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Tannins, Terpenoids, And Alkaloids: A Review of Their Pharmacognostic Importance in Anti-Inflammatory Therapy

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ABSTRACT

The significant followings of secondary metabolites plant-derived products are tannins, terpenoids, and alkaloids, which have significant pharmacognostic value in the treatment of anti-inflammation. Preclinical studies on animal models demonstrate that tannins, by means of their inhibitory effect on COX and LOX enzymes and their ability to scavenge reactive oxygen species, reduce edema, oxidative stress, and swelling of joints, whereas terpenoids (oleanolic and ursolic acid), by regulating the immune response and alleviating pro-inflammatory cytokine responses and anti-inflammatory effects on tissues, can be described as antioxidants. Alkaloids (such as berberine and colchicine) also work through distinct mechanisms of action, namely via inhibition of NF-KB, suppression of iNOS, and modulation of immune cell infiltration to yield therapeutic effects to specific gastrointestinal and joint inflammation. Taken together; these compounds can shed light on a variety of, but complementary mechanisms, which can provide safe and sustainable alternatives to traditional anti-inflammatory medicines. Although their potential remains encouraging, shortcomings including inefficient bioavailability, unstandardized extraction, and limited chronic model studies as well as their poorly studied translational potential, continue to represent a major obstacle. By filling these gaps with standardized approaches, pharmacokinetic/toxicological profiling, and designing synergistic formulations, the enhancement of their therapeutic value may be possible and allow their introduction in veterinary and biomedical practice.

Key Words:

Tannins, Terpenoids, Alkaloids, Pharmacognosy, Anti-inflammatory therapy, Animal models, Cytokine modulation, Bioavailability.

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1. INTRODUCTION

Animal models are of importance in pharmacognostic studies, since they give a confirmed and regulated background on which studies on efficacy, safety and mechanism of action with regard to the natural compounds are done[1]. Replicating certain characteristics of pathology, e.g., inflammation, animal-based research allows the researcher to evaluate the interaction of plant-derived bioactive molecules with physiological mechanisms. These types of investigations are important as they narrow the divide between traditional knowledge and biomedical confirmation, presenting evidence-based and clinically applicable insights into how therapies should be applied.

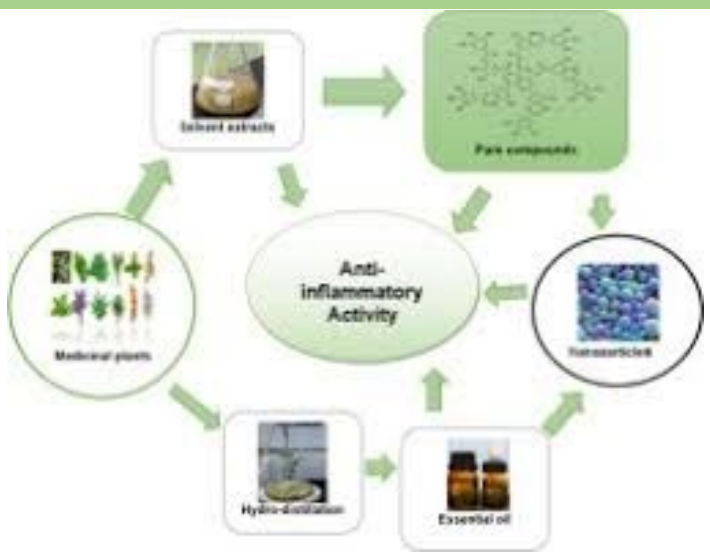

Figure 1: Pharmacognostic Importance of Tannins, Terpenoids, and Alkaloids in Anti-Inflammatory Therapy[2]

Animal-based experimental research has grown in use in the last 10 years to test plant metabolites that have anti-inflammatory property. These models offer the opportunity of measuring pharmacological responses, toxicity profile and mechanisms of action which are vital in attaining scientific credibility. They can also be used as the basis of a translational research to set the groundwork on future clinical studies on veterinary and human medicine studies[3].

1.1 Background and Context

Defence Properly termed as an inflammatory process, it is a critical physiological process that is activated when there is tissue injury or infection or when tissue or body processes are subjected to an aberrant metabolism. Although it facilitates protection and maintenance of homeostasis, chronic or long-lasting inflammation promotes numerous pathological changes in animals such as negating the onset of arthritis, dermatitis, colitis, and other immune-mediated disorders. Traditional anti-inflammatory drugs, like corticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDs) are still used but their chronic application is usually stilted by the side effects and slowing efficacy as well as the fear of resistance. This has fuelled an increase in scientific interest in natural alternatives, especially secondary metabolites derived by plants. Of them, tannins, terpenoids, and alkaloids have caused a lot of attention, being studied because of diverse pharmacological action and a well-established application in traditional veterinary medicine[4].

