHACIN | JAGSONPALPHARMACEUTICALS LIMITED | [INDOCAP] |

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**B)** Instruments:

**Table 3 List of Instruments used in the study**

| Sr. No. | Instruments | Make | Calibrated Yes / no |
|---|---|---|---|
| 1 | Centrifuge Machine | Remi RM -1215 | Yes |
| 2 | UV Spectrophotometer | Shimatzu UV-1800, Japan | Yes |
| 3 | Chem.5 plus $V_2$ Autoanalyzer | ERBA Mannheim analyzer by Transasia | Yes |

**1 A) Collection and authentication of the plant material**
The leaves of Moringa Oleifera were collected from local area of Sagar,Madhya Pradesh, India, during July 2021.

**1B) Authentification of the plant:**
The Plant Herbarium was submitted for identification and authentication at the Department of Botany, Dr. HS Gaur Central University, Sagar, Madhya Pradesh, India. The Voucher specimen (Number 1149 ) was the authentication number of the Herbarium after validation.

**1C) Drying:**
Plant was shade dried at room temperature.

**1D) Preparation of Plant Extract:**
The extraction includes the process of yielding of the extracts from plants species. This depends on the solvent polarity which determines qualitatively and quantitatively the quality of the extracted compounds. Ethanol is one of the most widely used solvent for the extraction because of its low toxicity and high extraction yield with the advantage of modulating the polarity of the solvent by using mixtures at different ratios. The plant Leaves were shade dried to control temperature, humidity and damage of active constituents . Then dried plant material of leaf was powdered individually by using grinder and defatted with petroleum ether. Defatted 500 gm of each powder was extracted by 95% ethanol in a soxhlet apparatus for 72hours as by cold maceration followed by concentrated in a rotator evaporator under reduced pressure at temperature 40-50°C and then lyophilized to get a dry residue. Some part of the total extract was used for qualitative and quantitative phytochemical investigation and rest of the extract was used for preliminary pharmacological screening.

**Preliminary Phytochemical studies of Ethanolic extracts of M.oleifera leaf** [319-320]
The therapeutic potentials of plant and animal origin are being used from the ancient times by the simple process without the isolation of pure compounds i.e. in the form ofcrude drugs or the galenicals prepared from them. The pharmacological action of crude drug is determined by the nature of its constituents. Thus the plant species may be considered as a biosynthetic laboratory not only for the chemical compounds e.g. carbohydrates, proteins and fats that are utilized as a food by humans and animals, but also for a multitude of compounds including alkaloids, Flavonoids, glycosides etc. which exert definite pharmacological effects. These chemical compounds are responsible for the desired therapeutic properties. To obtain these pharmacological effects, the plant materials are used as such in their crude form or may be extracted with suitable solvents to take out the desired components and the resulting principle being employed as therapeutic agents. The phytochemistry of herbal drugs embraces a thorough consideration of these chemical entities that are termed as constituents. As the herbal drugs contain so many chemical compounds, it is essential to single out those responsible for the

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therapeutic effect to be called as active constituents.

By considering the above facts, it is necessary to evaluate the nature of extract before evaluating the biological activity of same. So we have selected Ethanolic extract for pharmacological activity which contains large number of chemical constituents. Hence for this purpose, following tests are used to evaluate the chemical nature of extracts qualitatively.

**1] Test for alkaloids**

**A] Mayer's Reagent**

**Procedure**

1.5 ml of extract was taken in a test tube. 0.2 ml of dilute hydrochloric acid and 0.1 ml of

Mayer's reagent are added.

**Inference**

Formation of cream color precipitate gives positive test for alkaloids.

**B] Dragendroff's Reagent**

**Procedure**

Take 0.1 ml of dilute hydrochloric acid and 0.1 ml of Dragendroff's
ml solution of extract in a test tube.

