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A Review study on mechanisms of anti-inflammatory action of various Drugs and Ayurvedic formulations (Anti-inflammatory medications)

Review Article

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Abstract

Inflammation is primarily a defensive and healing mechanism, to save the human body when challenged with trauma, infection, autoimmune, toxic and ischemic injuries. While chronic inflammation needs to be controlled almost in all pathological conditions like diabetes, cardio-vascular conditions, autoimmune diseases and carcinomas; most of the time even acute inflammation needs a control to certain extent like to control pain, swelling and fever for comfort and health. While a number of medications are available for same and newer formulations are still under work, various ayurvedic drugs are also well known to possess a significant anti-inflammatory effect with better adverse effect profile at times. Since there is a compulsion to move our efforts from curative to preventive aspects of healthcare, like the need of a diet with anti-inflammatory properties, it always is beneficial to understand how various plants and plant products possesses anti-inflammatory properties. An attempt is made to compile the mechanisms of action of various medicines and anti-inflammatory ayurvedic formulations, to give an overview of how all products come in the ambit of same group of biochemical interactions and pharmacological affects. This also emphasises, why is it essential for every new formulation and conventionally used plant products to undergo studies to know exactly how it ensues its affects, herein anti-inflammatory actions. This also underlines how such knowledge helps to hypothesize newer mechanisms of action and novel drugs which may act by same or similar mechanisms of actions. This also provides the guidelines for approaches to develop newer medicines.

Keywords: Anti-inflammatory drugs, Properties, Ayurveda, Painkillers, Anti-pyretics.

Introduction

On the road of "Survival of the fittest" our body has developed a robust system of protection offered by specialized cellular and humoral components. This system helps us to fight various diseases and other microbial attacks. Inflammation results from activation of the immune system in response to a number of stimuli. It is an essential part of body's healing system. There are five cardinal signs of inflammation are heat (calor), pain (dolor), redness (rubor), swelling (tumor) and loss of function (function laesa) (1).

Innate immunity has capacity to produce general responses to any antigen while adaptive immunity mounts specific responses to a particular antigen. Depending on onset and duration of pathophysiological process inflammation can be divided into Acute and chronic forms. In acute inflammation innate immunity forms the first line of defense while a specific or adaptive immunity follows, while in chronic inflammation the adaptive immune responses cause excessive and continuous activation of innate immunity. Although inflammation is a protective phenomenon, most of the time it is prudent to curb it for relief of symptoms and management of diseases. Like to control pain in a wound, or fever in an infection, or swelling in blindness due to retinal swelling relieves the signs and symptoms of diseases. In certain diseases there is indirect involvement of inflammation in pathophysiology like – Coronary artery diseases, Diabetes mellitus and Alzheimer's disease. While other diseases we find a direct involvement like – Rheumatoid arthritis, Ulcerative colitis, Crohn's disease and fibromyalgia. This brings a frequent need for control of inflammation with medicines. Both modern medicine and Ayurveda has been using anti-inflammatory properties of various formulations. Here is an attempt to enlist these medicines and to draw parallels between mechanisms by which these medicines act.

Aims & Objectives

The aim of this review is to explore and compare the mechanisms of anti-inflammatory action of various modern drugs and Ayurvedic formulations.

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The objectives include analysing the mechanisms of action of commonly used drugs such as NSAIDs, corticosteroids, and biologics, alongside key Ayurvedic herbs like Ashwagandha, Turmeric, Guggul, and Boswellia. The study seeks to evaluate the efficacy, safety profiles, and side effects of both systems, identifying commonalities and differences in the inflammatory pathways they target. Additionally, it aims to explore the potential for integrative approaches that combine modern and Ayurvedic treatments to enhance therapeutic outcomes and minimize adverse effects. Lastly, it will highlight gaps in current research on Ayurvedic formulations and suggest future directions for study.

Anti-Inflammatory properties

Inflammation – It is a body's response to injury or infection to restore healing. There are two types – Acute and chronic.

