Investigation of anti-inflammatory and anti-cancer activity of leaf extracts and fractions of Lantana camara linn

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Abstract- **Inflammation is when a wound swells up, turns red and hurts, it may be a sign of inflammation. Inflammation is the body's immune system's response to an irritant. the irritant might be a germ, but it could also be a foreign object. Pathogens, toxic mechanical and chemical agents, autoimmune reactions, and other stimuli can all cause inflammation. Hear the study was undertaken to investigate the possible anti-inflammation and anti-cancer activity of extract of leaf of *Lantana camara linn* in carrageenan induced rat paw oedema and MTT assay.**

For this current research leaf of *Lantana camara linn* was taken as a test drug. Carrageenan induced model, the oedema (inflammation) was developed in rats by intraperitoneal injection (IP) of carrageenan in normal saline i.e., 0.1ml of 1% Carrageenan sol followed by administration of test drug low dose 250mg/kg and higher dose 500mg/kg of body weight. After 1 to 5 Hrs the paw volume samples were collected to measure oedema (inflammation) levels as well as after 24hrs and then biological parameters paw volume were measured by using digital plethysmometer. Diclofenac sodium (10mg/kg) was used as standard drug for this study. So, the test drug shown significant decline in carrageenan induced paw volume whereas significant elevation of paw volume at 500mg/kg dose and the results were comparable with that of standard.

MTT assay was conducted to assess the anticancer effects of the Methanolic extract of *Lantana camara linn* at different concentrations on HCT 29 cell lines. As observed by MTT assay, The extract decreased the HCT 29, cell viability in a concentration-dependent way.

The result have-been shown that leaf of *lantana camara linn* have anti-cancer and anti-inflammation action. To isolate and identify that exact active constituents, additional research must be conducted.

Keywords: **Anti-Inflammation, Anti-Cancer, *Lantana Camara Linn*, 0.1ml Of 1% Carrageenan, HCT 29, Digital Plethysmometer.**

INTRODUCTION

Inflammation is when a wound swells up, turns red and hurts , it may be a sign of inflammation. Inflammation is the body's immune system's response to an irritant. the irritant might be a germ, but it could also be a foreign object. Pathogens, toxic mechanical and chemical agents, autoimmune reactions, and other stimuli can all cause inflammation, which is a complicated, tightly controlled series of events. Red-rashes on skin, swelling, heat, and pain are visible signs and symptoms of the succeeding chain of events. The vascularized connective tissue experiences an inflammatory reaction, which includes some components like plasma, blood vessels, circulating cells, cellular and extracellular cells. This results in increased leukocyte recruitment, improved vascular permeability, increased microvascular diameter, along with the release of inflammatory mediators**. [1]**

Body's principal mechanism for repairing tissue damage and defending itself from stressors is inflammation. In the physiological condition, the controlled response clears injured tissue and guards against additional injury. In pathologic circumstances, inflammation cause loss of tissue or worsen organ function.

Inflammation is characterized by a multitude of interactions between leukocytes, endothelial cells, and platelets, irrespective of etiology, inflammation causes endothelial activation.

Activated endothelial cells express cell adhesion molecules such as P and E selection, which mediate leukocytes rolling, the first step in the adhesion cascade leading to leukocytes extravasation.[1]

Inflammation is part of body's defense mechanism. it is the process by which the immune system recognizes and removes harm full and foreign stimuli and begins the healing process. No human has been shown to have a congenital lack of cell line, perhaps because macrophages are needed during fetal development to eliminate primitive tissues while new tissues form to take their place. We shall go through the function of macrophages in inflammation in this post.

Inflammation is reduced by a medicine or chemical. Anti-inflammatory medications operate by reducing production of specific chemicals which are responsible for inflammation.
They are used for treating a number of inflammatory effects. Some of these medicines are being studied for prevention and treating of cancer. [10]

Inflammation is broken down into acute and chronic patterns:
Acute inflammation: The major characteristics of acute inflammation are exudation of fluid, emigration of leukocytes and plasma proteins Primarily neutrophils. The tissue damage due to trauma, microbial invasion, or noxious compounds can induce acute inflammation. It's starts rapidly, becomes severe in a short time and symptoms may last few days for example cellulitis or acute pneumonia. Subacute inflammation is period between acute and chronic inflammation and last 2 to 6 weeks.
Acute inflammation begins within seconds to minutes following injury to tissues. it characterized by four cardinal features,

- Redness (rubor) : secondary to vasodilatation and increased blood flow.
- Heat (calor) : localized increased in temperature, also due to increased blood flow.
- Pain (dolor): caused by stimulation of the local nerve ending, from mechanical and chemical mediators.
- Swelling (tumour) : results from increased vessel permeability ,allowing fluid loss into the interstitial space. [2]

Chronic inflammation: Long-lasting chronic inflammation is summarized by presence of macrophage and lymphocytes, tissue necrosis, vascular proliferation. The progression and histologic characteristics of both acute and chronic inflammation are influenced by a variety of factors. Phagocytosis , Antigen presentation and immune modulation through the production of various growth factor and cytokines are macrophages three main roles in inflammation. Chronic inflammation referred to as slow, long term inflammation lasting for prolonged periods of several months to years .
Diabetes, cardiovascular disease, allergies and chronic obstructive pulmonary disease (COPD) are example of diseases mediated by chronic inflammation. Obesity, stress and insufficient diet are some of the factors that promote chronic inflammation. [2, 3]

Cancer is main reason for death in world. Cancer is disease in which some of the body's cells grow uncontrollably and spread to other part of the body. cancer can start almost anywhere in the human body, which is made up of trillions of cells. The longer life expectancies, changing lifestyles, and more rural-to-urban migration are all contributing to rising cancer rates in India, despite the fact that they are still lower than in Western countries. In India, the incidence of esophagus and oral cancers is among the highest. On the other hand, colorectal, prostate, and lung cancer rates are among the lowest. The most prevalent area for cancer in humans, skin cancer makes about 55% of all cancers. The second most prevalent type of skin cancer is squamous cell carcinoma, and it is spreading swiftly around the globe. 16% of incidences of skin cancer are caused by it. [4] Cell cycle regulation is lost, leading to a class of illnesses known as cancer. Cancer is combined with abnormal and uncontrolled cells proliferation. The exterior and internal causes of cancer, respectively, include chemicals, tobacco, infectious diseases, radiations and environmental factors**.** (Inherited mutations, hormones, immune conditions, and mutations that occur from metabolism)[5]
Finding affordable, efficient, and simple-to-produce cancer medications has always been a popular topic of research. There is no one treatment plan for all types of cancer, with the exception of conventional chemotherapy, which involves cytotoxic chemicals linked to serious side effects and occasionally chemoresistance. This poses a huge obstacle for cancer treatment. [6]
A wealth of bioactive chemicals found in medicinal plants are help full to treat a various disease and improve human health. It has been used as a home remedy and a cancer treatment by some traditional healers in developing countries. Among the organic compounds extracted from medicinal plants that had anticancer properties were alkaloids, triterpenoids, and flavonoids. Alkaloids are a class of phytochemicals that typically have a nitrogen atom in a heterocyclic ring in their structure. It has effective anticancer properties against a variety of malignancies. The bulk of cancer medications authorized by the FDA are alkaloids with natural sources, including vinblastine and camptothecin. Chemotherapy drugs are designed to interact with rapidly proliferating cancer cells. Numerous research shown that plant alkaloids including berberine, sanguinarine, and matrine can cause apoptosis and stop the growth of cancer cells.[7]
A fundamental pathogenic component of various diseases, including cancer, rheumatoid arthritis, obesity and coronary heart disease, is angiogenesis, which is the process of creating new blood vessels from the vasculature that already exists. Solid tumor development and metastasis depend on tumor angiogenesis. helps the tumor receive oxygen and nutrients. It also serves as a pathway for cancerous cells to spread to other organs. Consequently, tumor angiogenesis is an exciting target for the treatment and prevention of cancer. [8]

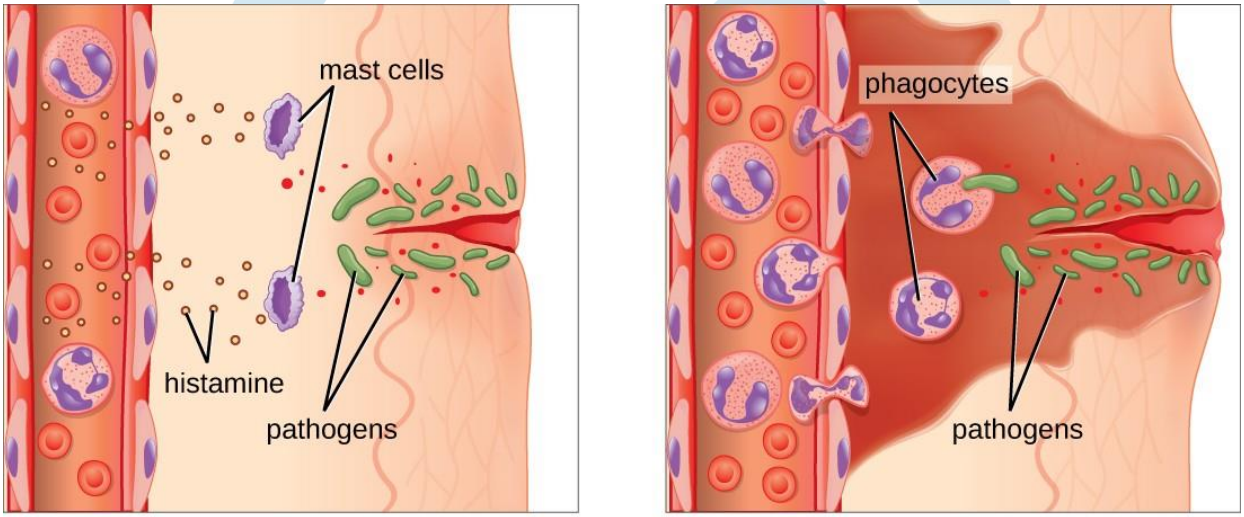
Colo-rectal cancer (CCR): This CCR is second most cause for death in humans around worldwide. Poor eating habits, smoking, intestinal inflammatory illness, gastric factors all increase the risk of acquiring this cancer. 90% of those who are given a colorectal cancer diagnosis are older than 50, with a median age of 64; nevertheless, the illness is more aggressive in those who are given a diagnosis earlier in life. The American Cancer Association estimates that more than 49,700 deaths in 2015 were attributable to cancer. With early diagnosis and treatment, the death rate is intended to be decreased. The survival rate is currently utilized to forecast a patient's prognosis. If a first-degree relative has had colonic polyps or colorectal cancer before the age of 60, or if two or more first-degree relatives have had cancer, the patient is said to have a positive family history. A number of tests, including the guaiac test, immunochemical stool test, DNA stool test, sigmoidoscopy, colonoscopy, and barium enema, can be used to identify colorectal cancer. The prognosis, survival, and course of therapy for the patient depend on the stage at when the cancer is discovered. Review the basics of colorectal cancer, its genetic foundation, risk factors, protective factors, clinical course, diagnostic techniques, treatment, and survival. [9]

REVIEW OF LITERATURE

When the immune system encounters harmful stimuli like viruses, damaged cells, toxins, or radiation, it responds by inducing **inflammation**, which has the twin benefits of removing the stimulus and kicking off the healing process. [11,12] Inflammation is an essential defense mechanism for optimal well-being.[13] Acute inflammatory reactions routinely successfully reduce the risk of harm or infection through cellular and molecular mechanisms and interactions. This mitigation procedure ends up in the decrease of the acute inflammation and an establishment of tissue homeostasis. Uncontrolled acute inflammation has the potential to develop a number of chronic inflammatory diseases. [14] Local immunological, vascular, and cell-mediated inflammatory responses to infection or damage include pain, discomfort, swelling, redness, and loss of tissue function, defining the signs of inflammatory at the tissue level. [15] Significant microcirculatory events that occur during the inflammatory phase include changes in vascular permeability, recruitment of leukocytes and accumulation, and the release of inflammatory compounds. [12, 16]

Pathogenic elements, such as illnesses, tissue injury, or cardiac infarction, can cause inflammation by harming tissue. Infection-related or non-infection-related factors can cause inflammation. The body initiates a biological signaling cascade when a tissue is harmed, which causes the tissues that were injured to respond by healing.

These messages cause lymphocyte chemo taxis from the bloodstream as a whole to move to the injured sites. Responses to inflammation are brought on by the cytokines that those activated leukocytes produce. [17]



(a) (b)

Figure: 1 Injury Inflammation (After injury)

Issues Of Concern Acute Inflammation:

Acute inflammation is an immediate, adaptive response with limited specificity caused by several noxious stimuli, such as infection and tissue damage (tissue necrosis). The controlled inflammatory response is generally beneficial, and this can be seen clearly in providing protection against infectious organisms, including mycobacterium tuberculosis, protozoa, fungi, and other parasites. However, it can become detrimental if not regulated, such as seen in septic shock.[103] The inflammatory pathway consists of a sequence of events involving inducers, sensors, mediators, and effectors.[104]

The process will initiate in the presence of inducers, which can be infectious organisms or non-infectious stimuli such as foreign bodies and signals from necrotic cells or damaged tissues. This will, in turn, activate the sensors, which are specialized molecules. The sensors will then stimulate the mediators, which are endogenous chemicals that can induce pain, activate or inhibit inflammation and tissue repair, and can activate the effectors, which are the tissues and cells.[105] These players can act together and give rise to multiple alternative pathways in the inflammatory process, depending on the type of stimuli. The goal of the inflammatory process is to restore homeostasis regardless of the cause.[103]

Symptoms of acute inflammation:

- Redness (rubor) : secondary to vasodilatation and increased blood flow.
- Heat (calor) : localized increased in temperature, also due to increased blood flow.
- Pain (dolor): caused by stimulation of the local nerve ending, from mechanical and chemical mediators.
- Swelling (tumour) : results from increased vessel permeability ,allowing fluid loss into the interstitial space [2]

Causes:

The causes or inducers of inflammation can classify into two main groups: exogenous and endogenous inducers.[103]

1. Exogenous inducers.

This grouping can further subdivide into two classes; microbial and non-microbial exogenous inducers.

A. Microbial inducers.

There are two classes of microbial inducers. The first class is pathogen-associated molecular patterns (PAMPs), which are carried by all microorganisms. The second class is virulence factors restricted to pathogens. Virulence factors trigger the inflammatory response due to the effects of their activity. Examples include enzymatic activity produced by helminths and exotoxins produced by bacteria, which will be sensed by known or unknown sensors.