**Inference**

Development of orange brown color precipitate suggested the presence of alkaloids.2]

**CARBOHYDRATES**

**Molish'stest**

**Procedure**

The extract (2ml) is added with 2 drops of 5% ethanol solution of alpha - naphthol
.Then few drops of H2SO4 are added by the side Millon's of the test tube.

**Inference**

Formation of coloured ring (violet) at the junction of the two liquids indicates the presence of carbohydrates.

3] **GLYCOSIDES**

**Keller-Killani Test Procedure**

For this test take 0.5 gm of the plant extract in a separate test tube .take test tube with 2 ml of glacial acetic acid containing a drop of ferric chloride solution. Add 1ml of concentrated tetra oxo sulphate (VI) acid. Then add the plant extract to the tube containing glacial acetic acid with ferric chloride .

**Inference**

Formation of brown ring formation at the interface indicated presence of glycosides. 4] PHENOLIC COMPOUNDS

**Ferric chloridetest Procedure**

To test solution few drops of neutral FeCl3 solution was added.

**Inference**

Formation of bluish black colour indicated the presence of phenolics.

**5] TANINS**

**Gelatin testProcedure**

To test solution 1% gelatin containing NaCl solution was added.

**Inference**

White precipitate formation indicates the presence of tannins.

**6] PROTEINS AND AMINO ACIDS**

**a) Ninhydrin test** (general test for amino acids)**:**

**Procedure**

3 ml of test solution was mixed with 3 drops of 5% v/v of Ninhydrin reagent.

**Inference**

The extract is heated with 3 drops of ninhydrin reagent on a water bath. The blue coloration appearance indicates presence of proteins and amino acids.

**b) Millon's test** (for proteins)**:**

**Procedure**

3 ml test solution is mixed with 5 ml .
r reagent. Heating of this solution on awater bath indicates results.

**Inference**

Red precipitate indicates the presence of proteins.

7] **SAPONINS**

**Forth Formation TestProcedure**

1 ml of extract solution was diluted with distilled water to 20 ml and shaken in a graduated cylinder for 15 minutes.

**Inference**

Development of stable foam suggested the

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presence of saponins.

**8] GUMS AND MUCILAGES**

**Procedure**

Small quantities of the extracts are added separately to 25 ml of absolute alcohol with constant stirring and filtered.

**Inference**

The precipitate is dried in air and examined for its swelling properties which indicates the presence of gums.

**9] FIXED OILS AND FATS**

**Procedure**

2.0ml of extract of Moringa Oleifera solution is shaken with 0.1 ml dilute sodium hydroxide. A small quantity of dilute HCl is added later .

**Inference`**

A white precipitate was formed with volatile oils.

**10] FLAVANOIDS SHINODATEST**

**Procedure**

The extract was dissolved in alcohol. A piece of magnesium is added which is followed by addition of concentrated hydrochloric acid added drop wise to test tube and then heated.

**Inference**

Magenta color of the solution indicates the presence of flavonoids in the Moringa Oleifera extract.

**ACUTE TOXICITY STUDIES** [321]

Principle: The acute toxicity test aims at establishing the therapeutic index. The acute toxicity study was done according to OECD (Organization of Economic Co- operationand Development) guidelines 420- Fixed Dose Procedure (FDP), as inannexure 2D.

**Procedure:** The suspension of ethanolic leaf extract of Moringa Oleifera was administrated orally to overnight fasted Albino Wistar Rats (number of animals = 6) in dose of 1000, 2000 and 4000 mg/kg body weight respectively. The animals were observed continuously for the initial 4hrs for behavioral changes and mortality and intermittently for the next 6 h and then again at 24 hrs and 48 h after dosing.

**Selection of Doses:** In this study dose of 1000 to 4000 mg / kg was found to be safe and no mortality was observed, so dose 1/10th i.e. 100, 200 and 400 mg / kg of the extract was chosen for the experimentation.

**EVALUATION OF ANTI-INFLAMMATORY ACTIVITY**

**Carrageenan induced paw oedema test** [324]

**Principle**

Carrageenan induced rat paw edema was done by the method described by of Winter et al.