Mechanism of action of anti-inflammatory drugs (2)

Antihistaminics

Histamine is an autacoid which is one of the important mediators of hypersensitive reactions. It is released from mast cells following antigen-antibody reaction on its surface involving IgE type reaginic antibodies. It causes immediate type of Hypersensitivity reaction causing urticaria, angioedema, broncho-constriction and anaphylactic shock. Four types of receptors have now been clearly delineated. H_1 antagonists can control these manifestations to considerable extent except asthma and anaphylactic fall of blood pressure wherein leukotrienes (LTC4, LTD4) and Platelet activating factors are more important. In inflammation histamine mediates vasodilatation, promotes adhesion of leukocytes to vascular endothelium through adhesion molecule P-selectin on endothelial cell surface, sequestrating leukocytes at the inflammatory site and regulates microcirculation. It has a role in tissue growth and repair as well. Few of the examples are – Diphenhydramine, chlorpheniramine, hydroxyzine, fexofenadine, levocetrizine and azelastine.

Eicosanoids (prostaglandins and leukotrienes) and Platelet activating factors

Eicosanoids are major lipid derived autocoids released from cell membrane phospholipids.

Drugs acting through inhibition of COX pathway – NSAIDS

Inhibits synthesis of COX products by reversible and competitive inhibition of COX. Most NSAIDS are non -selective COX-1 and COX-2 inhibitors, while some are selective COX-2 inhibitors like celecoxib and etoricoxib.

Other anti-inflammatory actions of NSAIDS –

- Inhibition of Adhesion molecules (ELAM-1, ICAM-1), Selectins and Integrins.
- Generation of free radicals and superoxide.
- Affecting Growth factors like GM-CFS, IL-6, Lymphocyte transformation factors and TNFα.
- Stabilising of lysosomal membrane of leukocytes and
- Antagonism of actions of kinins.

Aspirin (anti-inflammatory dosage – 3-5 gm / day): Acetylates COX at serine residue and causes irreversible inhibition.

Glucocorticosteroids: Inhibits release of arachidonic acid from membrane lipids, by enhancing production of proteins called annexins which inhibits phospholipase A_2.

Prostanoid receptors agonists and antagonists

Prostaglandins, Thromboxane and Prostacyclin receptors are physiologically categorised into –

- Excitatory or Contractile – EP, FP and TP.
- Inhibitory or Relaxant – DP_1, EP_2, EP_4 and IP
  - Enprostil – Selective EP antagonist.
  - Fuprostenol – Selective FP antagonist.
  - Cicaprost – Selective IP agonist.
  - Leukotriene receptors – Cysteinyl LT_1 and LT_2
  - Montelucast and Zafirlukast – Cysteinyl LT_1 receptor antagonists.
  - Platelet activating factor antagonist – Ginkogolide B (from a Chinese plant).

Disease modifying Anti-rheumatic Drug (DMARDs)

- Methotrexate – Inhibition of cytokine, chemotaxis and cell mediated immune response.
- Azathioprine – Suppresses inflammation, T-cells and Natural killer cells.
- Sulfasalazine (5-amino salicylic acid) – May suppress superoxide radicals and cytokines produced by inflammatory cells.
- Hydroxychloroquine / chloroquine – proposed mechanisms are reducing monocyte IL-1, consequently inhibiting B lymphocytes, interference with antigen processing, stabilizing lysosomes and free radical scavenging.
- Leflunomide – Inhibits proliferation of stimulated lymphocytes.
- Tofacitinib – Inhibits inflammatory mediators and release of cytokines.

Cytokines and Interleukins

Cytokines are proteins in nature and they are produced in response to pathogens and other antigens. It regulates and mediate inflammatory and immune responses.

Interleukin is a type of cytokine, which plays a critical role in immunological process homeostasis and classification; it was discovered initially from leukocytes, later other cells like macrophages and lymphocytic cells were found generating it.

Interleukin helps in transmitting information, activating and regulating immune cells especially proliferation and differentiation of T cells and B cells. Interleukin-1 contains IL-1α and IL-1β. While the former is produced by diverse cells, some specific tissues have the latter one.