1.2 Objectives of the Review

The objective of this review is:

- To evaluate the anti-inflammatory mechanisms of tannins, terpenoids, and alkaloids in animal-based models, focusing on their enzymatic, cytokine, and signaling pathway modulation.
- To compare the pharmacognostic strengths and limitations of tannins, terpenoids, and alkaloids in relation to bioavailability, therapeutic potential, and safety concerns.

- To assess the methodological approaches employed in experimental studies, including inflammation models, biochemical assays, and extract preparation techniques.
- To identify research gaps in standardization, chronic model evaluation, and translational applicability of plant-derived secondary metabolites.
- To propose future pharmacognostic perspectives for integrating tannins, terpenoids, and alkaloids into veterinary and biomedical anti-inflammatory therapies.

1.3 Importance of the Topic

There is great potential in exploring plant derived bioactive chemicals as anti-inflammatory tools lending into the development of safer and more sustainable anti-inflammatories than conventional medications. To ensure their traditional knowledge is valid, as well as to inform the future clinical development, it is important to understand their pharmacological properties in animal models. This review provides a comparative emphasis on the role of tannins, terpenoids, and alkaloids in the modulation of inflammation and their value as possible candidates of new anti-inflammatory treatment modalities in veterinary and biomedical practice[5].

2. EXPERIMENTAL INSIGHTS INTO THE ANTI-INFLAMMATORY POTENTIAL OF TANNINS, TERPENOIDS, AND ALKALOIDS

In preclinical studies the strong anti-inflammatory properties of tannins, terpenoids and alkaloids are associated with inhibiting enzymes and cytokines, as well as antioxidant activity, with some tannins, terpenoids and alkaloids inhibiting edema, others modulating immune signaling and others like alkaloids such as berberine protecting gastrointestinal tissue[6]. Animal inflammation models, biochemical assay, and solvent based extract preparation are normally used to assess therapeutic to determine therapeutic outcomes during research. They have the strengths of reproducibility and mechanistic knowledge but weaknesses of no standardized dosages, few studies investigating chronic inflammation, an insufficient number of comparative studies, and difficulties in translating their findings to clinical use[7].

2.1 Review of Key Research Studies

- **Tannins:** A number of preclinical studies exhibited the anti-inflammatory capacities of tannins mainly against experimental rat paw edema models. As an example, very high tannin contents of extracts used in Terminalia chebula resulted in a substantial decrease in carrageenan-induced paw swelling. This is explained by the blockage of various salient inflammation mediators notably the cyclooxygenase (COX) and the lipoxygenase (LOX) enzymatic pathways, which have been mentioned to be the core activity of the production of the prostaglandins and leukotrienes. That is indicative that tannins do not only eliminate acute inflammation but can play a role in regulating the presence of arachidonic acid cascade[8].
- **Terpenoids:** Terpenoids particularly oleanolic acid have been extensively researched using murine models of inflammation. Evidence demonstrates significant declines in the pro-inflammatory cytokines (TNF- alpha and IL-6) after the use of terpenoids. These immunomodulatory effects point to their capability of regressing inflammatory signaling and stabilizes immune actions. In addition, the terpenoids have also been linked to the

presence of antioxidants that indirectly prevent oxidative damage to the tissues that very frequently come about as a result of chronic inflammatory conditions.

- **Alkaloids:** Berberine in particular, has been widely studied as a protective agent to the gastrointestinal tract. Berberine has been demonstrated to inhibit excessive production of nitric oxide by inducible nitric oxide synthase (iNOS), at least in rat colitis models. It also achieved significant inhibition of NF-KB signal, a master regulator of inflammation and inflammatory cells amassed within mucosa were lesser and the mucosal healing got promoted. These observations explained the therapeutic potentials of alkaloids in the control of the occurrence of inflammation-related gastrointestinal disease[9].

2.2 Methodologies Employed

Secondary metabolites plant research has used diverse animal-based experimental models to initiate and measure inflammation. Carrageenan- or formalin-induced inflammation models have been traditionally used to induce an acute and subacute inflammatory response, and chronic inflammation has been mimicked with cotton pellet granuloma or acetic acid-induced colitis models. These various models give detailed understanding of a short-term inflammatory process and a long-term inflammatory process[10].