**Procedure**

**Table 4 Anti-Inflammatory Activity Group Description**

| Group | Description | Drug /Extract dose |
|---|---|---|
| 1 | Control | Normal saline 10 mg |
| 2 | Standard | Indomethacin 20mg/kg orally |
| 3 | Ethanolic extract moringa oleifera | 100 mg/kg orally |
| 4 | Ethanolic extract moringa oleifera | 200 mg/kg orally |
| 5 | Ethanolic extract moringa oleifera | 400 mg /kg orally |

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For the induction of inflammation carrageenan (1%) aqueous suspension in normal saline injection was taken. 0.1 ml of freshly injection was injected underneath the plantar tissue of the right hind paw of rats. Following one hour after administration acute inflammation was produced by injection of carrageenan. Inflammation was quantitated in terms of volume i.e. displacement of water by oedema using a plethysmometer at 0min before and 30, 60, 120, 180 min after carrageenan injection. Indomethacin was used as standard drug which has anti-inflammatory activity at both early and late phase of inflammation. The percentage inhibition of edema was calculated for each group with respect to its vehicle- treated control group using the following relationship.

Percentage inhibition of paw = $\frac{(Vt - Vo)control - (Vt - Vo)treated}{(Vt - Vo)control} \times 100$

Where, $V_O$=paw volume before drug administration Vt = Paw volume after drug administration

Fig 2. (A) PLETHYSMOMETER Fig. 2 (B) PLETHYSMOMETER

Herbal drugs play a restorative role in many diseases; most of them speed up the natural healing process. Previous literature indicates that a number of plant extracts and compounds isolated from various plant sources and minerals have shown activity against the various disease conditions. In the present investigation we have studied the Anti-inflammatory Activity of Ethanolic Leaf Extracts of Moringa oleifera oleifera in Albino Wistar Rats.

**Table 5 .Preliminary Phytochemical studies of Ethanolic leaf extracts of M.oleifera**

| **Extract** | **M.Oleifera leaf extract** |
|---|---|
| Alkaloids | **Present** |
| Carbohydrates | **Present** |
| Glycosides | **Present** |
| Phenolic compounds | **Present** |
| Tannins | **Present** |

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| | |
|---|---|
| Protein & Aminoacids | **Present** |
| Saponins | **Present** |
| Gums & mucilage | Absent |
| Fixed oils &fats | Absent |
| Flavonoids | **Present** |

**Acute toxicity studies:**

No mortality and signs of any toxicity were evidenced after the administration of a limit dose of 1000 mg/kg, 2000 mg/kg and 4000 mg/kg ethanolic extract of Moringa oleifera in acute oral toxicity test hence, for oral administration the doses selected were 100 mg/kg, 200 mg/kg and 400mg/kg.

**Table 6. Groups for study of Ethanolic leaf extracts of M.oleifera**

| GROUPS | TREATMENT | Abbreviation | Column |
|---|---|---|---|
| I | Control | C | A |
| II | Standard | Std | B |
| III | Moringa oleifera Ethanolic Extract (100mg/kg) | M0 100 | C |
| IV | Moringa oleifera Ethanolic Extract (200 mg/kg.) | Mo 200 | D |
| V | Moringa oleifera Ethanolic Extract (400mg/kg.) | Mo 400 | E |

**ANTI-INFLAMMATORY ACTIVITY**

For evaluation of Anti-inflammatory activity by carregenan induced rat paw method in group 1(control) Normal saline was administered.

In group 2 (standard) indomethacin 20 mg/kg intraperitoneally was administered.

In group 3 ethanolic extract of moringa oleifera in dose of 100 mg/kg was administered orally. In group 4 ethanolic extract of moringa oleifera in dose of 200 mg/kg was administered orally. In group 5 ethanolic extract of moringa oleifera in dose of 400 mg/kg was administered orally.