While the IL-1 receptor antagonist can inhibit the destruction of IL-1 through the competition of its receptor. IL-1 also affects the nitric oxides, adhesion molecules, cytokines and chemokines that destroy the cartilage.

IL-2 is vital for the immunotherapy of several diseases, including cancers.

Interleukin-10 is an anti-inflammatory responsive cytokine. By antagonist action on the receptor of IL-10, we can resolve the chronic viral infection.

Interleukin-18 is a regulator of autoimmune diseases and cancer' it also has a role in acute inflammation.

Biological agents

TNFα inhibitors: Inhibits TNFα mediated activation of membrane bound activation of macrophages and T-cells.

TNFα inhibitors, such as Etanercept, Infliximab, and Adalimumab, block TNFα-mediated activation of macrophages and T-cells. Etanercept is a recombinant fusion protein combining the TNF receptor with the Fc portion of IgG, inhibiting TNFα function. Infliximab is a chimeric monoclonal antibody that binds to and neutralizes TNFα, while Adalimumab is a fully human recombinant monoclonal anti-TNF antibody. Anakinra, another key biologic, is a recombinant human IL-1 receptor antagonist that inhibits the activity of interleukin-1, further reducing inflammation.

Drugs used in Gout

- Colchicine – Binds to fibrillar protein tubulin and hence inhibits granulocyte migration into the inflamed joint.
- Probenecid and Pebloticase – Promotes excretion of uric acid.
- Allopurinol and Febuxostat – Are Uric acid synthesis inhibitor.

Materials and Methods of the Study

This review examines the mechanisms of anti-inflammatory action in pharmaceutical drugs and Ayurvedic formulations. Data were collected from scientific databases (PubMed, Scopus), Ayurvedic texts, and relevant clinical studies. Pharmaceutical drugs like NSAIDs and corticosteroids were compared with Ayurvedic formulations such as *Boswellia serrata* and *Curcuma longa* based on their ability to target inflammation pathways (e.g., COX-2 inhibition, cytokine modulation).

Method of Selection of the Particular Drugs

The selection of drugs for this review was guided by several key factors. Priority was given to those with strong scientific evidence supporting their anti-inflammatory mechanisms. Ayurvedic formulations were chosen based on their traditional use in treating inflammation, as referenced in classical texts. Additionally, emphasis was placed on drugs known to target specific inflammatory pathways, including the regulation of prostaglandins, immune modulation, and cytokine activity. Drugs and formulations with abundant clinical data and research availability were prioritized to ensure a comprehensive and evidence-based review.

Limitations of the Search

The search faced several limitations. There is a lack of modern clinical studies on Ayurvedic formulations, and the variability in research designs made comparisons challenging. Many Ayurvedic studies had smaller sample sizes and less rigorous controls, increasing the risk of bias. Language barriers, with texts in Sanskrit or regional languages, restricted access to complete data. Additionally, the absence of long-term safety and efficacy studies on Ayurvedic formulations limits the strength of conclusions regarding their prolonged use.