B. Non-Microbial

Causes include allergens, toxic compounds, irritants, and foreign bodies that are too large to be digested or cause phagosomal damage in macrophages. Examples of foreign bodies include silica and asbestos.

2. Endogenous inducers.

These are signals released by tissues that are either dead, damaged, malfunctioned, or stressed.

As an alternative, we could also divide the inflammatory inducers into two large groups, which are the infectious factors and the non-infectious factors.

I. Infectious factors:

This category includes bacteria, viruses, and other microorganisms.

II. Non-Infectious factors:

This group can be due to physical injuries such as frostbite, burn, physical injury, foreign bodies, trauma, ionizing radiation, chemical compounds such as glucose, fatty acids, toxins, alcohol, and chemical irritants such as nickel and other trace elements. Apart from that, there are also biological inducers, including signals released by damaged cells and physiological due to excitement.[106]

Biochemical (Mediators) And Genetic Pathology:

Many mediators play a crucial role in initiating the cascade in the acute inflammatory process.

The first group of mediators is the **toll-like receptors (TLRs),** which are membrane-spanning proteins found on the surfaces of the innate immune system cells like macrophages and dendritic cells. These single-pass membrane-spanning receptors recognize the pathogen-associated molecular patterns (PAMPs) or can recognize endogenous signals activated during tissue or cell damage known as danger-associated molecular patterns (DAMPS). To date, research has identified more than ten TLRs. An important example is the CD14 (cluster of differentiation 14), a co-receptor for TLR4, which is present on the surface of innate immune system cells preferentially expressed in macrophages, monocytes, and neutrophils. TLR4 can recognize the Lipopolysaccharide, which is the major component of the outer membrane of the gram-negative bacteria (PAMPs). Then the transmission of PAMPs and DAMPs are mediated by MyD88 (myeloid differentiation 88) along with the TLRs. Subsequently, the signaling will transmit through a specific cascade that leads to nuclear translocation of transcription factors, such as NF-kB, activator protein-1 (AP-1), or interferon regulatory factor 3(IRF3).[106,107,108]

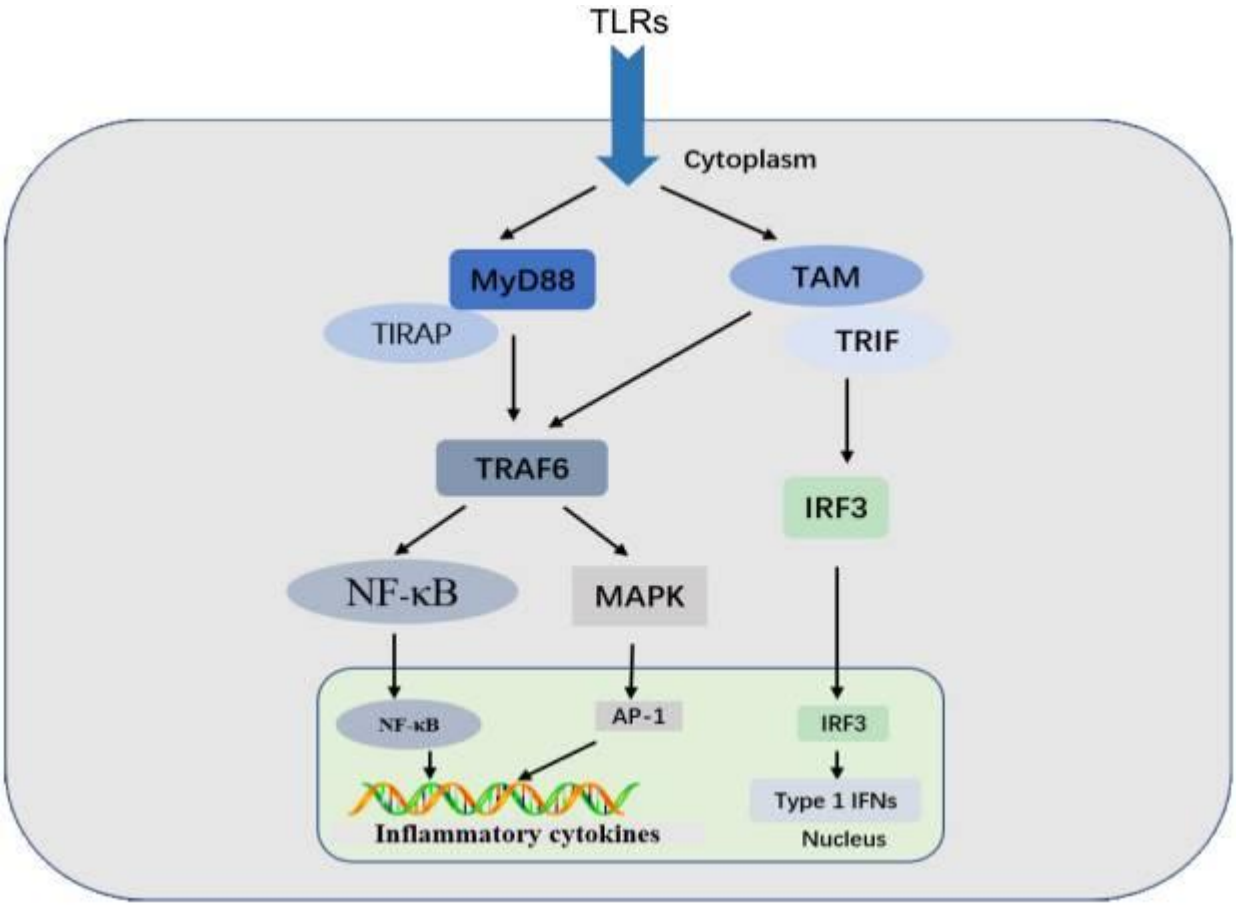


FIGURE:2

TLR signaling : MyD88-dependent and TRIF-dependent pathways are shown. Signaling through TLRs activates intracellular signaling cascades that lead to nuclear translocation of AP-1 and NF-κB or IRF3, which regulates the inflammatory response.

The second groups of mediators are **arachidonic acid (AA)** mediators. Arachidonic acid is a phospholipid that constitutes the membrane of the body's cells. Phospholipase can become activated by inducers, such as infection or tissue damage. This enzyme can act on this membrane phospholipids to liberate the arachidonic acid. This component can potentially metabolize into two main components through either the cyclooxygenase pathway or the 5-lipooxygenase pathway. The cyclooxygenase pathway forms the prostaglandins (PG) mediators; this includes the PGD2 and thromboxane, which are the bronchoconstrictive prostaglandins and the bronchoprotective or inhibitory PGE2 and prostacyclin. On the other hand, the 5-lipooxygenase pathway will form the leukotrienes (LTs). Examples of LTs include LTB4, which is neutrophil adhesive and chemotactic, LTC4, D4, and E4, which is involved in contraction of smooth muscle bronchioles, vasoconstriction, and edema formation.[109]

The third group of mediators are the **Mast cells**, derived from precursors in the bone marrow and widely distributed in the connective tissue. These cells will become activated by tissue damage. Other immune molecules also contribute to the activation of these molecules, including the C3a and C5a, which lead to degranulation of human mast cells. Mast cells can also be enhanced by cross-linking of their high-affinity receptors for IgE. After activation, mast cell secretes a few pro-inflammatory molecules such as histamine, TNF, kinin, and leukotrienes (Leukotrienes play an important role in the delayed response of acute inflammation caused by mast cell activation).[110]

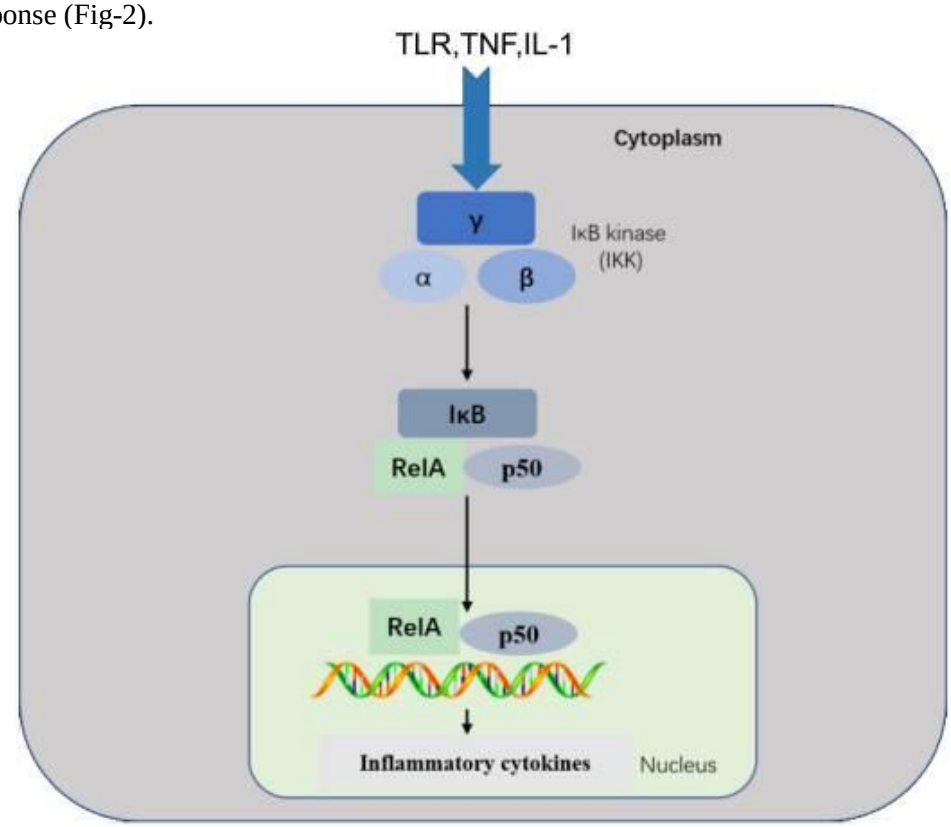
The fourth group of mediators that can activate the acute inflammation is the Complements. The complements are a set of proteins that interact with one another to create a cascade. A large number of these complements can become activated through several pathways like the classical, alternative, or mannose-binding lectin pathway. The most important complement in acute inflammation include the C3a and C5a that mediate the anaphylatoxins, and also the C5a consider as chemotactic for neutrophils, C3b for opsonin for phagocytosis. These complements can then activate the MAC (membrane attack complex) that can activate the neutrophils, monocyte, and mast cells.[111,112]

The last mediators are the **Hageman factor**, which is a part of clotting factors and also plays an important role in inflammation. Activation of this factor will lead to the activation of the kinin system and the formation of bradykinin.

Bradykinin increases the permeability of the walls of blood vessels. This leakage leads to the swelling considered as part of the acute inflammation. [113,114]
Other mediators and biomarkers of acute inflammation include Reactive oxygen and reactive nitrogen oxide species (ROS and RNOS), cytokines such as **IL-6**, Tumor Necrosis Factor **TNF-alpha**, and **chemokines**, the formation of DNA adducts, acute-phase proteins such as C-reactive protein (CRP), inflammation-related growth factors and transcription factors **(NF-KappaB)** and major immune cell types. The type of the mediators and immune cells involved all are variable and depend on several factors like the type of inducer, the duration of the injury, and multiple genetic loci.[115]

Inflammatory Response Mechanisms:
A response of inflammation is brought on by the interaction of pathways of signaling that regulate the levels of inflammatory mediators in surrounding tissue cells and cells of inflammation separated from the blood. [18] Inflammation is the root of many chronic illnesses including arthritis, cancer, diabetes, rheumatoid arthritis, heart disease, and intestinal problems. [19] Although the details of the initial stimulus and its place in the body affect how an inflammatory response process develops, they all have an identifiable mechanism.
Which can be summarized as follows:
1) Cellular pattern sensors detect harmful stimuli
2) The stimulation of inflammatory pathways,
3) The release of inflammatory markers,
4) The gathering of inflammatory cells.

NF-κB pathway:
The NF-κB transcription factor plays important roles in inflammatory, immune response, survival, and apoptosis processes. [116] The NF-κB family includes five related transcription factors: P50, p52, RelA (p65), RelB, and c-Rel. [117, 118] NF-κB activity is induced by a range of stimuli, including pathogen-derived substances, intercellular inflammatory cytokines, and many enzymes. [119, 120] Under physiological conditions, IκB proteins present in the cytoplasm inhibit NF-κB. [121] PRRs use similar signal transduction mechanisms to activate IκB kinase (IKK), which is composed of two kinase subunits, IKKα and IKKβ, and a regulatory subunit, such as IKKγ. IKK regulates NF-κB pathway activation through IκB phosphorylation. [123] IκB phosphorylation results in its degradation by the proteasome and the subsequent release of NF-κB for nuclear translocation and gene transcription activation. [122] This pathway regulates pro-inflammatory cytokine production and inflammatory cell recruitment, which contribute to the inflammatory response (Fig-2).



FIFURE:3 NF-κB pathway

This pathway is triggered by TLRs and inflammatory cytokines, such as TNF and IL-1, leading to activation of RelA/p50 complexes that regulate expression of inflammatory cytokines. NF-κB signaling requires IKK subunits. Which regulate pathway activation through IκB phosphorylation.

Etiology of inflammation:
1) Non-infectious factors
Physical: ionizing radiation, foreign bodies, physical injury, burn.
Chemical: chemical irritants, fatty acids, glucose, toxins.
Biological: A harmed cells
Psychological: excitement
2) Infectious factors
Bacteria, viruses, other microorganisms.