In group 2 (Indomethacin) there was significant decrease in the paw edema at 30 min ($p<0.05$) and 3hrs ($p<0.001$) as compared to control and results were highly significant at the end of 3hrs.

In group 3 (100mg) there was dose dependent decrease in paw edema compared to control group which was significant at the end of 3hrs.

In Group 4 (200mg) there was significant reduction of paw edema at 30 min ($p<0.05$) and 3hrs ($p<0.001$) at 30 min and 3hrs respectively which was highly significant at the end of 3 hrs.

In group 5(400 mg) there was significant reduction of paw edema throughout the period from 30 min. to 3hrs and highly significant results were obtained at end of 3 hrs comparable with the standard drug

**Table 7 Comparison of Anti-Inflammatory activities and paw edema (ml) at different time**

| Groups - | 0min | 30 min | 60min | 120min | 180min |
|---|---|---|---|---|---|

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| | | | | | |
|---|---|---|---|---|---|
| Group1 mean ± S.E.M | 0.79 ±0.01$^{ns}$ | 1.70±0.29 $^{ns}$ | 1.29 ±0.04$^{ns}$ | 1.69 ± 0.09 Ns | 1.67 ± 0. 04$^{ns}$ |
| Group 2 [std] mean ± S.E.M | 0.89 ± 0.02 Ns | 1.19 ± 0.07 * | 1.27 ± 0.09 * | 1.53 ± 0.16* | 0.52 ± 0.03* * |
| Group3 [mo100] mean ± S.E.M | 0.92 ±0.01$^{ns}$ | 1.22 ±0.07** | 1.37 ±0.04* | 1.34 ±0.08* | 0.87 ±0.04** |
| Group4[mo200] mean ± S.E.M | 0.90 ± 0.03 ns | 1.21 ±0.11** | 1.19 ±0.07* | 1.16 ±0.01** | 0.82 ±05** |
| Group5mo[400] mean ± S.E.M | 0.90 ±0. 02$^{ns}$ | 1.18 ± 0.08 ** | 1.3 ± 0.08$^{ns}$ | 1.36 ± 0.02** | 0.70 ± 0.05** |

Values are * p<0.01 significant, **P<0.001 -- Highly Significant, ns non significant

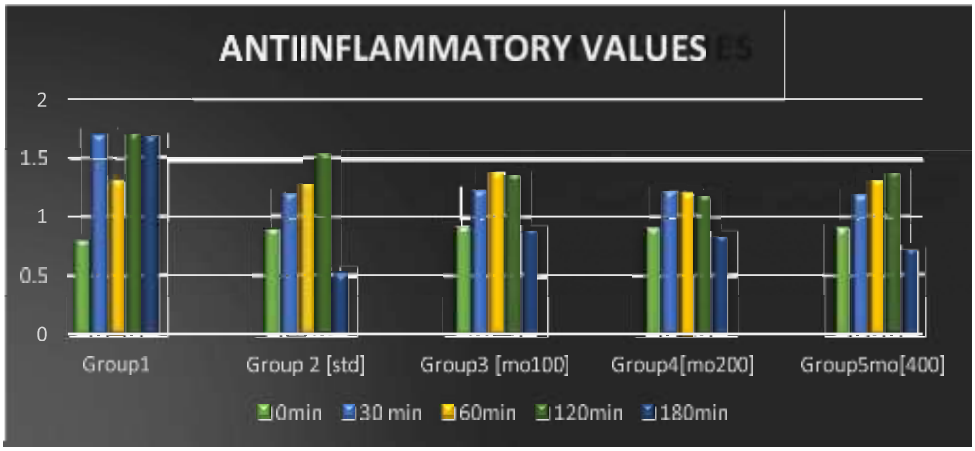


Fig 3. **Graph Showing Values By Carragenan Induced Rat Paw Edema Method**

**PERCENTAGE OF INHIBITION**

In group 2 (Indomethacin )the percentage of inhibition of paw volume was 30% and 68.86% at 30min and 3hr respectively. In group 3 (100mg ) the percentage of inhibition of paw volume was28 % and 47.90 % at 30min and 3hrs respectively. In group 4 (200mg) the percentage inhibition of edema was 28 % and 50.89 % at 30 min and 3hrs respectively. In group 5(400 mg) the percentage inhibition of edema was 30 % and 58.08% at 30 min. and 3hrs respectively.