Observation & Results

Mechanism of actions for various Ayurvedic formulations

Ayurvedic formulations which works through inhibition of Cyclo-oxygenase pathway

- *Adenanthera pavonina* L. (Fabaceae)– Ethanolic leaf extracts from *Adenanthera pavonina* L. (Fabaceae) were administered in dosage of 250 and induced paw inflammation, and cotton pallet granuloma (3,4,5). It was found to produce significant anti-inflammatory activity. The probable mechanism of anti-inflammatory action may be due to its influence on the cyclooxygenase pathway. It has also shown to delay castor oil induced diarrhea in rats which could be due to inhibition of prostaglandin synthesis.
- *Saraca asoca (Roxb.) De Wilde (Fabaceae)*– two procyanidin dimers found to have inhibitory effects on prostaglandin H2 synthatase. (6)
- *Abies pindrow (Royle) Royle ex Carrière (Pinaceae)* – Has shown anti-inflammatory affects in rats, by down regulation of cyclooxygenase-2by its active component – Pinitol (3-O-methyle-chiroinositol). (7)
- *Strychnos nux-vomica L. (Loganiaceae)*– Brucine and brucine N-oxide were found to have anti-inflammatory effects through suppression of Prostaglandin E2 release. (8)
- *Commiphora wightii (Arnott) Bhandari (Burseraceae)*– A plant sterol derived from the gum resin (guggulu) suppresses COX-2, MMP-9, and iNOS expression for its anti-inflammatory action. (9)
- *Acacia catechu (L.f.) Willd. (Fabaceae)*– A mixed extract Flavocoxid (baicalin and catechin) inhibits COX-2, 5-LOX and inducible nitric oxide synthase. (10)
- *Alpinia galanga (L.) Willd. (Zingiberaceae)*– Extract can inhibit COX-2, TNFα, IL-1β, MIP-α and NF-κB. (11)
- *Curcuma longa L. (Zingiberaceae)*– it suppresses COX-2 promoter activity induced by TNF. (12,13)
- *Piper longum L. (Piperaceae)*– Inhibits Prostaglandin and leukotrienes COX-1 inhibitory effects. (14,15)
- *Pterocarpus marsupium Roxb. (Fabaceae)*– extract is reported to selectively inhibit COX-2. (16)
- *Withania somnifera (L.) Dun. (Solanaceae)*– Withanolide sulfoxide inhibits COX-2 expression. (17)
- *Vernonia cinerea (L.) Less. (Asteraceae)*– Downregulates mediators like COX-2, iNOS, TNFα, IL-1β and IL-6. (18)

Ayurvedic formulations which works through inhibition of Lipoxygenase pathway

- *Boswellia serrata Roxb. (Burseraceae)*– It inhibits 5-Lipooxygenase (LOX)and hence suppresses leukotriene biosynthesis. (19)
- *Tamarindus indica L. (Fabaceae)*- Flavonoids' ability to inhibit 5-lipoxygenase enzyme plays a key role in the suppression of leukotriene biosynthesis and hence reducing the body inflammatory reactions. (20)
- *Cinnamomum camphora (L.) J.Presl (Lauraceae)*– Anti-inflammatory mechanisms blocked the production of IL-1, IL-6, TNFα, NO and PGE2. (21)
- *Nyctanthes arbor-tristis L. (Oleaceae)* – Oral intake of leaf and fruit extracts reduces expression of IL-1β, IL-6 AND TNF-α. Has a potential anti-inflammatory action by inhibiting histamine and serotonin induced edema. (22)

Ayurvedic formulations which works through inhibition of NF-κB mediated activation of inducible Nitric oxide synthase pathway

- *Indigofera tinctoria L. (Fabaceae)*– It exhibits its anti-inflammatory activity through suppression of transcription factor NF-κB. (23)
- *Acorus calamus L. (Acoraceae)*– anti-inflammatory affects might be mediated though suppression of NF-κB and interferon regulatory factor 3. (24)
- *Embelia ribes Burm.f. (Myrsinaceae)*– Embelin inhibited both inducible and constitutive NF-κB activation. (25)
- *Aloe vera (L.) Burm.f. (Asphodelaceae)*– Its active component Emodin suppresses the activation of NF-κB in human umbilical vein endothelial cells. (26)
- *Berberis aristata DC. (Berberidaceae)*– It acts against experimental herpetic uveitis by inhibiting activation of NF-κB. (27)
- *Andrographis paniculata (Burm.f.) Wall. ex Nees (Acanthaceae)*– Exibits anti-inflammatory action by inhibition of suppression of NF-κB, TNF-α, IL-6, MIP-2, iNOS and COX-2. (28)
- *Foeniculum vulgare Mill. (Apiaceae)*– Anethole is the main constituent which suppresses TNF induced NF-κB activation through inhibition of IκBα phosphorylation and degradation. (29)

Ayurvedic formulations which are known to have shown anti-inflammatory affects in Carrageenin induced rat paw edema, Freund's complete adjuvant or Cotton pallet granuloma