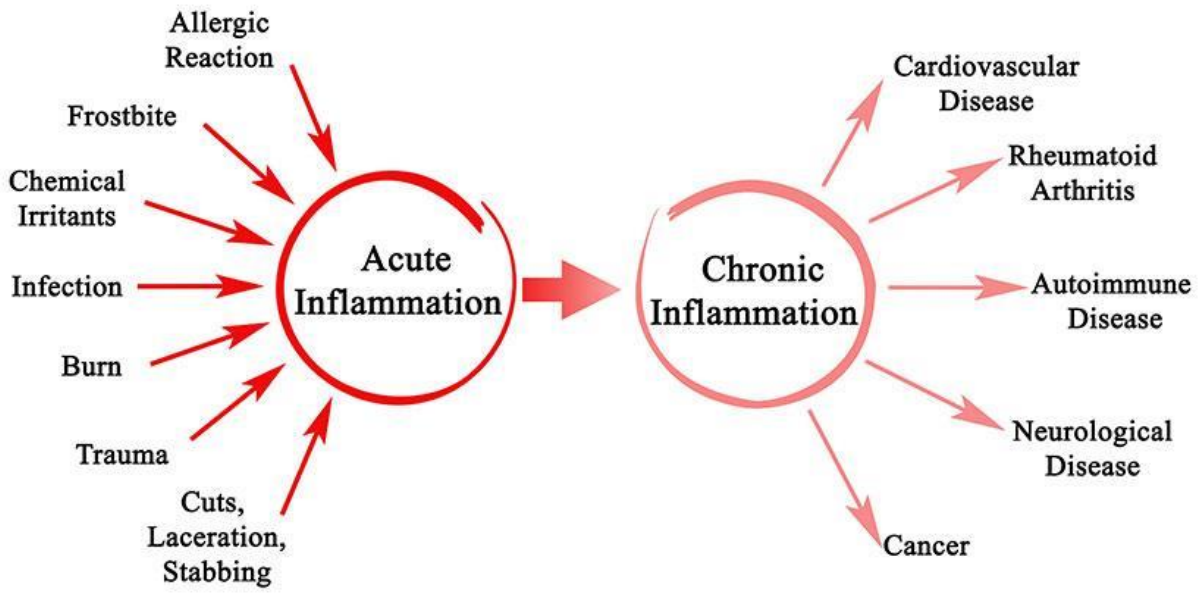


Figure 04: Types of Inflammation

Symptoms of Chronic Inflammation:
The following is a list of some of the typical warning signs and symptoms that appear during chronic inflammation:

- Myalgia, arthralgia, body pain.
- Insomnia and chronic fatigue
- Mood disorder, anxiety, depression.
- Acid reflux, GI complexation like constipation.
- Gain or loss of weight
- Often infections

Pathophysiology:
A large number of the hallmarks of acute inflammation, namely vasodilation, higher blood flow, capillary permeability, and neutrophil diapedesis (the migration of neutrophils into the infected tissue through the vessel wall), persist as the inflammation develops into chronic inflammation. However, as the composition of white blood cells changes, lymphocytes and macrophages soon take the place of the transient neutrophils. As a result, the tissue site is invaded by primary inflammatory cells, including macrophages, lymphocytes, and plasma cells, which then release inflamed cytokines, growth factors, and enzymes. As a result, it encourages progression of injuries to tissue and secondary repairs such fibrosis and granuloma formation.[20]

Types of Chronic Inflammation
Nonspecific proliferative: marked by the presence of non-specific granulation tissue, which is generated by the growth of fibroblasts, connective tissue, vasculature, and epithelial cells as well as the invasion of mononuclear cells (lymphocytes, macrophages as and plasma cells). Lung abscesses and inflammatory polyps that resembled nasal or cervical polyps being two examples.

Granulomatous inflammation: A particular form of chronic inflammation that is defined as the presence of distinct nodular lesions or granulomas composed of functional macrophages or their descendant cells, epithelioid cells, which are generally ringed by lymphocytes. Aschoff, Reed-Sternberg, and tumor giant cells are a few types of the Langhans or gigantic cells that typically develop when the macrophages or epithelioid cells within the granules congregate.
There are two types:
Foreign body granuloma, such as silicosis which is caused by T-cell mediated immune response.
Infectious granuloma, which are caused by tuberculosis and leprosy due to prolonged infection. [22]

History and physical:
Factors that are included with chronic inflammation:
Several risk factors promote a low-level inflammatory response. These include:
Age: • Elevated levels of a number of inflammatory chemicals are positively linked with advancing age. It's possible that age-related factors like an increase in visceral body fat or mitochondrial malfunction are to blame for the age-related increase in inflammatory chemicals.
Obesity: • Elevated levels of a number of inflammatory chemicals are positively linked with advancing age. It's possible that age-related factors like an increase in visceral body fat or mitochondrial malfunction are to blame for the age-related increase in inflammatory chemicals.
Diet: People with diabetes or those who are overweight are more likely to produce more pro-inflammatory molecules when they consume a diet high in saturated fat, trans-fats, or refined sugar.
Smoking: Smoking cigarettes is linked to reduced levels of anti-inflammatory chemicals and inflammation.
Low Sex Hormones: Studies have found that sex hormones, such as testosterone and estrogen, can inhibit the generation and secretion of a number of pro-inflammatory indicators, and it has been found that keeping sex hormone levels stable lowers the risk of a number of inflammatory disorders.
Stress and Sleep Disorders: Both physical and emotional stress are associated with the release of inflammatory cytokines. Stress can additionally lead to sleep problems. Due to the fact that people with irregular sleeping patterns are more likely to experience chronic inflammation than those who sleep regularly, sleep disturbances are also recognized as one of the distinct risk factors for chronic inflammation.[23]

Treat and Management:
The following list of dietary and lifestyle modifications may be useful in lowering chronic inflammation and removing inflammation triggers. Obesity management is the most successful. For instance, weight loss alone has been demonstrated to be independently associated with clinically meaningful improvement in disease activity and inflammation in patients with psoriatic arthritis, a chronic inflammatory arthritis.
Low-glycemic diet: High glycemic index diet is associated with increased risk of stroke, coronary heart disease, and type 2 diabetes. It is advantageous to restrict the intake of items that cause inflammation, such as sodas, processed carbs, and fructose corn syrup.
Reduce intake of total, saturated fat and trans fats: While omega-3 polyunsaturated fats seem to be anti-inflammatory, some dietary saturated and artificial trans-fats seem to exacerbate inflammation. Trans fats should be avoided in processed and packaged foods, baked products (including those made with soy and corn oil), and processed seed and vegetable oils.
Fruits and vegetables: Foods strong in polyphenols, natural antioxidants, and other anti-inflammatory substances, such as blueberries, apples, Brussels sprouts, cabbage, broccoli, and cauliflower, may help reduce inflammation. Consuming cherries and cherry juice has been demonstrated to be uricosuric and IL-1 inhibitory in gout sufferers.
Fiber: High dietary soluble and insoluble fiber intake is linked to decreased IL-6 and TNF-alpha levels.
Nuts: such as almonds are linked to a lower incidence of diabetes and cardiovascular disease.
Green and black tea polyphenols: In human clinical research, tea polyphenols have been linked to a decrease in CRP.
Curcumin: In animal studies, a component of turmeric has been linked to a considerable improvement in a number of inflammatory disorders.
Fish Oil: the most abundant source of omega-3 fatty acids. Lower levels of TNF-alpha, CRP, and IL-6 are linked to higher intake of omega-3 fatty acids.
Mung bean: Flavonoid-rich, especially vitexin and isovitexin. It is an ancient herbal remedy and meal that is well-known for its anti-inflammatory properties.
Micronutrients: (Magnesium, vitamin D, vitamin E, zinc and selenium). One of the most anti-inflammatory dietary components is magnesium, whose consumption is linked to decreased levels of hsCRP, IL-6, and TNF-alpha activity. By inhibiting inflammatory mediators including prostaglandins and nuclear factor kappa-light-chain-enhancer of activated B cells, vitamin D exerts its anti-inflammatory effects. In the body, antioxidants such as vitamin E, zinc, and selenium work.

Sesame Lignans: Sesame oil consumption is renowned for its possible hypotensive activity and decreases the production of prostaglandin, leukotrienes, and thromboxane.

Physical Exercise

Exercise decreases several pro-inflammatory cytokines and molecules, regardless of weight loss, as shown by human clinical trials.

Conventional Drugs that Combat Chronic Inflammation

Metformin is widely used to treat type II diabetic patients who have mild inflammation and dyslipidemia. Metformin's anti-inflammatory effects are demonstrated by the patients' decreased levels of blood TNF-alpha, IL-1beta, CRP, and fibrinogen.

Statins have an anti-inflammatory effect because they reduce a number of circulating and cellular mediators that induce inflammation. This pleiotropic effect appears to have reduced the amount of cardiovascular events.

Corticosteroids also prevent several mechanisms involved in inflammation. Glucocorticoids are prescribed for several inflammatory conditions including inflammatory arthritis, systemic lupus, sarcoidosis, and asthma.

Herbal supplements like ginger, turmeric, cannabis, hyssop, and Harpagophytum procumbens are shown to have anti-inflammatory properties however one should always consult with a doctor before their use and caution should be taken for using some herbs like hyssop and cannabis.[21]

NSAIDs (non-steroidal anti-inflammatory medicines), which include aspirin, ibuprofen, and naproxen, reduce inflammation by blocking the action of the COX enzyme. The pain associated with inflammation in people with arthritis is often treated with these drugs.

Additionally, a variety of mechanisms linked to inflammation are blocked by corticosteroids. Among the inflammatory diseases for which steroids are used are systemic lupus, inflammatory arthritis, sarcoidosis and asthma.

Several herbal supplements, including ginger, turmeric, cannabis, hyssop, and Harpago phytum procumbens, have been found to have anti-inflammatory effects; however, before using any herbal supplement, a doctor should always be consulted.

When abnormal cells divide quickly, they can invade nearby tissues and organs, a condition known as cancer. These incredibly fast-expanding cells could be giving rise to tumors. Additionally, they could obstruct the body's usual processes.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are a drug class FDA-approved for use as antipyretic, anti-inflammatory, and analgesic agents.[92] These effects make NSAIDs useful for treating muscle pain, dysmenorrhea, arthritic conditions, pyrexia, gout, migraines, and used as opioid-sparing agents in certain acute trauma cases.[93,94,95]

NSAIDs are typically divided into groups based on their chemical structure and selectivity: acetylated salicylates (aspirin), non-acetylated salicylates (diflunisal, salsalate), propionic acids (naproxen, ibuprofen, acetic acids (diclofenac, indomethacin), enolic acids (meloxicam, piroxicam) anthranilic acids (meclofenamate, mefenamic acid), naphthylalanine (nabumetone), and selective COX-2 inhibitors (celecoxib, etoricoxib).

Topical NSAIDs (diclofenac gel) are also available for use in acute tenosynovitis, ankle sprains, and soft tissue injuries. [96,97,98,99]

Listed below are the FDA-approved NSAIDs (organized alphabetically):

Non-selective NSAIDs

- Diclofenac
- Diflunisal
- Etodolac
- Fenoprofen
- Flurbiprofen
- Ibuprofen
- Indomethacin
- Ketoprofen
- Ketorolac
- Mefenamic acid
- Meloxicam
- Nabumetone
- Naproxen
- Oxaprozin
- Piroxicam
- Sulindac

- Tolmetin

COX-2 Selective NSAIDs

- Celecoxib
- Rofecoxib
- Valdecoxib

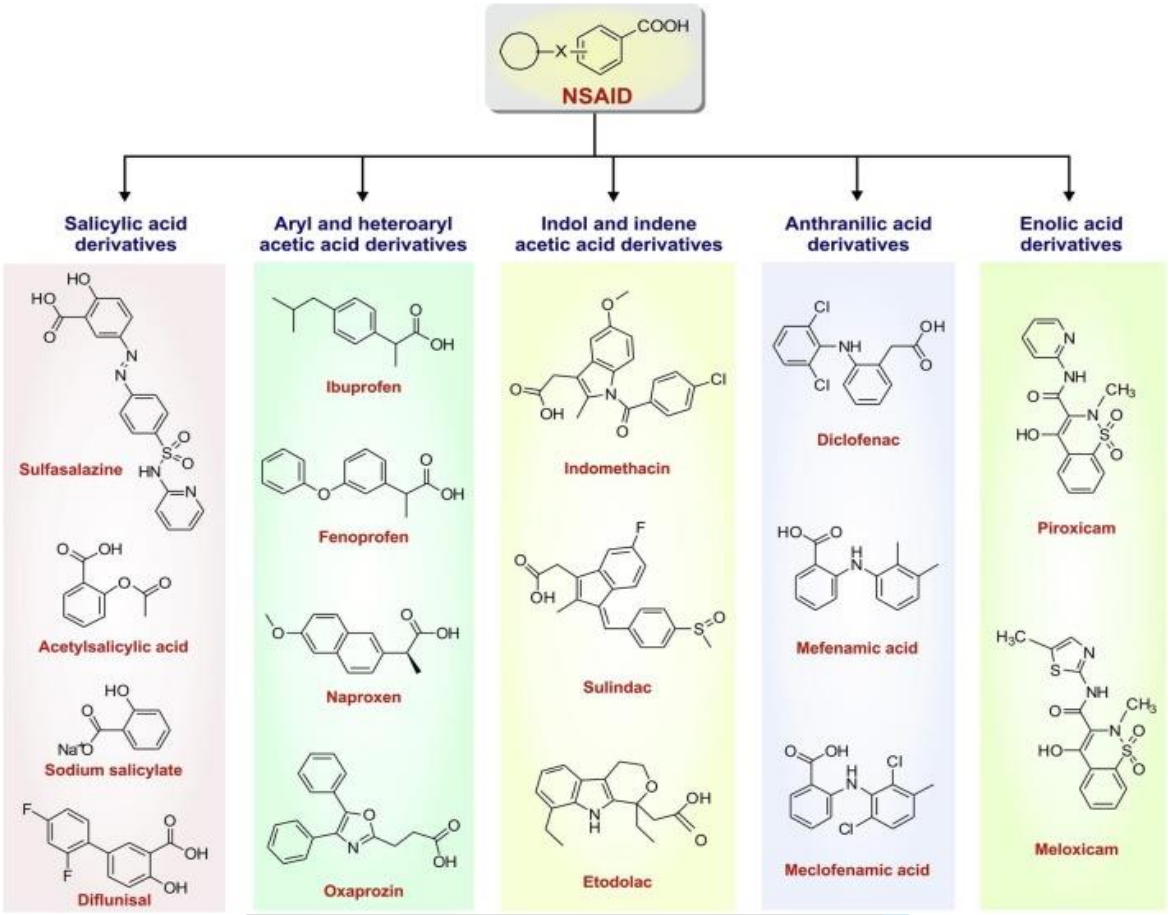


Figure 05: **Chemical structures of common NSAIDs**

Mechanism of Action:

The main mechanism of action of NSAIDs is the inhibition of the enzyme cyclooxygenase (COX). Cyclooxygenase is required to convert arachidonic acid into thromboxanes, prostaglandins, and prostacyclins.[100] The therapeutic effects of NSAIDs are attributed to the lack of these eicosanoids. Specifically, thromboxanes play a role in platelet adhesion, prostaglandins cause vasodilation, increase the temperature set-point in the hypothalamus, and play a role in anti-nociception.

There Are Two Cyclooxygenase Isoenzymes,

COX-1 and COX-2.

➢ COX-1 gets constitutively expressed in the body, and it plays a role in maintaining gastrointestinal mucosa lining, kidney function, and platelet aggregation.