**Table 8 .Percentage of inhibition of paw volume in different groups at different times**

| Groups | 30 min | 60min | 120min | 180min |
|---|---|---|---|---|
| Group 2[std] Indomethacin 20 mg/kg | 30 % | 5 % | 10 % | 68.86 % |
| Group3[mo100] Moringa extract 100mg /kg | 28 % | 10 % | 20 % | 47.90 % |

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| | | | | |
|---|---|---|---|---|
| Group4[mo200] Moringa extract 200mg /kg | 28 % | 6 % | 31 % | 50.89 % |
| Group5mo[400] Moringa extract 400mg /kg | 30 % | 1 % | 19 % | 58.08 % |

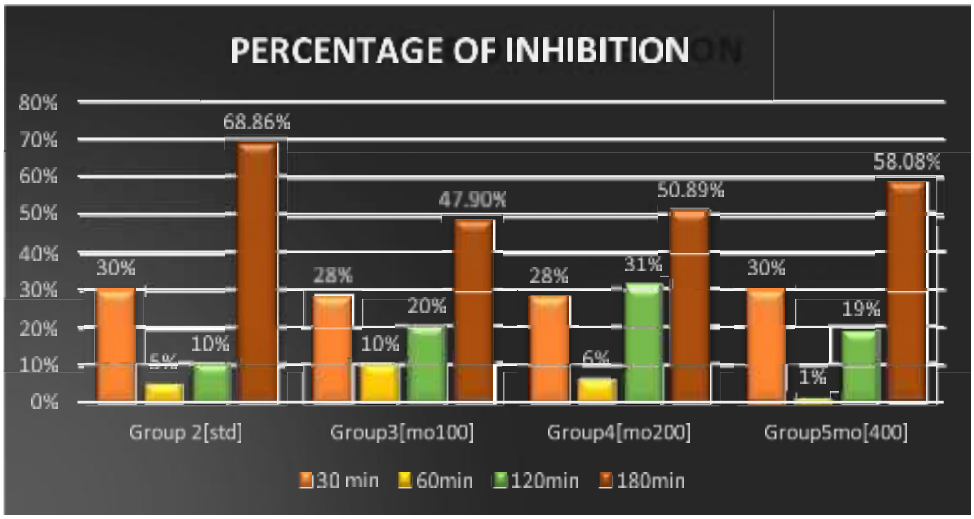


**Fig 4 Graph Showing Percentage Of Inhibition In Different Groups**


**Fig 5** Macroscopic images of carrageenan-induced hind paw oedema and the effects of ME (400 mg/kg) and indomethacin (10 mg/kg). (A) Normal; (B) control; (C) ME (400 mg/kg); (D) Indomethacin (10 mg/kgb.w.)

The aim of research is to find out new herbal origins from plants, which are potent and non toxic agents. These plants are traditional medicinal plants. Generally herbal drugs are free from side effects /adverse effects and are low cost medicines which will be beneficial for the people of our country. The improvement in quantity control and standardization of herbal drugs and their products have led to the development of effective quality medicines from plants. In present investigation we have not only authenticated the leaf of Moringa oleifera but also standardized the leaf extract with various physical parameters like total ash, acid insoluble ash, loss on drying, water and ethanol soluble extractive values.

Acute toxicity study revealed the non-toxic nature of the extract at dose of 4000 mg/kg. Experiment was carried out on normal healthy rats. No deaths were observed in rats the extract

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treated group and the behavior of the treated groups also appeared normal. There was no toxic reaction found at any dose selected until the end of the study.