- *Cedrus deodara (Roxb. ex D.Don) G.Don (Pinaceae)* - Anti-inflammatory and anti-arthritic activity has been proven with various studies. The stem bark of *Cedrus deodara* was air dried and aqueous extract was made. In carrageenan induced inflammation utilizing the technique of Winter et al 1962. Cedrus deodara extracts were compared with the anti-inflammatory drug - betamethasone. Although anti-inflammatory activity was established but found to be less effective than standard. (30)
- *Achyranthes aspera L. (Amaranthaceae)* – Extract shows anti-inflammatory effects in rat paw edema. (31)
- *Argyreia speciosa (L.f.) Sweet (Convolvulaceae)* – the ethanolic extract has strong action to inhibit paw edema and against Freund's complete adjuvant. (31)
- *Uraria lagopoides (L.) DC. (Fabaceae)*– Aqueous extract of aerial parts showed anti-inflammatory effects in rat paw edema. (32)
- *Quercus infectoria G.Olivier (Fagaceae*) – oral intake of extract inhibits – carrageenan, histamine, serotonin and prostaglandin induced rat paw edema and PMA induced ear inflammation. (33)
- *Gaultheria yunnanensis (Franch.) Rehder & E.H.Wilson (Ericaceae)* – Found effective against Freund's complete adjuvant and rat's paw edema. (34)
- *Bambusa arundinacea (Retz.) Willd. (Poaceae)* – the methanol extract has shown prominent reduction in carrageenin induced rat paw edema. (35)
- *Carum copticum (L.) Benth. & Hook.f. (Apiaceae*)– total alchoholic extract and total aquous extract of seeds of Carum copticum had found to reduce carrageenan induced edema and cotton pallet induced granuloma. (36)
- *Mentha piperita L. (Lamiaceae)*– showed anti-inflammatory action against Xylene induced ear edema and cotton pallet granuloma. (37)
- *Stereospermum suaveolens (Roxb.) DC. (Bignoniaceae*)– The ethanol extract exibits anti-inflammatory action in carrageenan, dextran and histamin induced rat paw edema. (38)
- *Azadirachta indica A.Juss. (Meliaceae)* - Anti-inflammatory affect was found in cotton pallet granuloma assay in rats. Many biochemical parameters like DNA, RNA, lipid peroxide, acid phosphatase and alkaline phosphatase were found to be lowered in cotton pallet exudates. Though the efficacy was not comparable to dexamethasone. (39)
- *Hemidesmus indicus (L.) R.Br. (Apocynaceae*)– Ethyl extract of roots of Hemidesmus indicus has shown to have significant anti-inflammatory activity in inflammation induced by carageenin, bradykinin, S-hydroxy tryptamine, employing granuloma pouch and cotton pallet implantation method in rats. It was not found as active as phenyl butazone or beta-methasone against granuloma pouch and cotton pallet implantation. It was ineffective in dextran induced inflammation. (40)

Ayurvedic formulations which have anti-inflammatory actions through other pathways

- *Abrus precatorius L. (Fabaceae*)– Abruquinones, the isoflavanquinones isolated form roots suppresses anti-inflammatory actions through suppressing release of mediaters from mast cells and inhibition of vascular permeability increase. (41)
- *Adhatoda vasica Nees (Acanthaceae*) – An alkaloid, Ambroxol inhibits IgE depended basophil mediated release. (42)
- *Cassia occidentalis L. (Fabaceae*) – It reduces the availability of arachidonic acid, precursor of prostaglandin biosynthesis, and stabilization of lysosomal membrane. (43)

- *Allium sativum L. (Amaryllidaceae)*– it inhibits inflammation by cell mediated T-helper-1 and inflammatory cytokines (TNF – α, IL-1 α, IL-6, IL-8, T-cell IFN- γ and IL-2). (44) The water-soluble allyl sulfur containing compound, inhibits pro-inflammatory cytokine induced adhesion of monocyte to endothelial cells by inhibiting the MAPK signaling and related ICAM-1 expression. (45)

Limitations of the study

- This review might have missed relevant studies due to search strategy limitations of restricted databases.
- If some studies lacked rigor e.g., small sample sizes and bias, this will adversely influence final conclusions of review.
- If due to publication bias the review may primarily include studies with positive outcomes, possibly skewing the overall findings.
- The studies in the review are highly heterogeneous limiting ability to draw generalised conclusions.
- The review does not include a meta-analysis, hence its ability to quantitatively assess the overall effect size across studies is limited.