➢ COX-2 is not constitutively expressed in the body; and instead, it inducibly expresses during an inflammatory response. Most of the NSAIDs are nonselective and inhibit both COX-1 and COX-2. However, COX-2 selective NSAIDs (ex. celecoxib) only target COX-2 and therefore have a different side effect profile. Importantly, because COX-1 is the prime mediator for ensuring gastric mucosal integrity and COX-2 is mainly involved in inflammation, COX-2 selective NSAIDs should provide anti-inflammatory relief without compromising the gastric mucosa. [101]

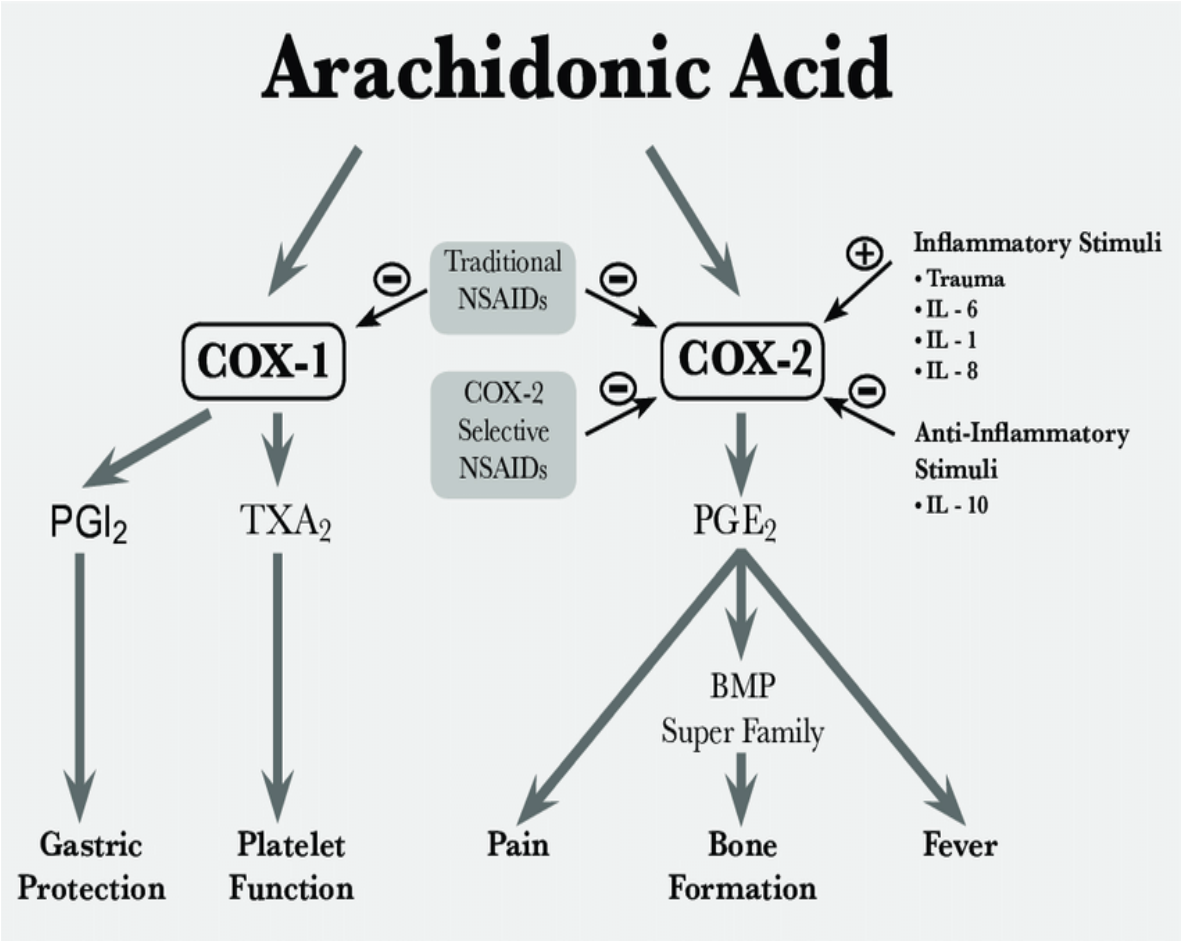


Figure 06: COX-1 and COX-2 pathways

Cancer:
One of the biggest causes of death worldwide is cancer. Nearly 1 in 6 fatalities in 2020 were attributed to cancer, according to a trusted source from the World Health Organization (WHO). Every day, professionals are putting innovative cancer treatments to the test.

Types of Cancers:
1) Cancers of Blood and Lymphatic Systems
- Hodgkin's disease
- Leukaemia's
- Lymphomas
- Multiple myeloma
- Walden Strom's disease

2) Skin Cancers
- Malignant Melanoma

3) Cancers of Digestive Systems
- Oesophageal cancer
- Stomach cancer
- Cancer of pancreas
- Liver cancer
- Colon and Rectal cancer
- Anal cancer

4) Cancers of Urinary system
- Kidney cancer
- Bladder cancer
- Testis cancer

- Prostate cancer

5) Cancers in women
- Breast cancer
- Ovarian cancer
- Gynaecological cancer
- Choriocarcinoma

6) Miscellaneous cancers
- Brain cancer
- Bone cancer
- Carcinoid cancer
- Nasopharyngeal cancer
- Retroperitoneal sarcomas
- Soft tissue cancer
- Thyroid cancer

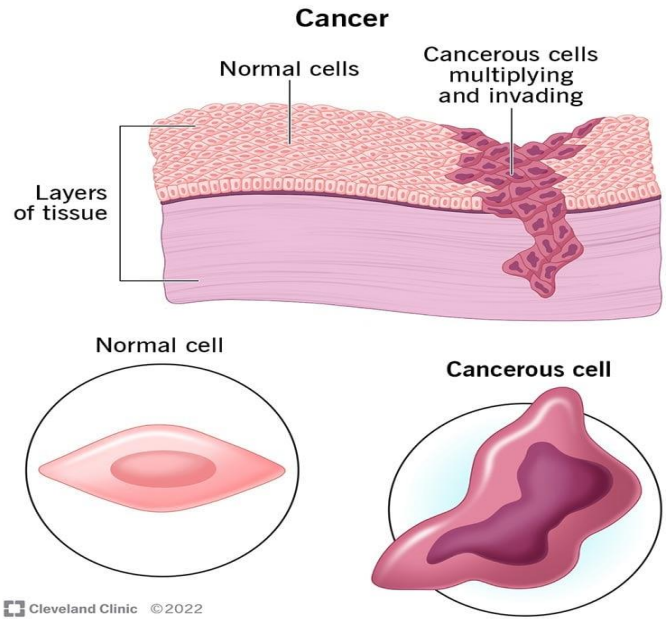


Figure 07: Normal cells and multiplying cells

Colo-rectal cancer (CCR): colorectal cancer starts in your colon (large intestine),the long tube that helps carry digested food to your rectum and out of your body.
The adult large intestine includes the colon, rectum, anal canal .The colon can be divided into the right colon and left colon. The blood supply of the colon is mainly from the mesenteric artery, the veins are accompanied by the arteries of the same name, And lumphatic network drain through the regional lymph nodes.[24]
It is the second-leading cause of cancer-related deaths in both men and women around the world, the third-most prevalent cancer overall, and the primary killer of gastrointestinal cancer. Poor eating habits, smoking, intestinal inflammatory illness, polyps, genetic factors, and aging all increase the risk of acquiring this cancer. 90% of those who are given a colorectal cancer diagnosis are older than 50, with a median age of 64; nevertheless, the illness is more aggressive in those who are given a diagnosis earlier in life. The American Cancer Association estimates that more than 49,700 deaths in 2015 were attributable to cancer. With early diagnosis and treatment, the death rate is intended to be decreased. The survival rate is currently utilized to forecast a patient's prognosis. If a first-degree relative has had colonic polyps or colorectal cancer before the age of 60, or if two or more first-degree relatives have had cancer, the patient is said to have a positive family history. A number of tests, including the guaiac test, immunochemical stool test, DNA stool test, sigmoidoscopy, colonoscopy, and barium enema, can be used to identify colorectal cancer. The prognosis, survival, and course of therapy for the patient depend on the stage at when the cancer is discovered. Review the basics of colorectal cancer, its genetic foundation, risk factors, protective factors, clinical course, diagnostic techniques, treatment, and survival. [9]

The colon, rectum, and anal canal are all parts of the adult large intestine. Right and left colons can be distinguished by the cecum, ascending colon, and right 2/3 of the transverse colon. The left colon can be identified by the left 1/3 of the transverse colon, descending colon, and sigmoid colon. The mesenteric artery provides the colon with the majority of its blood flow, along with its veins and arteries. The lymphatic system empties through the local lymph nodes. [24, 25]
The vagus and pelvic nerves innervate the colon. While the left colon's primary job is to store and expel excrement, the right colon's primary job is to absorb water and some nutrients. Notably, digestive hormones and alkaline mucus components are secreted by the colon.
The lower end of the rectum connects to the anal canal at the dentate line, and it joins the sigmoid colon. The superior and inferior rectal arteries deliver the majority of the blood to the rectus muscles. The superior rectal vein is mostly where venous reflux to the liver travels. The pararectal lymph nodes, superior and inferior rectal artery lymph nodes, etc. are some examples of the regional lymph nodes of the rectum. The primary physiological function of the rectum, which is innervated by the autonomic nerves, is defecation. It also takes in a tiny bit of water, salt, glucose, and some medications. [26]
Rectal cancer accounts for 49.66% of cases, colon cancer accounts for 49.09%, and both sites combined account for 1.25% of cases of cancer. [27] The sigmoid colon (55% of cases), followed by the ascending colon (23.3%), transverse colon (8.5%), descending colon (8.1%), cecum (8.0%), and crossing site (2.1%), are the most frequent sites for colon cancers. [27]

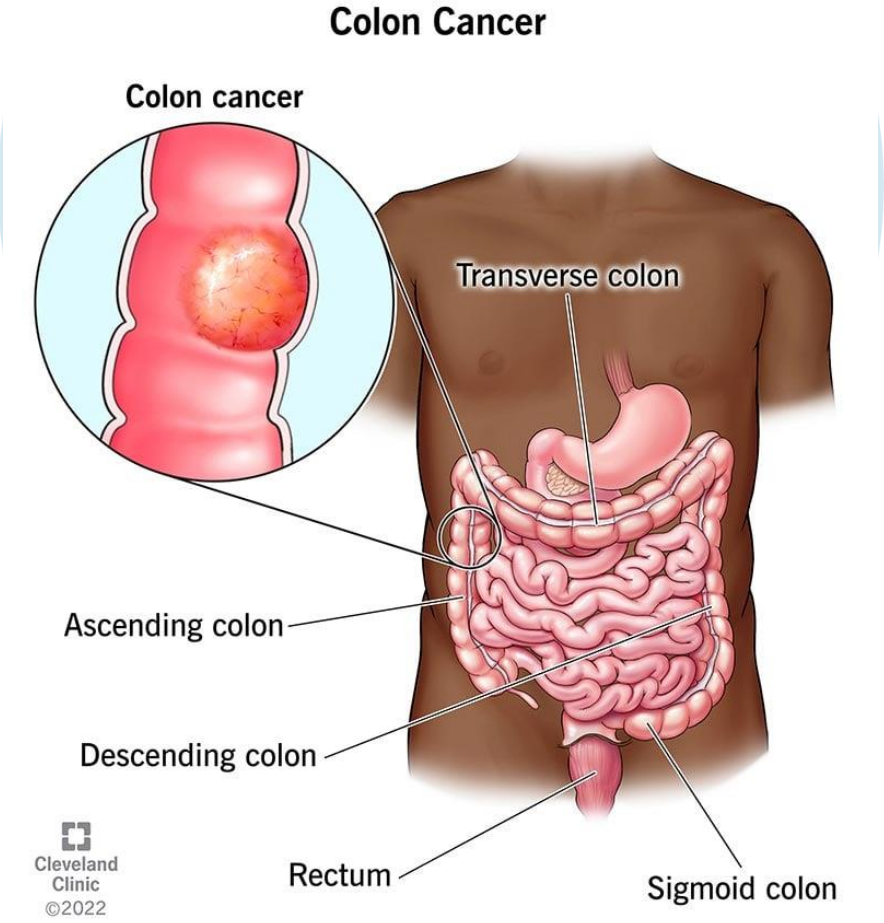


Figure 08: Colon cancer starts as polyps in your colon. It can start in any part of your colon

Etiology:
The etiology of CRC remains unclear, but it may be related to the following factors:
Genetic factors: Investigations have revealed a threefold greater risk of cancer in first-generation relatives of CRC patients, who account for 20% of instances of CRC. A genetic condition called familial adenomatous polyposis (FAP), as well as the mismatch repair gene (MMR), have both been associated to inherited CRC.[32]
Dietary factors: Currently, it is thought that a diet high in fat, high in animal protein, and low in cellulose contributes to the prevalence of CRC. Consuming too much fat will increase intestinal carcinogens, bile acid breakdown, bile secretion, and the activity of anaerobic bacteria in the gut. [33]
Non-cancerous diseases: CRC can be influenced by non-cancerous conditions such colorectal polyps, colorectal adenomas, ulcerative colitis, and Crohn's disease, among others. The incidence of malignant transformation is greater

than 10% in individuals with ulcerative colitis lasting longer than 20 years, according to research, and roughly 3-5% of ulcerative colitis patients will acquire CRC. Colonic polyps, which have a precancerous course of 2–5 years, are thought to be the source of 15–40% of colon malignancies. Adenomas with a diameter of less than 1 cm have a less than 2% probability of developing cancer, whereas those with a diameter of more than 3 cm have a more than 40% chance of doing so. [26, 34]

Other factors: Carcinogenic exposure and lifestyle, such as sedentary and overweight, are risk factors for CRC, and the incidence of sigmoid and rectal cancer is higher in patients undergoing pelvic radiation therapy. **[26]**

Epidemiology:

CRC is the third most common cancer to be diagnosed globally, with men suffering it at a higher rate than women.[28] The second most frequent reason for cancer-related fatalities worldwide is CRC. CRC is the second most common tumor overall in China, with an age-standardized incidence of 23.7 per 100,000 people. Male and female patients are ranked third and third, respectively, with age-standardized incidences of 28.1 and 19.4 per 100,000 people. The incidence of CRC is substantially correlated with environmental variables, lifestyle, and food, but there is no clear connection between ethnicity and CRC, according to research linking migration, religious factors, and the disease. The incidence of CRC varies by region, with North America, Western Europe, and Oceania reporting the greatest incidence and Africa, Asia, and South America reporting the lowest prevalence. The incidence of CRC similarly exhibits an east-to-west gradient in the Chinese main land.While the incidence of CRC is significantly lower in the economically depressed western parts, it is higher in the economically developed eastern coastal districts. [29] Second-generation immigrants' incidence and mortality rates from CRC's low-occurrence areas to its high-incidence areas are comparable to those of locals. [30]

With age, the risk of CRC rises. However, a large proportion of cases still involve teenagers. The incidence and mortality of CRC are low until the age of 45 and then significantly rise after that, peaking in the age range over 80. In China, 10-20% of CRC patients are under the age of 30, and the age of onset is 12–18 years earlier than in western nations.[27, 31]

Over time, the morbidity and mortality of CRC have changed. Regional differences exist in the change. While the low-incidence regions, like China, demonstrate an increasing trend, the initial high-incidence regions' rising rate slows or even stops. In China, especially in cities, the incidence and mortality of CRC have been rising steadily over the past 30 years. The aging of the population, shifting habits, and shifting environments could all be contributing factors. [26, 29]

In general, the epidemiological characteristics of CRC in China has been summarized below: [26, 27]

- Higher in males than in females, males to female ratio is 1.3:1
- Medium age of onset is 58years
- Rectal cancer is common comparatively to colon cancer.
- In well developed regions, most common site of colon cancer has changed from rectum to colon and proportion of right colon cancer increased.