## III. PHYTOCHEMICAL ANALYSIS

In our study we found the presence of alkaloids. Alkaloids group are mostly basic nitrogen atoms chemical compounds which are naturally occurring and possess a variety of pharmacological actions.

We also found the presence of Glucosinolates which are also present in Moringa oleifera leaves. Glucosinolates play an important role in health promoting and prevention of disease. Tannins are water-soluble phenolic compounds which bind to alkaloids, gelatin and other proteins. They display various activities like anti-cancer, antiatherosclerotic, anti-inflammatory, Hepatoprotective, antibacterial and anti-viral activity. Moringa oleifera leaves have an appreciable source of tannins. In Moringa Oleifera leaf extract in our study we found the presence of Saponins .saponins are group of natural compounds that contain isoprenoidal-derived aglycone, structure which is covalently linked to one or more sugar moieties. Saponins are known to possess antioxidant and anti-cancer properties.

In our study we also found the presence of Phenolic acids which are are a sub-group of phenolic compounds derived from hydroxybenzoic acid and hydroxycinnamic acid, naturally present in plants. The scientific literature shows its beneficial effects on human health, as a food supplement is a subject of increasing interest. These compounds are mainly known to possess antioxidant, anti-inflammatory, antimitotic and anticancer properties .

We also found presence of flavonoids which are are a sub-group of polyphenolic compounds having a benzo- -pyrone structure and are ubiquitous in plants.Studies have consistently shown that high intake of flavonoids has protective effects against many infectious (bacterial and viral diseases) and also has a protective action against degenerative diseases such as cardiovascular diseases, cancers, and other age- relateddiseases .

## IV. ANTI-INFLAMMATORY ACTIVITY

The most commonly used basic model for the screening of anti-inflammatory agents is carrageenan induced edema. The edema develops in the paw of the rats after injection of carrageenan and is biphasic in nature.[351] The initial phase of inflammation which is observed during the first hour is attributed to a release of histamine and serotonin and the second phase is due to a release of prostaglandin like substances.[352] In the present study, ethanolic extract Moringa oleifera leaf extracts at 400 mg dose showed significant reduction of edema in both the phases of inflammation but maximum reduction was observed in the second phase of inflammation (68.86%) which was comparable with indomethacin (58.08%).

The anti-inflammatory activity observed could possibly be attributed to the secondary metabolites present in the leaves of moringa oleifera . In previous studies alkaloids, isolated from plant extract have shown inhibitory effect on eosinophil recruitment, leukotriene production in the pleural cavities, as well as inhibiting in the production of nitric oxide mediators which result in anti-inflammatory effect. Flavonoids also inhibit inflammatory processes by inhibiting phosphodiesterases which involved in cell activation. In addition, polyphenols exert their anti-inflammatory properties through inhibition of the production of inflammatory cytokines and chemokines and suppressing the activity of cyclooxygenase (COX)) and inducible nitric oxide synthase (iNOS) and thereby decreasing the production of reactive oxygen and nitrogen species (ROS/RNS) .

Intergroup comparisons showed that the ethanolic leaf extracts showed statistically significant different effect in 100 mg/kg , 200 mg/kg and 400 mg/kg versus indomethacin in 10 mg/kg dose statistically significant effect was observed

Indomethacin showed highly significant anti-inflammatory effect in this model. This indicates that the ethanolic extracts showed lower anti-inflammatory effect than the Indomethacin.

Similar few studies have been done on Moringa Oleifera . A study done by Caceres A et al has showed anti-inflammatory activity of hot water infusion of Moringa Oleifera leaves against carrageenan induced hind paw edema. The crude ethanolic extract of Moringa dried seeds was tested for anti-inflammatory activity using carrageenan induced inflammation the hind paw of mice and found to inhibit 85 % of

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inflammation at a dose of 3 mg/kg. body weight, while the mature green seeds inhibited edema by 77 % at the same dose.