There have been biochemical, molecular and histological methods of evaluation of therapeutic outcomes. IL- 1 B, TNF a and IL 6 are the pro inflammatory cytokines routinely measured by ELISA assay and MDA, SOD and antioxidants are the markers of redox homeostasis. Biochemical results can be reinforced by histopathological studies of affected tissue that show structural results of decreased cellular infiltration, edema, and tissue destruction.

Common solvent extraction methods applied during extraction preparation generally include ethanol, methanol, and aqueous solution, and the bioactive parts should be isolated. Such extracts are screened preliminarily via phytochemical screening to establish the presence of tannins, terpenoids and alkaloids after which they are subjected to dose-dependent studies. This type of systematic approach guarantees reliability and contributes to the isolation of active principles that have a therapeutic value[11].

2.3 Strengths and Weaknesses

- **Strengths:** Experimental designs are controlled and well-established animal models give a high level of reproducibility and reliability. The models have permitted the clear mechanistic insights of molecular and biochemical host-pathogen interactions especially cytokine signaling, oxidative host responses and enzymatic pathways. In addition, dose-response studies are made possible which augments the knowledge on therapeutic windows as well as potency[12].
- **Weaknesses:** These strengths notwithstanding, there are a number of weaknesses that also exist. Lack of standardised dosage and extraction methodologies is another key issue of concern, since it is hard to make comparisons on individual research. Moreover, majority of studies have been conducted by investigating acute models of inflammation and comparatively less studies in chronic or systemic inflammation are carried out which are more clinically relevant. There is also absence of comparative studies conducted on direct comparison of tannins, terpenoids and alkaloids under comparable experiment conditions

to allow identification of the most effective type of molecules. Lastly is the translation of animal models to human clinical trials which has not learned to the full yet, thus begs the question of efficacy, safety and pharmacokinetics in practical practice[13].

3. PHARMACOGNOSTIC ROLES OF TANNINS, TERPENOIDS, AND ALKALOIDS IN ANTI-INFLAMMATORY THERAPY

Other important plant-based metabolites, which have demonstrated significant anti-inflammatory activity, are tannins, terpenoids, and alkaloids, and their associated mechanisms of action vary markedly (including enzyme inhibition, COX, LOX, modulation of signaling pathways, MAPK, NF-BD, JAK/STAT, antioxidant activity, and cytokine suppression)[14]. Tannins also decrease joint swelling, oxidative stress, terpenoids improve edema, granuloma, and inflammatory pain also provide antioxidant protection and alkaloids such as berberine and colchicine modulate immune response and restrict inflammatory cell migration. All of them show considerable pharmacognostic use in the treatment of acute and chronic inflammation in human and veterinary situations[15].

3.1 Tannins in Anti-inflammatory Therapy

Tannins constitute a varied assortment of compounds (polyphenolic compounds) that have strong anti-inflammatory characteristics. Protein binding, pro-inflammatory enzyme inhibition, and reactive oxygen species scavenging are the major mechanisms of therapeutic efficacy of these compounds[16]. Condensed tannins are administered in a swollen joint of the arthritis rat model, which results in significant reduction in joint swelling, decrease and ameliorate cartilage destruction as well as reducing oxidative stress through curbing signs of lipid peroxidation. Tannins also suppress the synthesis of prostaglandin and leukotriene through the inhibition of cyclooxygenase (COX) and lipoxygenase (LOX). They also consist of astringents, which increases tissue shrinkage and alleviates the ability of vasculature to leak, which will help to curtail edema and inflammation[17]. The use of tannins has also been found useful in giving mucosal defense as well as wound healing effects on veterinary applications, and in relation to this aspect, their pharmacological significance continues to increase in inflammatory diseases.

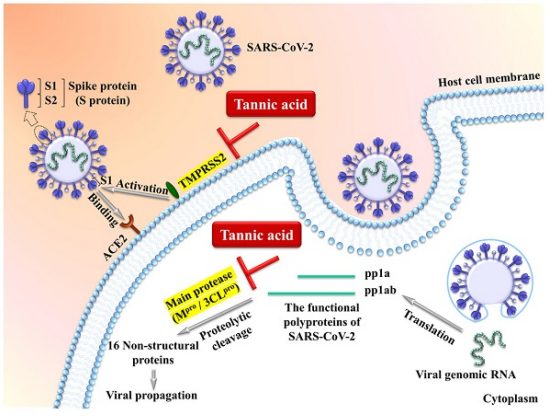

Figure 2: Mechanism of Tannic Acid Inhibition of SARS-CoV-2 Infection[18]