Pathogenesis:

A number of factors contribute to CRC. The colon mucosal epithelial cells can experience adenomas, mild, moderate, or severe atypical hyperplasia, and hyperplasia, all of that can progress to develop into cancer. This process is typically started by carcinogenic agents that alter DNA structure and cause malignant cell transformation into cancer. Adenomas, which may eventually turn into carcinomas, include epithelial hyperplasia, atypical hyperplasia, adenoma development, carcinoma in situ, and invasive carcinoma severe. [35] Fearon and Vogelstein presented a molecular event model for the development and incidence of CRC in 1990.[36] Three molecular processes linked to the occurrence and progression of CRC have been confirmed as research has advanced: (i) Chromosome instability, which primarily affects FAP [37] (ii) genetic mutations such as in Lynch syndrome and other sporadic MMR mutations [38] (iii) hypermethylation of CPG islands in specific gene promoter regions [39]

Pathological type and metastasis:

Early stages of CRC are limited to the mucosa and submucosa of the intestine. Early CRC typically does not have lymphatic metastases. About 10% of patients experience lymphatic metastasis when the tumor penetrates the submucosa. The most common gross forms of CRC are elevation, ulceration, and infiltration.[35] Papillary adenocarcinoma, tubular adenocarcinoma, mucinous adenocarcinoma, signet-ring cell carcinoma, undifferentiated carcinoma, adenosquamous carcinoma, squamous cell carcinoma, and carcinoid carcinoma are the main pathological histopathological forms. [35] The most common type of colon cancer, accounting for more than 90% of cases, is

adenocarcinoma. The clinical data of 1092 primary CRC patients were analyzed, and it was discovered that adenocarcinoma accounted for 93.4% of cases, mucinous adenocarcinoma 3.9%, signet ring cell carcinoma 0.6%, and carcinoid 0.2% (43). The four pathways listed below are primarily used by CRC to spread and metastasize:

Local invasion: The original lesion's immediate vicinity as well as nearby structures get infiltrated by the tumor.

Lymphatic metastasis: About 60% of CRC metastasis takes place through this pathway, where the neoplastic cells travel through the intramucosal lymphatic system to local lymph nodes before finally generating distant lymph node metastases. [26]

Hematogenous metastasis: Blood arteries were used by the cancer cells to spread. About 30% of CRC are spread via hematogenous metastasis, which primarily affects the liver and lungs as target organs. [26]

Implantation and metastasis: The cancer cells are implanted in the abdominal and pelvic peritoneum after they have shed, creating metastatic foci.[26]

Diagnosis:

The majority of CRC patients do not exhibit any overt clinical signs in the early stages, which lowers the rate of early diagnosis. Many patients receive diagnoses that are too late to allow for drastic treatment. Clinically, it is typically advised that those over 20 with the following symptoms get additional testing.

(i) Recent persistent abdominal discomfort, such as abdominal pain.
(ii) Changes in defecation habits.
(iii) Blood in stool
(vi) Abdominal mass.[44]

Routine physical exams and other tests are included in further examination. Patients with a suspicion of rectal cancer should undergo a digital rectal examination. Additional tests include:

(i) Fecal occult blood test (FOBT)—It has some clinical utility for the detection and diagnosis of CRC because positive results can be obtained with as little as 5 ml of digestive tract bleeding[26]

(ii) Tumor markers—There are currently no specific tumor markers for CRC, but CEA (carcinoembryonic antigen) and CA19-9 (carbohydrate Antigen 19-9) are frequently used, and their combined detection is more sensitive than either one of them alone, which has significant clinical significance for determining the effectiveness of treatment and keeping track of disease recurrence.[26]

(iii) Endoscopy—The most crucial step in colorectal endoscopy is a practicable pathological tissue biopsy, which allows for direct observation of the location, size, and form of the lesion.

(iv) X-ray—Following a barium enema, an X-ray scan can reveal filling defects and mucosal damage at the tumor location. However, it is not appropriate for individuals who have intestinal blockage. Gas-barium double contrast works to detect colon cancer with tiny lesions.

(v) Ultrasound—Intestinal tumors and abdominal lymph nodes can be found with ultrasonography in some cases.

(vi) Computed tomography (CT)—The size of lesions, their relationship to surrounding tissues and organs, abdominal lymph nodes, and other diseases can all be seen on a CT scan, which has considerable diagnostic value and can help with clinical staging.

(vii) Nuclear magnetic resonance (NMR)—comparable to a CT scan but with more tissue resolution than a CT scan, preoperative evaluation is extremely valuable clinically, especially for pelvic lesions like rectal cancer.

(viii) Positron emission computed tomography (PET/CT) —It offers details on the tumor's anatomical location and metabolic features and is very helpful for CRC diagnosis, preoperative staging, and recurrence evaluation. [26, 44, 45]

Treatment:

Surgery is the primary form of treatment for CRC, but additional methods such as chemotherapy, radiation, molecular targeted therapy, immunotherapy, and other treatments may also be used. [44, 46] According to studies, people with early CRC who receive surgical treatment had a 5-year survival rate of more than 90%. [47] As a result, surgery continues to be the mainstay of CRC treatment. In order to maximize the chance of surgical treatment, the feasibility of surgery should be assessed following neo adjuvant therapy for some CRC patients who were initially inoperable and for some CRC patients with metastases. Radial surgery and palliative surgery are the two basic types of surgery. [44]

Neoadjuvant chemotherapy, adjuvant chemotherapy following radical surgery, and palliative chemotherapy are the three primary types of CRC chemotherapy.**[48]** Neo adjuvant chemotherapy is frequently used in conjunction with radiotherapy to improve patient quality of life, decrease postoperative recurrence, and decrease the clinical stage of the tumor. After radical surgery, adjuvant chemotherapy can eradicate any remaining tumor cells and strengthen the effects of major surgery. Palliative chemotherapy is used to prolong survival and enhance quality of life in patients with advanced CRC. The chemotherapeutic medicines fluorouracil, irinotecan, oxaliplatin, and raltitrexed are frequently utilized. Combination chemotherapy regimens that frequently use the afore mentioned chemotherapeutic agents include FOLFOX, FOLFIRI, CAPEOX, and FOLFOXIRI, among others. [49]

For patients with CRC, the use of molecularly targeted medications has had a considerable positive impact. The majority of molecularly targeted medications utilized in the clinical therapy of CRC today fall into two categories:

bevacizumab, an anti-angiogenesis drug, and cetuximab, an anti-epidermal growth factor agent. Clinically, it is advised to employ molecular-targeted medications in combination with chemotherapeutic drugs since they are non-cytotoxic and have modest side effects that typically do not significantly worsen the side effects of chemotherapy.[46]
The use of molecularly targeted drugs has significantly improved outcomes for CRC patients. Bevacizumab, an anti-angiogenesis medicine, and cetuximab, an anti-epidermal growth factor agent, make up the majority of molecularly targeted drugs used in clinical therapy for CRC today. Since molecular-targeted therapies are non-cytotoxic and have mild side effects that often do not significantly worsen the side effects of chemotherapy, it is advised clinically to use them in combination with chemotherapeutic treatments.[50]
Recent studies have shown that immunotherapy can prolong survival in CRC patients. [51] Other therapies include biotherapy, conventional Chinese medicine, local cryotherapy, radiofrequency therapy, and palliative care, as well as hyperthermia combined with chemotherapy or radiotherapy. [44]

Essential medicines for cancer on the national essential medicines lists [102]

On WHO 2013 Model List

- Asparaginase
- Bleomycin
- Calcium folinate
- Carboplatin
- Chlorambucil
- Cyclophosphamide
- Cytarabine
- Dacarbazine
- Dactinomycin
- Daunorubicin
- Docetaxel
- Doxorubicin
- Etoposide
- Fluorouracil
- Hydroxycarbamide
- Ifosfamide
- Mercaptopurine
- Mesna
- Methotrexate
- Paclitaxel
- Procarbazine
- Tamoxifen
- Tioguanine
- Vinblastine
- Vincristine

Added to WHO Model List via 2015 revision

- All-trans retinoic acid
- Aromatase inhibitors
- Bendamustine
- Bicalutamide
- Capecitabine
- Cisplatin
- Fludarabine
- Gemcitabine
- Granulocyte colony stimulating factorsc
- Imatinib
- Irinotecan
- Leuprolin class
- Oxaliplatin
- Rituximab
- Trastuzumab
- Vinorelbine

Other medicines

- Arsenic trioxide

- Dasatinib
- Diethylstilboestrol
- Erlotinib
- Gefitinib
- Nilotinib

Prevention and prognosis:

The following are some approaches for preventing CRC in accordance with its pathogenic factors:

(i) Diet—consumption of raw fiber-containing foods, fresh fruit and vegetables, and the right minerals and trace elements, such as calcium, magnesium, and vitamin D [48]

(ii) Lifestyle management—reducing alcohol consumption, getting enough exercise, and managing your weight.

(iii) Active management of benign colorectal illnesses include Crohn's disease, ulcerative colitis, polyps, and adenomas.

(iv) Regular screening--early screening to prevent CRC is very important.[52]

Primary prevention has been reported to reduce CRC death by 35%, secondary prevention through early screening for CRC has been reported to reduce CRC mortality by 53%, and prescribing treatment for patients with CRC has been reported to reduce CRC mortality by 12%, according to the literature [52,54]

The most crucial prognostic factor for CRC is the disease stage at initial diagnosis. According to reports, patients with localized CRC who can undergo surgical resection have a 5-year survival rate of roughly 90%, compared to patients with advanced CRC who are unable to undergo surgery, who have a 5-year survival rate of only 10%.[55] Normally, it takes 5 to 10 years for benign lesions like adenomas and cancer to develop naturally from normal colorectal epithelial cells[47] Multiple aberrant gene alterations, including those in the APC, DCC, P53, K-RAS, C-MYC, BRAF, MCC, and MMR-related genes, are frequently involved in this process. Clinical intervention and early detection of limited-stage lesions are essential for improving the prognosis of CRC patients. [47, 56]

Currently, FOBT, fecal immune histochemistry (FIT), tumor markers, and colonoscopy are frequently used for CRC screening and diagnosis. Although FOBT is a cheap and non-invasive screening tool, it is only 50% sensitive to the detection of CRC. Dietary restriction is not necessary, and FIT has greater sensitivity and specificity than FOBT (78% and 96%, respectively) **[57],** but the detection results of FIT are susceptible to non-hemorrhagic tumors and hemorrhagic non-tumor illnesses.[58, 59]

However, the development of this examination is hampered by patients' and their families' reluctance to handle stool samples. Only 50% of patients receiving FOBT had a specimen sent in, according to data from the UK research[60] Although more approachable DNA-based stool tests have been made available in the UK, delivering fecal samples still poses a significant issue. Blood samples are simple to obtain and can dynamically represent the physiological and pathological state of the body in real time. The most common CRC indicators found in blood samples are CEA and CA19-9, which are now used therapeutically to assess the effectiveness of anti-tumor therapy and track the disease's recurrence with poor sensitivity and specificity (40–70% and 73–90%, respectively). [60, 61] The utility of CEA in screening asymptomatic patients and detecting CRC has been questioned due to reports that it fluctuates significantly in healthy individuals, with its variance in the same individual reaching 30%. [62] As a result, CEA and CA19-9 are inadequate for use as CRC screening and diagnostic indicators. Colonoscopy allows for visual inspection of the colorectal lesions' size, shape, and location. Most notably, it can collect abnormal biopsy samples, a crucial tool for CRC detection and diagnosis. [55, 63] Colonoscopy screening could lower colon cancer mortality due to the high prevalence of CRC cases and the fact that early diagnosis and removal of colorectal adenomas or early-stage CRC can prevent deaths. [64] However, because a colonoscopy needs intestinal preparation, it is an intrusive examination technique that can increase the risk of intestinal perforation and poor patient compliance. [55]

The accuracy of a colonoscopy varies substantially depending on both disease- and technology-related factors, including operator expertise, bowel preparation, and the length of the examination. [42]

The Mechanism on Cancer Therapy:

• Directly reducing the growth of cancer cells by promoting macrophage phagocytosis and raising killer cell production.

• Increasing the synthesis of interferon-1, interleukin-2, immunoglobulin, and complement in blood serum to encourage the death of cancer cells.

• By preventing the tumor tissue's blood supply, a tumor is forced to die, and its translocation and spread are prevented.

• Increasing leukocyte and platelet counts by promoting haemopoietic activity.