Ahemad B et al has studied methanol extract of the Moringa fruit was alsoscreened for antiinflammatory effect using the rat paw edema and the rat 6 days at pouch inflammatory models following oral administration, the extract inhibited carrageenan induced rat pow edema in a dose dependent manner, with dose of 660 mg/kg in the six dayat pouch acute inflammation model induced with carrageenan, the extract was much more potent. They proposed that antiinflammatory activity may be useful in the treatment of both the acute and chronic inflammatory conditions. Moringa oleifera was investigated for analgesic effect against thermal stimuli usinghot plate test and Analgesiometer test and for antipyretic effect.

The inhibitory effect of Moringa Oleifera leaf extract on first phase inflammation could be due to inhibition of the serotonin and histamine mediated effect and on second phase could be due to the inhibition of the prostaglandin synthesis probably due to the edema formationby carrageenan. The activity of our extract of moringa oleifera could be due to bioactive compounds naturally present in such as phenolic acids and flavonoids, which may have been involved in to anti-inflammatory process.

The acute oral toxicity studies of herbal preparation of ethanolic extract of Moringa oleifera leaves was showed no mortality up to dose of 4000 mg/kg orally.

The study shows that plant contains phytochemicals like phenolic, flavonoids and tannins,glycosides; saponins could be responsible for the potential activity of the plant.

The ability of the extract suppressing the carrageenan-induced inflammation confirms the anti- inflammatory activity of the extract. The data collectively indicates the ethanolic extract of Moringa oleifera possesses anti-inflammatory properties, which are probably mediated by both central and peripheral inhibitory mechanisms as well as via inhibition of prostaglandin synthesis. The moringa oleifera plant can therefore be proposed to have a potential benefit in the management of pain and inflammatory disorders.

In conclusion animal models have demonstrated the anti-inflammatory effects of Moringa Oleifera leaves. Many phytochemicals may be involved in the anti- inflammatory process. Among them, quercetin and many other bioactive compounds such as other like flavonoidsand phenolic acids naturally present in Moringa oleifera leaves may be involved in to anti- inflammatory process. Further studies should be devoted to investigate the potential anti- inflammatory action and the mechanism of action of other bioactive compound naturally present in Moringa oleifera leaves. Finally, human studies are needed to evaluate the anti-inflammatory property of Moringa oleifera leaves also in human beings.

It can be concluded that the Ethanolic Leaf Extract of Moringa Oleifera possess Anti-Inflammatory activity.

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In India the sources 1of medicinal plants have been used as medicines since the days of historic Vedic glory. A few therapeutic plants and spices structure part of our eating regimen as flavors, vegetables and organic products Plants are being used in traditional medicine since history of mankind.1The knowledge of these medicinal plants has accrued in the course of many centuries leading to medicinal systems in India such as Ayurveda, Unani and Siddha. It is anticipated that herbal drugs used globally were discovered following leads from local medicine. According to WHO reports that about 25% of modern medicines have been derived from plants which were first used traditionally many synthetic analogues are built on modelsof compounds isolated from plants. The use of rudimentary drugs and herbal formulations has a important role in new drug discoveries so it is important to justify their acceptability in modern system of medicine. On the other hand the major problems faced by the herbal drug industry is non availability of rigid quality control profile for herbal material and their formulations due to which there is a need for studies in animals and humans to assess the safety and efficacy of herbs or plant extracts which are claimed to have a very good therapeutic potential Pain can be defined as , unpleasant sensation, usually evoked by an external or internal noxious stimulus. Analgesic decrease the pain by acting on the CNS or peripheral pain mechanisms, without altering So analgesic activity means capacity of asubstance to neutralize the pain sensation. The environment has provided a vast collection ofremedies to cure all ailments of mankind. Since the beginning of human era, along with the food crops, man has cultivated herbs for his medicinal needs.