Discussion

Inflammation first came to picture during first century in Rome by Cornelius Celsus, later it was linked with diseases by Rudolf Virchow. Once pathophysiology of inflammation is substantially recognised, formulations can be tried to antagonise the pro-inflammatory substrates, catalysts and receptors. Most ayurvedic formulations seems to be acting through very similar mechanisms as modern drugs. Cyclo-oxygenase pathway, interleukin suppression and free radical control are invariably suggested. But there are sufficient clues for the scope of discovering newer mechanisms by which inflammation can be controlled, like the transcription factor, Nuclear Factor-kappa B that controls over 500 different gene products is now known as major mediator of inflammation. Various Ayurvedic plants used for long time to treat several chronic diseases may serve as the source for various novel anti-inflammatory agents by the method of reverse pharmacology. Studying plant products for the treatment of human diseases can indeed guide us to develop new drugs, and this approach has several benefits and scientific underpinnings. Many traditional medicines, such as those from Ayurvedic, Chinese, and Native American medicinal practices, have relied on plant products. For example, aspirin was derived from willow bark, and quinine, used to treat malaria, comes from the bark of the cinchona tree. A significant number of modern drugs are derived from plants. Examples include paclitaxel (Taxol) from the Pacific yew tree, used in cancer treatment, and digoxin from foxglove plants, used to treat heart conditions. While developing anti-inflammatory drugs plant products can guide us in a systematic manner.

1. Bioactive Compounds: Discovery: Plants produce a wide array of bioactive compounds as part of their defence mechanisms against pests and diseases. These compounds can have pharmacological effects on humans. Researchers can isolate and identify these compounds for their potential therapeutic effects. Once a bioactive compound is identified, it can serve as a lead compound. This is a starting point for drug development, where the structure of the compound can be optimized for better efficacy, safety, and pharmacokinetic properties.
2. Novel Mechanisms of Action: Plant-derived compounds can work through unique mechanisms that may not be targeted by existing drugs. By studying these mechanisms, researchers can develop drugs that act on new targets, which can be particularly valuable in treating diseases that are resistant to current therapies.
3. Diversity of Chemical Structures: Plants produce a vast array of chemical structures that are not found in synthetic chemical libraries. This structural diversity can lead to the discovery of new drug classes. Nature's vast chemical diversity offers a reservoir of novel scaffolds that synthetic chemistry may not easily replicate.
4. Synergistic Effects: Some plant extracts contain multiple compounds that work synergistically to produce a therapeutic effect. Understanding these synergies can help in designing combination therapies or multi-target drugs.
5. Ecosystem and Ethnobotanical Knowledge: Ethnobotanical studies, which explore how different cultures use plants for medicinal purposes, can provide valuable clues about which plants to study. Indigenous knowledge often points to plants with significant therapeutic potential.

Developing anti-inflammatory drugs from plant products involves a series of systematic steps, from initial identification and extraction of bioactive compounds to clinical testing and regulatory approval. Here is a detailed outline of the process:

1. Identification of Plant Sources:

Ethnobotanical Research: Literature Review - Study ethnobotanical and traditional medicine literature to identify plants used for anti-inflammatory purposes. Field Studies should be done with Collaboration with ethnobotanists and indigenous communities to gather information on plants with reputed anti-inflammatory effects.

2. Collection and Preparation

Plant Material Collection: Source Verification is done to ensure accurate botanical identification and classification of plant species. Sustainable Harvesting is done by collecting plant material sustainably to avoid ecological damage. Preparation is done by drying and storage. Extraction is done by the use of solvents like water, ethanol, or methanol to extract bioactive compounds. Techniques like maceration, percolation, and Soxhlet extraction can be employed.