• Supporting the process by which tumor cells become normal cells in reverse. Enhancing metabolism and halting the development of cancer in healthy cells. Stimulating appetite, improving quality of sleep, relieving pain, thus benefiting patient's health

Table 01: Global scenario on types of cancer

Sl.no	Type of cancer	No. of Patient's Affected / year
1	Lung	1.2million
2	Breast	Over 1 million
3	Colorectal	940000
4	Stomach	870000
5	Liver	560000
6	Cervical	470000
7	Oesophageal	410000
8	Neck and Head	390000
9	Urinary bladder	330000
10	Malignant Non-Hodgkin lymphomas	290000

Table 02: Indian Medical plants having anticancer activity

S.no	Name of the plant	Family	Parts used
1	Calotrophisgigantean	Asclepiadaceae	Whole plant
2	Cajanuscajan	Fabaceae	Leaves
3	Butcamonosperma	Fabaceae	Bark

4	Bauhiniavariegate	Caesalpinaceae	Root
5	Bacopamonnieri	Scropulariaceae	Wholeplant
6	Azadirachtaindica	Meliaceae	Bark
7	Asparagusracemosus	Liliaceae	Root
8	Aphanamixispolystachya	Meliaceae	Bark
9	Aloebarbadensis	Liliaceae	Leaf juice
10	Aliumcepa	Liliaceae	Bulb
11	Acoruscalamus	Araceae	Rhizome
12	Cassiaabsus	Caesalpinaceae	Leaves
13	Cassiaauriculata	Caesalpinaceae	Roots
14	Catunaregumspinosa	Rubiaceae	Bark/Fruit
15	Citrulluscolocynthis	Cucurbitaceae	Root
16	Citrusmedica	Rutaceae	Root
17	Cissusquadrangularis	Vitaceae	Whole plant
18	Clerodendrumserratum	Verbanaceae	Root
19	Clerodendrumviscosum	Verbanaceae	Leaves

20	Crinumasiaticum	Amaryllidaceae	Bulb

Lantana camara L. *(L. camara)* is a tropical plant that exists in 60 countries.Few research have documented the separation of certain bioactive substances from L. camara, such as the common pentacyclic triterpenoid *Lantadene*. *Lantadene* had anticancer activity against cervical, colon, lung, and human promyelocytic leukemia cells. Alkaloids in *L. camara* are present in relatively small amounts and are challenging to find or extract. Using standard techniques for phytochemical screening, alkaloids in the leaves of *L. camara* have been discovered qualitatively, in a very small percentage. Due to the alkaloids' low concentration in the plant tissues or the possibility that other chemicals in the extract were masking their presence, some phytochemical experiments on *L. camara* failed to discover them. In the current study, a novel technique was developed to separate particular alkaloids by their preferential and selective adsorption on iron oxide magnetic nanoparticles (MNPs), which are negatively charged. To the best of our knowledge, this study is the first to document the isolation of *L. camara's* alkaloids employing cutting-edge methods that enlist the MNPs as a separating medium. The anticancer potential of the crude alkaloids and the separated HPAF (highest peak of the alkaloid fraction) was examined. [66]

Linnaeus gave the Verbenaceae family member *Lantana camara* its name in 1753. It is well known for producing essential oils.

The majority of it is made up of seven species, six of which have been documented from America and one from Ethiopia. Although it originated in South America, there are about 50 additional countries where elements of the levies are used. It can also be grown in some of those countries. It is also known as red sage and is used as a common garden attractive plant. L. camara flourishes in tropical, subtropical, and temperate climates at high heights of up to 2000 m. The flowering plant has a woody stem and a range of colors, including red, white, and pink. Additionally, it has prickles or spines. The genus contains 650 cultivars, however the majority of them are related to the *L.camara* complex.

It is also considered as a noxious weed globally. Moreover, it is stated that the ash of Manganese and potassium, which are beneficial for coconut palms, are found in *L. camara*. Few sources list it as a plant that is harmful to both humans and animals. *L. camara* has historically been used to cure a wide range of ailments, including cancer, tumors, tetanus, wounds, eczema, measles, chickenpox, fevers, rheumatism, and asthma. Because it contains a number of bioactive components, including steroids, *L. camara* has the potential to be therapeutic. [67]

Figure 09: whole plant

History and Distribution:

Small, perennial, evergreen *Lantana camara linn* can reach heights of 2 meters and a width of 2.5 meters. Because the leaves and stems are bent and covered in rough hairs, the leaves are simple, opposite, ovate, sharp, dentate, and rough

on both sides. Flowers are tubular in shape and have four petals that are placed in clusters in the terminal parts. The color of the flower and stem varies depending on the location, age, and maturity of the plant as well as the inflorescence. Even after numerous cuttings, the plant still produces new, fresh shoots from its robust roots. When fully grown, fruits have a meaty, glossy appearance and are either black, purplish-black, or bluish-black in color. Throughout the year, there is flowering and fruiting, with the first two months of the rainy season being the apex**.** [68]

Leaves: perennial

1. seed propagated
2. Shrub
3. vine / climber
4. Woody

Botanical Description: [69]

Synonyms:

Kannada- kasooti Hoo

Marathi- Ghaneri

Hindi- Raimuniya

Sanskrit- vanacchedi

English- Arch man

Botanical name: *Lantana Camara Var .aculeata*

Biological source: it is obtained from whole plant of *Lantana Camara Linn*

Table 03: Taxonomy [70]:

Kingdom: Plantae
Phylum: Spermatophyta
Subphylum: Angiospermae
Division: Magnoliophyte
Class: Magnoliopsida
Order: Lamiales
Family: Verbenaceae
Genus: Lantana
Species*: Lantana Camara Linn*

Table 04: *LANTANA CAMARA LINN* PLANT DISCRIPTION [71]:

Leaves	Leaves are strong aromatic when crushed.
Stem	The stems and branches are angular, bearing curved spines, arranged along the edges.
Flowers	Flowers are red, pink, orange, yellow, white in colour and it changes after maturation
Fruits	Fruits are green to dark purple in colour

Seeds	The green balls on lantana are the seed pods, which will eventually mature to a deep, purplish-black colour when fully ripe. Pick the pods when they are fully ripe and the skin is slightly wrinkled.
Colour	Flowers when bloom, young flowers are in yellow colour and old are in red colour

Fig 10: Flower

Fig 11: Leaves

Fig 12: stem

Fig 13: Root

Fig 14: seeds

Traditional uses:

Lantana camara linn leaves can exhibit antibacterial, fungicidal, and insecticidal qualities, according to studies done in India. Leprosy, skin rashes, leprosy, chicken pox, measles, asthma, and ulcers are just a few of the conditions that have been treated using *L. camara* in traditional herbal remedies.[71]

Pharmacologic Activities of *lantana camara linn*

L. camara is a vital member of the Verbenaceae family of medicinal plants. This herb has recently been linked to a number of stated medical benefits.

Antibacterial activity:

There have been reports of antibacterial activity in the leaves and flowers of many *L. camara* plant types. A high amount of antibacterial activity against E. coli, Bacillus subtilis, and P. aeruginosa was shown by three separate solvent extracts of the leaves and flowers of four different varieties of *L. camara*, but not against Staphylococcus aureus.

Ethanolic extracts of *L. camara* leaves and roots were reported for antibacterial activity. The microdilution method was used to test the in vitro antibacterial activity. Escherichia coli, Proteus vulgaris, Pseudomonas aeruginosa, V-briocholareae, and two multiresistant strains of E. coli and S. aureus were all susceptible to the extracts' antimicrobial effects.

By using the disk diffusion method and the broth microdilution method, methanolic extracts of various sections of L. camara were tested for antibacterial activity against 10 bacteria and 5 fungi. The maximum activity against Gram positive Bacillus cereus and Gram-negative bacteria was seen in the L. camara leaves extract. Typhi salmonella.[72]

Antifungal activity:
The antifungal ability of *L. camara* was tested against the plant pathogen Alternaria sp., which is particularly harmful to vegetable plants. The food poison plate method was used to test the antifungal activity at three distinct extract concentrations, namely 10 mg/ml, 15 mg/ml, and 20 mg/ml. L. camara demonstrated considerable antifungal efficacy against Alternaria sp. at a dosage of 20 mg/ml.
L. camara was put to the test against the plant pathogen Alternaria sp., which is highly detrimental to vegetable plants, to see if it has any antifungal properties. The antifungal activity of three different extract concentrations—10 mg/ml, 15 mg/ml, and 20 mg/ml—was tested using the food poison plate method. At a dosage of 20 mg/ml, L. camara showed notable antifungal effectiveness against Alternaria sp. [73]

Antiulcerogenic activity:
On aspirin, ethanol, and cold resistance stress caused stomach ulcers in rats, methanol extract of leaves of *L. camara* was reported to have antiulcerogenic potential. Aspirin-induced, ethanol-induced, and cold restraint stress-induced ulcers in rats were significantly protected when the extract was pre-treated with the affected animals (200 and 400 mg/kg body weight). In all models, the extract had dose-dependent antiulcerogenic efficacy [74]

Hemolytic activity:
The hemolytic activity of the L. camara liquid extract and its solvent fractions was evaluated using a modified spectroscopic method at four distinct concentrations (125, 250, 500, and 1000 g/ml). The hemolytic activity toward human erythrocytes by the aqueous extract and its solvent fractions was extremely low. The different extracts' hemolytic activity was detected in the following order: Aqueous extract followed by ethanol extract, methanol fraction, chloroform fraction, and finally, a 50/50 mixture of hexane and ethyl acetate.[75]

Antihyperglycemic activity:
In rats with diabetes induced by alloxan, methanol extract of leaves from *L. camara* was found to have antihyperglycemic action. In alloxan-induced diabetic rats, oral treatment of the methanol extract of *L. camara* (400 mg/kg body weight) leaves caused a drop in blood glucose to 121.94 mg/dl.
In streptozotocin-induced diabetic rats (Wistar albino rats), the methanol extract of *L. camara* Linn fruits were tested for its hypoglycemic action. In streptozotocin-induced diabetic rats, extract therapy at doses of 100 and 200 mg/kg body weight led to a dose-dependent drop in serum glucose level. Improvements in body weight, HbA1c profile, and liver cell regeneration were also seen after extract administration.[76]

Wound healing activity:
Rats were used to test the aqueous extract of *L. camara* leaf's wound-healing abilities. Topical application of the extract (100 mg/kg/day) to the wound dramatically increased wound contraction (98%), collagen synthesis, and speed of wound healing.
The ability of an ethanol extract of *L. camara* leaf to promote wound healing in adult male Wister rats has been documented. The extract's topical administration to the wound dramatically accelerated wound healing. The role of extract in healing was established by histological examination of cured lesions. [77]

Antimotility activity:
It has been reported that a methanol extract of *L. camara* leaves has antimotility activity in mice. Mice were used in a charcoal meal test to measure intestinal motility. The extract fully prevented the transit of charcoal in healthy mice at a dose of 1 g/kg body weight. Mice suffering from castor oil-induced diarrhea had their fecal output significantly reduced when the extracts were administered intraperitoneally at doses of 125 and 250 mg/kg body weight.[78]

Mosquito controlling activity:
Aedes aegypti, Culex quinquefasciatus, Anopheles culicifacies, An. fluvialitis, and An. stephensi mosquitoes have been shown to be susceptible to the essential oil from the leaves of *L. camara*, with LD50 values of 0.06, 0.05, 0.05, 0.05, and 0.06 mg/cm and LD90 values of 0.10, 0.10, 0.09, 0.
Methanol and ethanol extracts of the leaves and flowers of *L. camara* have been shown to have larvicidal activity against mosquito larvae in their third and fourth in stars of the Ae. aegypti and Cx. quinquefasciatus species. Both extracts had considerable larvicidal action against both mosquito species, however at low concentrations (1 mg/ml), Ae. aegypti extracts were more potent than Cx. quinquefasciatus extracts. [79]

Anti- filarial activity:

It was noted that the crude extract of *L. camara* stem had antifilerial properties. In the mouse model Mastomyscoucha, the extract and its chloroform fraction killed adult Brugiamalayi and sterilized the majority of the remaining female worms.[80]

Anti-inflammatoryactivity:
In albino rats, aqueous extract of *L. camara* was found to have anti-inflammatory properties. In a rat test of carrageenan-induced paw oedema, extract therapy (500mg/kg body weight) considerably reduced the volume of the paws.[81]

Anti fertility activity (Embryo toxicity):
Female albino Wistar rats were used to study the effects of a hydroalcoholic extract of *L. camara* leaves on fertility, overall reproductive performance, and teratology. Without showing any evidence of maternal toxicity, the extract caused embryotoxicity as assessed by post-implantation loss and reduced the prevalence of fetal skeletal abnormalities in dams treated with the extract. [82]

Antiurolithiasis activity:
The leaves of *L. camara* were reported to have antiurolithiasis effect against calcium oxalate urolithiasis caused by ethylene glycol and ammonium chloride in male albino rats. The use of extracts considerably reduced the deposition of calcium and oxalate as well as the excretion of calcium, oxalate, and creatinine from the urine. [83]

Anticancer and antiproliferative activity:
A375 (malignant skin melanoma), Hep2 (epidermoid laryngeal carcinoma), and U937 (lymphoma) are three human cancer cell lines that were used to test the anticancer activity of oleanonic acid, which was derived from *L. camara*. When used against A375 cells, oleanonic acid showed promising cytotoxicity.
According to reports, *S* leaves have a cytotoxic impact on Vero cell line. Using the MTT assay, an in vitro cytotoxicity test was conducted. Cell growth was 2.5 times less inhibited by the methanol extract (500 g/ml) concentration than by Triton 100 1%.

L. camara leaves have been shown to have antiproliferative properties against the lung cancer cell line NCI-H292 and the HEp-2 laryngeal cancer cell line. By using the MTT assay, an in vitro antiproliferative test was conducted. Antiproliferative effect of methanol extract against NCI-H292 cells (% live cells=25.80.19) [83]

Anti mutagenic activity:
L. camera produced 22-acetoxylantic acid and 22-dimethylacryloyloxylantanolic acid that had antimutagenic properties. Swiss mice were used for the micronucleus test to determine the antimutagenicity. When mice were exposed to Mitomycin C-induced mutagenesis, both drugs demonstrated strong antimutagenic efficacy**.** [84]

Antioxidant activity:
In vivo investigations using ethanol extract of *L. camara* revealed considerable antioxidant activity. In the kidneys of urolithic rats, the extract therapy reduced the degree of lipid peroxidation. Nitric oxide free radical scavenging assay and DPPH radical scavenging assay were used for in vitro studies. In both experiments, extract displayed high antioxidant activities.
The 1, 1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging assay and reducing power activity of the leaves of *L. camara* were used to measure their antioxidant activity. The antioxidant effect of leaf extracts was substantial, but younger leaves had stronger antioxidant activity than older or more developed leaves. [85]

Phytochemical constituents [86]**:**
Test for tannins: Five milliliters of water were combined with a pinch of the powdered plant sample. Following a water bath boil, the mixture was filtered. To the filtrate, a few drops of 0.1% ferric chloride were applied. Tannins are present when the color is brownish green or blue-black.

Test for proteins and amino acids (Ninhydrin test): Different solvents were used to extract the plant powder, and the solvent-free plant extract was combined with a little amount of diluted HCl and filtered. The filtrate was mixed with two drops of ninhydrin solution (10 mg of ninhydrin in 200 ml of Acetone). The material was thoroughly blended. Protein and amino acid presence is indicated by the color purple.