Inflammation is the natural response by a living tissue to various kinds of injury. Cyclooxygenase (COX) is the key enzymes in the synthesis of Prostaglandins, Prostacyclin and Thromboxane which are involved in Inflammation, Pain and Platelet Aggregation. Steroidal and non-steroidal anti-inflammatory drugs (SAIDs and NSAIDs, respectively) are currently the most widely used drugs in the treatment of acute inflammatory disorders, though despite their Renal and Gastric negative secondary effects . These drugs block COX-1 and COX-2 enzyme activity. COX enzymes assist with Prostaglandin Production. NSAIDs, Steroidal Anti-Inflammatory drugs are being used till now, As a result long term uses of these drugs cause adverse side effects and damage human biological system such as liver, gastrointestinal tract, etc on long term use. As a result of adverse side effects can lead to complications, like gastric lesions, cardiovascular, renal failure and gastrointestinal damagein long term.

The term inflammation is derived from the Latin "inflammare" means to burn. It is a physiological response of living tissues to injury. It is not a disease, but a manifestation of disease. Diseases in which an inflammatory reaction is a major component are classified accordingly with suffix. They are usually named from the organ affected followed by the suffix '-itis'. Thus, acute inflammation of the meninges is called meningitis. But like any rule, it has its own exceptions such as in case of pneumonia, typhoid fever, etc. Inflammation is fundamentally a protective response intended to remove the initial cause of cell injury as well as the necrotic cells and tissues due to damage by noxious agent. It achieves its protective function by diluting, destroying, or otherwise neutralizing harmful agents (e.g., microbes or toxins). These events eventually heal and reconstitute the sites of injury. Thus, inflammation is intimately interlaced with repair processes whereby damaged tissue is replaced by the regeneration of parenchymal cells, and/or by filling of any

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residual defect with fibrous scar tissue. Cardinal signs of inflammation include, among others, swelling (tumour), redness (rubor), heat (calor), pain (dolor), and loss of function (functeo laesa). Inflammation requires the participation of various types of cells expressing and reacting to diverse mediators along a very precise sequence.

Inflammation is generally classified based on the lesion and histological appearances in acute and chronic inflammation. However, these basic forms of inflammation can overlap, and many factors modify their course and histological appearance.

Acute inflammation, in the initial phase is transient series of tissue reactions to injury, of very short duration, lasting from a few minutes to few days, and is characterized by fluid and plasma protein exudation with predominantly neutrophilic leukocyte accumulation. It is associated with increased vascular permeability, capillary infiltration and emigration of leukocytes. The classical symptoms of redness, heat, edema and pain are associated with acute inflammation.

Herbal drugs play a role in the diseases and most of them speed up the natural healing process. Numerous medicinal plants and their formulations are used for various disorders in ethno medical practices as well as traditional systems of medicines in India.

Since prehistoric days attempts are being made to find out suitable drugs from natural sources for treatment of different diseases. The rational approaches, experiences of folk medicines provide a valuable approach in search for the development of new and useful therapeutic agents. Gradually keeping in pace with the scientific interpretation of drug actions, the causes of the diseases and the development in field of chemistry and technology, intensive efforts are being directed towards the design and the synthesis of new drugs.

The acute oral toxicity studies of herbal preparation of ethanolic extract of Moringa oleifera leaves was showed no mortality up to dose of 4000 mg/kg orally.

The study shows that plant contains phytochemicals like phenolic, flavonoids and tannins, glycosides; saponins could be responsible for the potential activity of the plant.

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In conclusion animal models have demonstrated the anti-inflammatory effects of Moringa Oleifera leaves. Many phytochemicals may be involved in the anti- inflammatory process. Among them, quercetin and many other bioactive compounds such as other like flavonoids and phenolic acids naturally present in Moringa oleifera leaves may be involved in to anti- inflammatory process. Further studies should be devoted to investigate the potential anti- inflammatory action and the mechanism of action of other bioactive compound naturally present in Moringa oleifera leaves. Finally, human studies are needed to evaluate the anti-inflammatory property of Moringa oleifera leaves also in human beings.

It can be concluded that the Ethanolic Leaf Extract of Moringa Oleifera possess Anti-Inflammatory activity.

Sources

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