3. Screening for Anti-Inflammatory Activity

In Vitro Screening: Assays is done with the use of cell-based assays to test extracts for anti-inflammatory activity. Common assays include - Enzyme Inhibition Assays which assess inhibition of enzymes like COX-1, COX-2, and LOX. Also the cytokine assays which measure the inhibition of pro-inflammatory cytokines like TNF-α, IL-1β, and IL-6. This is followed by bioactivity-Guided Fractionation. Fractionation does separate the extract into different fractions using chromatographic techniques (e.g., HPLC, TLC). Fractions are followed by test each fraction for anti-inflammatory activity to identify the most active components.

4. Isolation and Characterisation of Active Compounds

Isolation – Purification is done using techniques such as column chromatography, preparative HPLC, and crystallisation to isolate pure compounds. Characterisation is then done using structural analysis which does determine the chemical structure of isolated compounds using spectroscopic methods like NMR (Nuclear Magnetic Resonance) Spectroscopy, Mass Spectrometry (MS), Infrared (IR) Spectroscopy and X-ray Crystallography.

5. In Vivo Testing

Is done in Animal Models - Inflammation Models which uses animal models to evaluate the anti-inflammatory efficacy of isolated compounds. Common models include - Carrageenan-Induced Paw Edema in Rats/Mice, Collagen-Induced Arthritis in Mice, Ear Edema Models etc.

6. Pharmacokinetics and Toxicity is studied next -

- Pharmacokinetics: Study the absorption, distribution, metabolism, and excretion (ADME) of the compounds.
- Toxicity: Conduct acute and chronic toxicity studies to determine safe dosage ranges.

7. Optimization of Lead Compounds

Structure-Activity Relationship (SAR) - Modify the chemical structure of lead compounds to enhance their anti-inflammatory activity, reduce toxicity, and improve pharmacokinetic properties. This is followed by process to synthesize analogs of the lead compound and test for improved efficacy and safety.

8. Preclinical Development

Drug Formulation is developed (e.g., tablets, capsules, injectables) that ensures stability and bioavailability. Good Laboratory Practice (GLP) Studies are conducted for comprehensive preclinical studies in compliance with GLP to gather detailed safety and efficacy data.

9. Clinical Trials

- Phase I Trials are done for Safety and Dosage - Test the drug in a small group of healthy volunteers to assess safety, tolerability, and pharmacokinetics.
- Phase II Trials is to be done for efficacy and side effects by testing the drug in a larger group of patients with inflammatory conditions to evaluate efficacy and monitor side effects.
- Phase III Trials: Large-Scale Testing is conducted by large-scale studies in diverse patient populations to confirm efficacy, monitor adverse reactions, and collect data for regulatory approval.

10. Regulatory Approval

- Regulatory Submission: Prepare and submit a New Drug Application (NDA) or similar dossier to regulatory authorities (e.g., FDA, EMA) including all preclinical and clinical data.
- Regulatory Review: Respond to any queries or additional information requests from the regulatory authorities.
- Approval: Obtain approval to market the drug.

11. Post-Market Surveillance

Pharmacovigilance: Continuously monitor the drug's safety and efficacy in the general population and report any adverse effects to regulatory bodies.

Further Research ongoing studies for conducting further studies to explore additional therapeutic uses, long-term effects, and potential for drug combinations.

Conclusion

Thus, the mechanisms of anti-inflammatory action of various modern drugs and Ayurvedic formulations is explored and compared.

By following these detailed steps, researchers can systematically develop new anti-inflammatory drugs from plant products, ensuring efficacy, safety, and compliance with regulatory standards. This methodical approach maximises the potential for discovering effective new treatments derived from natural sources. Studying plant products is a valuable approach to drug discovery because it leverages the natural chemical diversity and biological activities evolved over millions of years. This approach can lead to the development of novel drugs with unique mechanisms of action, potentially providing new treatments for a wide range of diseases.

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