Test for flavonoids: 10 ml of ethyl acetate was added to some of the filtrate, boiled in a water bath, and filtered. The filtrate was mixed thoroughly before 1 cc of diluted ammonia solution was added. The presence of flavonoids is indicated by a yellow.

Test for saponins:2-3 ml of distilled water were mixed with a pinch of the dried, powdered herb. The mixture was vigorously shaken. The presence of saponin is shown by the formation of foam.

Test for oils and fats: The extract was pressed between the two filter papers in a tiny amount. The presence of oils and fats is indicated by oil stains on the filter sheets.

Test for phenolic: compounds 50 mg of the test extract were dissolved in 5 ml of distilled water. A few drops of 5% neutral ferric chloride solution were then added to this. Phenolic substances are indicated by a dark green color.

Test for carbohydrates: 5 ml of water were used to dissolve 100 mg of the plant extract, which was then filtered. Benedict's reagent was added to 0.5 cc of the filtrate and cooked over a boiling water bath for 3 minutes. Carbohydrates are indicated by a distinctive color.

Test for alkaloids: 2 gram of the powdered plant sample were combined with 20 ml of distilled water, heated in a water bath, and then filtered. To create a stable, long-lasting froth, 10 ml of this filtrate was combined with 5 ml of Wagner's reagent and vigorously shaken. Alkaloids are present, as evidenced by the reddish-brown precipitate.

Glycosides (Brontrager's Test): For two hours on a water bath, 50 mg of the extract was hydrolyzed with strong HCl. After the hydrolyzed mixture was filtered, 1 ml of the filtrate was combined with 3 ml of chloroform. The mixture was shaken, and the layer of chloroform was removed. The chloroform layer was then mixed with a 10% ammonium solution; the presence of glycosides is shown by the pink color.

Phytosterols: In 2 ml of acetic anhydride, 50 mg of the extract was dissolved. A few drops of strong sulfuric acid were then poured gently along the test tubes' walls. The presence of phytosterols was indicated by a variety of color changes.

Toxicology:

L. camara is one of the top ten or one of the most dangerous plants currently known. There have been reports of *L. camara* toxicity in Australia, India, New Zealand, South Africa, and America. However, toxicity only manifests itself when a significant amount of plant material is consumed. According to reports, *lantadenes* A, B, and D as well as icterogenic acid poisoning can affect sheep, cattle, and goats, but not horses, rats, lambs, or neonatal calves. Photosensitivity and jaundice are two prominent clinical symptoms of poisoning.

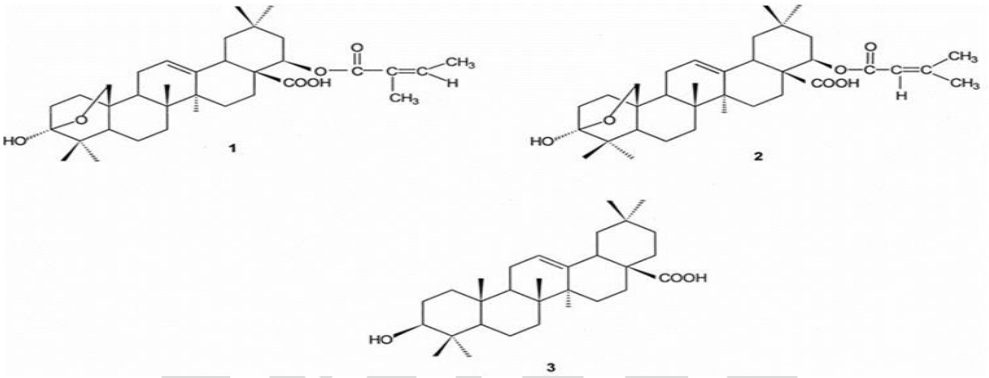
Animals poisoned have loss of appetite and a decrease in appetite within 24 hours. The most seriously poisoned animals pass away after two days of exposure, but in most cases, death happens one to three weeks following exposure. The liver is enlarged, the gall bladder is visibly distended, and the kidneys are bloated and pale in color. For sheep, the hazardous dose of *Lantadene* A administered orally is 60 mg/kg and administered intravenously is 1-3 mg/kg. [87]

Table 05: Phytochemical screening of *Lantana camara leaf* [88]

Phytochemicals *Lantana camara linn*

Phenolic compound	++++
Flavonoids	+++
Alkaloids	+++
Tannins	++
Saponins	++
Phytosterols	++
Carbohydrates	+
Proteins	–
Oil and fats	–
Glycosides	–

Here, + : present, - : not present



1) *Lantanilic acid* (2) *Oleanolicacid* (3) through spectral studies

Table 06: Nutritional profile of *lantana camara linn* leaves

Mineral composition of *lantana camara linn* leaf [89]

Minerals	Composition (ppm)
Phosphorus	0.07±0.0
Calcium	0.54±0.01
Manganese	0.99±0.02
Sulphur	0.73±0.03
Potassium	1.05±0.02
Iron	0.84±0.01
Zinc, Magnesium	0.43±0.03
Copper	0.53±0.01

Values are expressed as Mean ± SEM (n = 3). Nd: not detected

METHODOLOGY

Plant material:

Lantana camara linn. leaves are gathered from areas outside of Vijayapura. Dr. Ramchandra Naik, the head of botany at KCP Science and Arts College in Vijayapura, authenticates the plant. The pods were then ground into powder using a grinder, and the aqueous was extracted from the methanol using a Soxhlet device. The aqueous was then formed into a suspension, and it was stored in a cool, dark location with an airtight glass container.

Drugs and Chemicals: Diclofenac sodium, MTT, DMEM, DMSO, Methanol, Petroleum ether, Carrageenan powder, phosphate buffer Saline (PBS), Trypsin EDTA and other chemicals.

Experimental animals:

A both sex of well healthy Wistar albino rats were used in this research study weighing between 150-200gm. All the rats and mice were taking care as per the CPCSEA guidelines. These animals were housed in polypropylene cages under standard laboratory conditions (35 to 40% relative humidity, temperature: 24±2°C, 12/12 hr. light/dark cycle) in animal experiment lab. All these animals were fed with standard diet and purified water ad *libitium.* The study protocol was approved by institutional animal ethical committee for the motive of control and supervision of animals (CPCSEA, New Delhi).

Determination of acute toxicity:

According to the rules established by the Organization for Economic Cooperation and Development (OECD), the acute oral toxicity study will be conducted. By using the fixed dosage approach described in OECD Guideline No. 423, the acute toxicity will be evaluated in Swiss/Albino mice. Mice used in the investigation were Swiss albino mice. This investigation demonstrated that the extracts were not harmful even when given at the maximum beginning dose of 2000 mg/kg of animal body weight [90].

Figure 15: Soxhlet apparatus

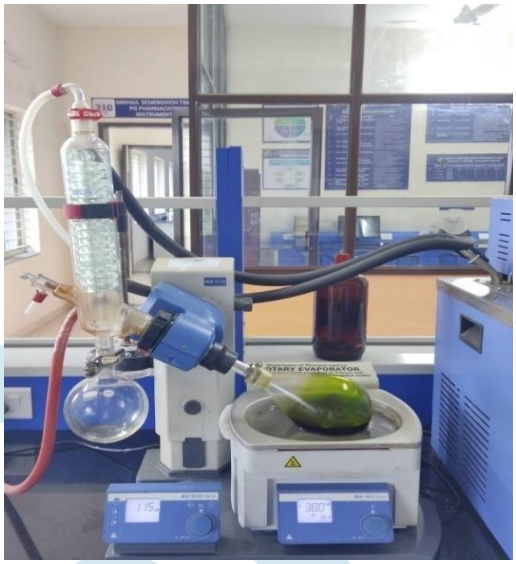


Figure 16 Evaporation method

Fig: 17 Methanolic Extract

Extraction of Plant Materials:

The aerial part of plant leaves will be washed thoroughly with distilled water. The leaves will shade dried for five days, The dried leaves of *lantana camara linn* will be finely grinded using electrical grinder and stored in air tight container for further use.

One kilogram of the powdered leaves will be extracted by petroleum ether (5 L) for 4 hrs by using Soxhlet extractor to remove the essential oils and fatty materials. The extraction will repeated with methanol in the Soxhlet extractor until further extraction will be given a colorless solution. The methanol extract will be separated, and the residues assumed to contain alkaloids, then exhaustively extracted with Methanol by Soxhlet the extract will be concentrated to dryness using a rotary evaporator [122].

TABLE: 7 Phytochemical Results of Methanolic Extract of *Lantana Camara .Linn*

SL.NO	TEST	METHANOLIC EXTRACT OF *LANTANA CAMARA .LINN*

1.	**Carbohydrates** a) Mollish's Test b) Benedict's test	 +ve +ve
2.	**Alkaloids** a) Mayer's test b) Dragendorff's test c) Hager's test d) Wagner's test	 +ve +ve +ve +ve
3.	**Cardiac glycosides** a) Keller - Killani test b) Lugols test	 +ve +ve
4.	**Proteins** a) Biuret test b) Million's test c) Xanthoproteic test d) Precipitation test	 -ve -ve -ve -ve
5.	**Flavonoids** a) Shinoda test b) Lead acetate test c)Ferric Chloride test d)Zinc Hydrochloride acid Reduction test	 +ve +ve +ve +ve
6.	**Steroids** a) Liberman Burched reaction b) Salkowskis test	 +ve +ve
7.	**Tannins** a) Neutral ferric chloride Test b) Gelatin solution test	 +ve +ve
8.	**Saponins** a) Foam test b) Haemolysis test	 -ve -ve
9.	**Triterpenes** a) Salkowski test b) Liberman Burchard test	 -ve -ve

Hear , + is present - is not present

Anti-Inflammatory Activity:

Carrageenan induced rat Paw Oedema:

Five sets of thirty albino Wistar rats of each sex were created. Group 1 serves as the control group and receives standard saline. Diclofenac sodium (5 mg/kg) is given to Group 2 as a normal dose. Group 3 has received carrageenan. Groups 4 and 5 received the methanolic lower dose and higher dose extracts, respectively. Which was used as an inducer 0.1 ml of 1% carrageenan solution was injected under the skin of all animals right hind paws an hour after the administration (per the experimental protocol). The volume of the paw was measured using a mercury plethysmometer at 1,2,3,4,5 and after 24 hours following the carrageenan therapy in order to evaluate the anti-inflammatory activity. [91]

Group I- Normal control
Group II- Standard (Diclofenac sodium 10mg/kg)
Group III- Control (0.1ml of 1% Carrageenan sol)
Group IV- Lower dose (Carrageenan + treated with 250mg/kg/b.w./p.o.*Lantana camara linn methanolic* extract)
Group V- Higher dose (Carrageenan + treated with 500mg/kg/b.w./p.o.*Lantana camara linn methanolic* extract)

Cell viability assay

HCT -29 colon cancer cells were grown in DMEM containing 10% FBS media in T-20 flask to ~ 80% confluence. The cells were treated with Trypsin EDTA. The separated cells were counted and plated in 96 well plates, and were treated with different concentrations of extract along with the vehicle/DMSO control for about 24 h., the media was removed and wash the cells with phosphate buffer Saline (PBS). MTT solution at 0.5 mg/ml was added to each well and the plate was incubated at 37 °C for 4 h in the dark following which the MTT solution was replaced with 200 µl of DMSO.The plate was shaken at 180 rpm for 10 min and the optical density was measured at 570 nm by using a plate reader (Tecan) . The experiment was repeated for two times before the data was calculated to plot a graph.

RESULTS

Effect of methanol extract of *Lantana Camara L* on carrageenan induced paw edema in rat.

Methanolic extract of *lantana camara linn* (250 and 500 mg/kg) treated groups are shown in table 8.in comparison with normal control group, carrageenan caused a significant (after applying student's t- test) increase in paw oedema level. The results were compatible with previous literature. Treatment with methanolic extract o *lantana camara linn* (250,500 mg/kg) significantly (P<0.001) reduced the level of paw oedema after 1 to 5 hrs and 24 hrs of carrageenan injection.

Sl.no	Group	After 1hrs	After 2 hrs	After 3hrs	After 4 hrs	After 5 hrs	After 24 hrs
1.	Normal control	1.15±0.013	1.15±0.013	1.15±0.013	1.15±0.013	1.15±0.013	1.15±0.013
2.	Disease Control	2.28±0.0088$	2.27±0.0113$	2.25±0.0117$	2.23±0.0084$	2.20±0.061$	1.93±0.0076$
3.	Standard 10 mg/kg	1.92±0.0049*	1.82±0.0062*	1.75±0.0067	1.65±0.0073**	1.52±0.0056	1.24±0.0061***
4.	MELCL 250 mg/kg	2.19±0.0056	2.11±0.009	1.94±0.014*	1.86±0.0103**	1.78±0.0076**	1.62±0.021**
5.	MELCL 500 mg/kg	2.17±0.057	1.93±0.0049*	1.87±0.0067*	1.73±0.0037**	1.63±0.0067**	1.34±0.0081***

TABLE: 8 Effect of leaf of *lantana camara linn* on carrageenan induced paw oedema after 15 and 24 Hrs.

The value represented as Mean ± SEM, n=6. *P<0.001 by using One-way ANOVA followed by bartlett's test and $P<0.05 as per Student's t-test.
(ns= non-significant)

EFFECT OF CARRAGEENAN INDUCED RAT PAW OEDEMA AFTER 5 HRS AND 24 Hrs RESPECTIVELY

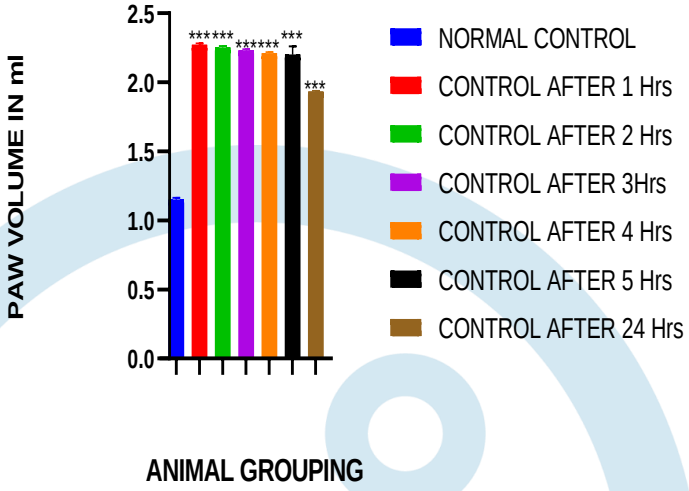


Figure: 18

EFFECT OF DICLOFENAC SODIUM AFTER 1 TO 5 AND 24 Hrs RESPECTIVELY

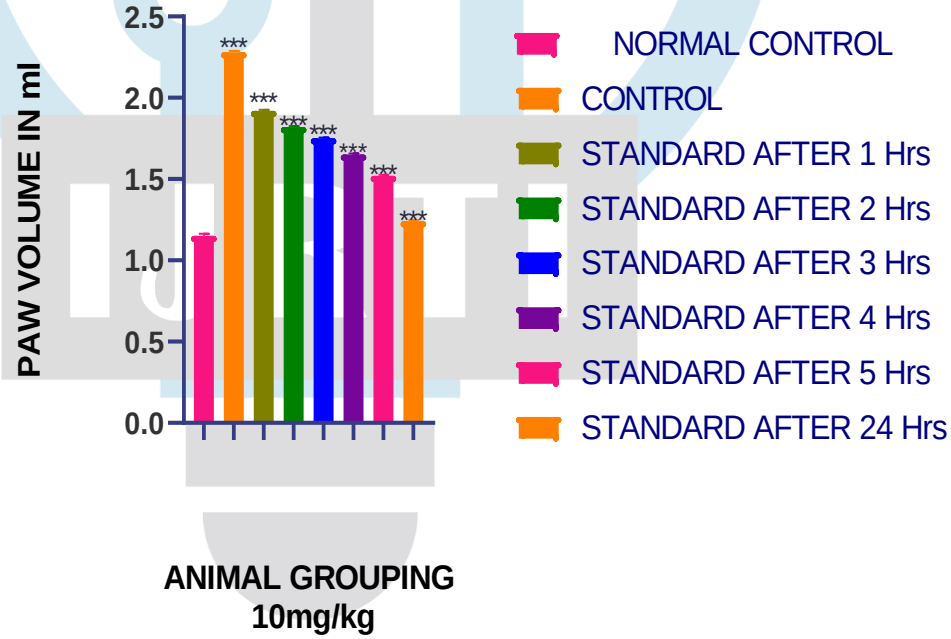


Figure: 19

EFFECT OF LOWER DOSE OF MELCL AFTER 1 TO 5 AND 24 Hrs RESPECTIVELY

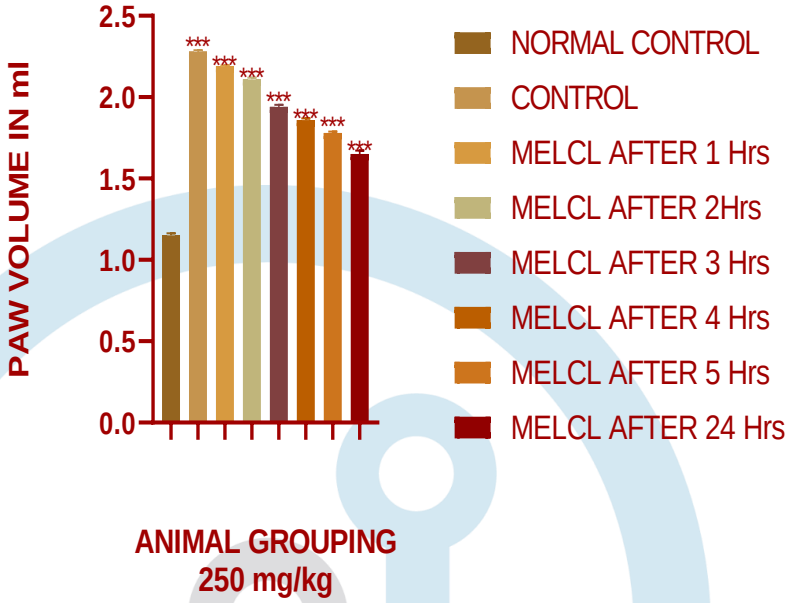


Figure:20

EFFECT OF HIGH DOSE OF MELCL AFTER 1 TO 5 AND 24 Hrs RESPECTIVELY

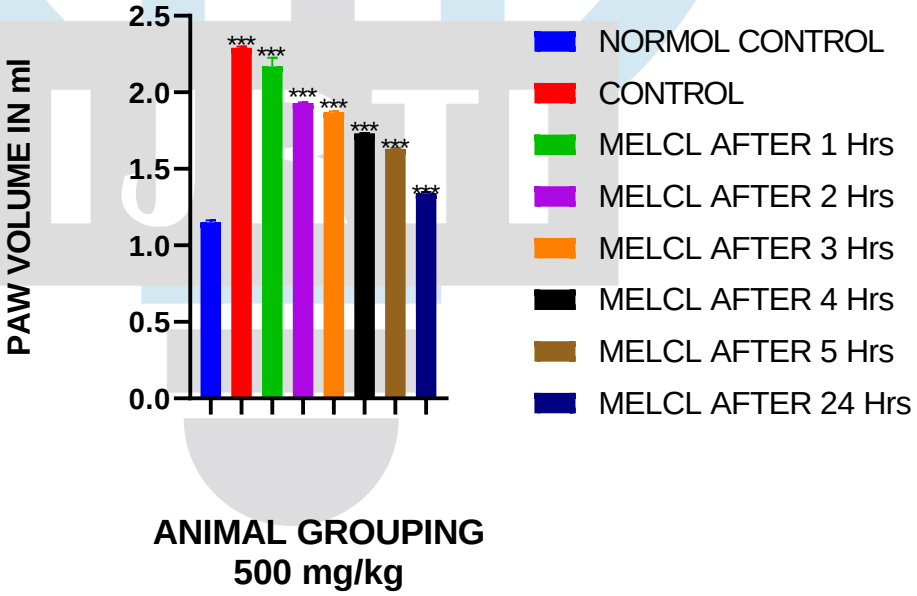


Figure:21

Effect of methanol extract of *Lantana Camara L* in MTT Asaay:

Cell Viability Assay:
MTT assay was conducted to assess the anticancer effects of the **Methanolic extract of *lantana camara . linn*** at different concentrations on HCT 29 cell lines. As observed byMTT assay and depicted in Figure below. The **extract** decreased the HCT 29, cell viability in a concentration-dependent way. The IC_{50} of the extract is **80µg/ml.**

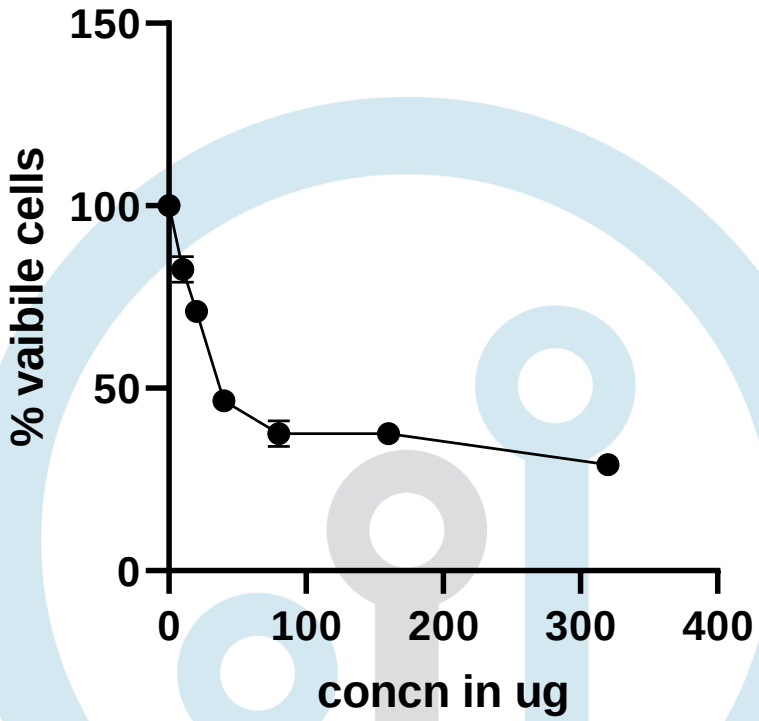


Figure: 22 IC $_{50}$ Value of MELCL

DISCUSSION

Lantana camara L, a member of the *Verbenaceae* family and a notable producer of essential oils, was given its name by Linnaeus in 1753.
Seven species make up the majority of it, with six reported from America and one from Ethiopia. Although it is native to South America, some of the taxes may be found in approximately 50 other nations. In certain of those nations, it can also be grown. It is utilised as a common ornamental plant in gardens and is also referred to as red sage. *L. camara* thrives at high elevations of up to 2000 m in tropical, subtropical, and temperate climates. The plant has a woody stem with flowers in a variety of hues, including red, white, and pink. It also includes spines or prickles. There are 650 cultivars in the genus, however most of them are connected to the *L.camara* complex.

- It is also considered as a noxious weed globally . Moreover, it is stated that the ash of *L.camara* contains manganese and potassium, which are useful for coconut trees . Few reports consider it as a poisonous plant for humans as well as animals . Traditionally, *L. camara*has been used as a medication to treat various diseases such as cancer, tumors, tetanus, cuts, eczema, measles, chickenpox, fevers, rheumatism, and asthma .*L.camara* possesses therapeutic potential because of various bioactive components, including steroids.[67]

- The outcoms acquired from the phytochemical examination on methanolic extract of *lantana camara linn* leaf executed the presence of carbohydrates, proteins and alkaloids, phenols, flavonoids, glycosides and saponins and oils and fats

Cancer is main reason for death in world. Cancer is disease in which some of the body's cells grow uncontrollably and spread to other part of the body. cancer can start almost anywhere in the human body, which is made up of trillions of cells. The longer life expectancies, changing lifestyles, and more rural-to-urban migration are all contributing to rising cancer rates in India, despite the fact that they are still lower than in Western countries. In India, the incidence of esophagus and oral cancers is among the highest. On the other hand, colorectal, prostate, and lung cancer rates are among the lowest. The most prevalent area for cancer in humans, skin cancer makes about 55% of all

cancers. The second most prevalent type of skin cancer is squamous cell carcinoma, and it is spreading swiftly around the globe. 16% of incidences of skin cancer are caused by it. [4]

- **Colo-rectal cancer (CCR)**: Colorectal cancer develops from certain polyps or growths in the inner lining of your colon, colon cancer that is not treated may spread to other area of your body, lead to cause severe harm and death. This CCR is second most cause for death in humans around worldwide. Poor eating habits, smoking, intestinal inflammatory illness, gastric factors all increase the risk of acquiring this cancer. 90% of those who are given a colorectal cancer diagnosis are older than 50, with a median age of 64; nevertheless, the illness is more aggressive in those who are given a diagnosis earlier in life. A number of tests, including the guaiac test, immunochemical stool test, DNA stool test, sigmoidoscopy, colonoscopy, and barium enema, can be used to identify colorectal cancer. [9]

Inflammation is when a wound swells up, turns red and hurts , it may be a sign of inflammation. Inflammation is the body's immune system's response to an irritant. the irritant might be a germ, but it could also be a foreign object. Pathogens, toxic mechanical and chemical agents, autoimmune reactions, and other stimuli can all cause inflammation, which is a complicated, tightly controlled series of events. Red-rashes on skin, swelling, heat, and pain are visible signs and symptoms of the succeeding chain of events. The vascularized connective tissue experiences an inflammatory reaction, which includes some components like plasma, blood vessels, circulating cells, cellular and extracellular cells. This results in increased leukocyte recruitment, improved vascular permeability, increased microvascular diameter, along with the release of inflammatory mediators**.** [1]

Body's principal mechanism for repairing tissue damage and defending itself from stressors is inflammation. In the physiological condition, the controlled response clears injured tissue and guards against additional injury. In pathologic circumstances, inflammation cause loss of tissue or worsen organ function. [2]

Methanolic extract of *lantana camara linn* (250 and 500 mg/kg) treated groups. In comparison with normal control group, carrageenan caused a significant (after applying student's t- test) increase in paw oedema level. The results were compatible with previous literature. Treatment with methanolic extract of *lantana camara linn* (250,500 mg/kg) significantly ($P<0.001$) reduced the level of paw oedema after 1 to 5 hrs and 24 hrs of carrageenan injection.

MTT assay was conducted to assess the anticancer effects of the **Methanolic extract of *lantana camara linn*** at different concentrations on **HCT 29** cell lines. As observed by MTT assay, The **extract** decreased the HCT 29, cell viability in a concentration-dependent way. The **IC_{50}** of the extract is **80µg/ml.**

CONCLUSION

According to the results of the present findings it can be concluded that extracts of *lanana camara linn* leaf significantly lower paw volume levels in carrageenan induced paw oedema experimental wister rats and MTT assay was conducted to assess the anticancer effects at different concentrations on HCT 29 cell lines. As observed by MTT assay, The **extract** decreased the HCT 29.

SUMMARY

Inflammation is when a wound swells up, turns red and hurts , it may be a sign of inflammation. Inflammation is the body's immune system's response to an irritant. the irritant might be a germ, but it could also be a foreign object. Pathogens, toxic mechanical and chemical agents, autoimmune reactions, and other stimuli can all cause inflammation. If inflammation not treated

increases the risk of swelling, severe abdominal pain, chest pain, fatigue, fever (tuberculosis), joint pain, mouth sore and chronic inflammation is involved in the disease process of many conditions like cancer, asthma , alzheimer's disease, heart disease, rheumatoid arthritis, type II- diabetes.

Cancer is disease in which some of the body's cells grow uncontrollably and spread to other part of the body. cancer can start almost anywhere in the human body, which is made up of trillions of cells,

Colorectal cancer develops from certain polyps or growths in the inner lining of your colon, colon cancer that is not treated may spread to other area of your body, lead to cause severe harm and death.

In order to screen natural or synthesized medication, carageenan has been extensively to induce acute oedema (inflammation) in experimental animal.

Lantana camara linn belongs to the family *verbenaceae* is one of the ost widely used ass the herbal plants. The leaf of *lantana camara linn* were collected from outside the city of vijayapura, Karnataka , India .The leaf of *lantana camara linn* crushed ,powder were extracted and stored in closed in air-tight container .

Carageenan induced rat paw oedema model were used in the current study to screen for inflammation activity. *Lantana camara linn* leaf were extract at concentration of 250 mg/kg , 500 mg/kg . in the Carageenan induced rat paw oedema model, level of paw volume were taken after 1to 5 hrs and 24 hrs in Digital plethysmometer . At a dose of 500 mg/kg , the leaf of *lantana camara linn* have shown significant effects.

The result have been shown that leaf of *lantana camara linn* have anti-cancer and anti-inflammation action. To isolate and identify that exact active constituents , additional research must be conducted.
MTT assay was conducted to assess the anticancer effects of the Methanolic extract of *lantana camara linn* at different concentrations on HCT 29 cell lines. As observed byMTT assay, The extract decreased the HCT 29, cell viability in a concentration-dependent way.

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