3.2 Terpenoids in Anti-inflammatory Therapy

It contains terpenes such as ursolic acid, oleanolic acid and limonene which have broad anti-inflammatory results through the regulation of several intracellular signaling mechanisms. These

substances have been found to inhibit the pro-inflammatory cytokines through inhibition of the mitogen-activated protein kinase (MAPK) and nuclear factor kappa B (NF-κB) by decreasing expression of IL-1- b, IL-6, and TNF-a. Murine studies performed in the preclinical setting have shown terpenoids to be effective in reducing acute inflammation or edema (reducing alveolar edema through the inhibition of influx) and in inhibiting chronic inflammation or granuloma formation[19]. Terpenoids cure inflammatory analgesia as well since they can help in modulation of nociceptive signaling and also lower cyclooxygenase-2 (COX-2) expression. In addition to this, they have a two-fold benefit of being antioxidants in nature and therefore reduce the ROS mediated destruction caused to cells that is oftentimes a correlate of chronic inflammation. In combination, these pharmacognostic traits emphasize terpenoids as an effective therapy amid acute-level and chronic inflammation.

3.3 Alkaloids in Anti-inflammatory Therapy

Alkaloids form a structurally varied group of structurally related nitrogen-containing compounds with well recognized anti-inflammatory properties. Their activity is based on neurotransmitter regulation, anti-inflammatory action at the level of pro-inflammatory cytokines, and blocking of intracellular signaling cascades (NF-κB and JAK/STAT)[20]. An example is berberine, which has proven to have GI protective effects via the inhibition of inducible nitric oxide synthase (iNOS) and a reduction in oxidative stress in colitis-based models. Colchicine as conventionally employed in the treatment of gout slows down the infiltration of neutrophils and the polymerization of microtubules therefore constraining the movement and activation of the inflammatory cells. Besides their analgesic effects, morphine derivatives have the indirect anti-inflammatory effects of their immune modulation responsibilities on the function of immune cells and decreasing the liberation of cytokines. The colchicine prevented the recruitment of inflammatory cells and has been confirmed by experimental evidence in rat models of peritonitis, which supports the mechanistic usefulness. All in all, the representative alkaloids are an essential type of therapy, and the combination of analgesic, immunomodulatory, and anti-inflammatory therapeutic activity functions in different pathological conditions[21].

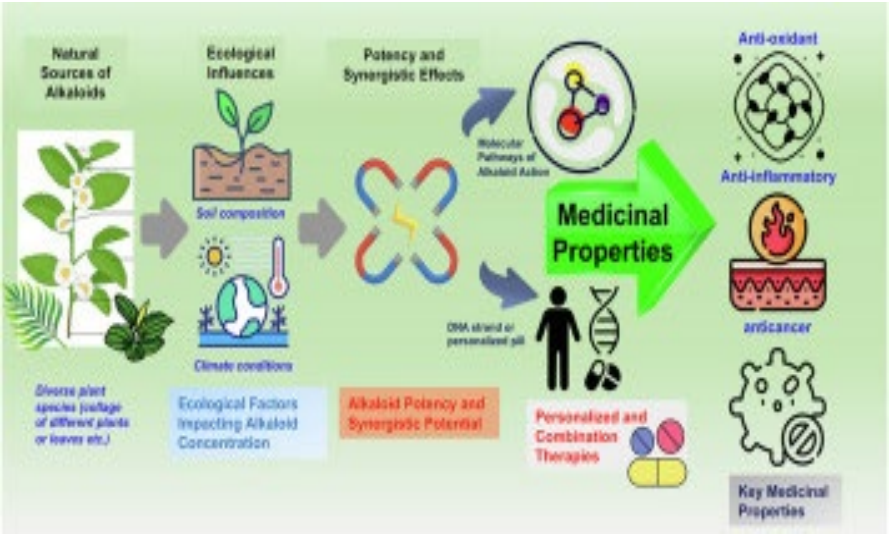

Figure 3: Alkaloids Unveiled[22]

4. COMPARATIVE PHARMACOGNOSTIC EVALUATION OF TANNINS, TERPENOIDS, AND ALKALOIDS

A comparative pharmacognostic comparison can give valuable observation that tannin, terpenoids and alkaloids vary in their actions and therapeutic advantages and draw capsules as well as the means by which they may overcome each other in a way that complements to make anti-inflammatory treatment[23].

- **Tannins:** Tannins are mostly known to have antioxidant properties, to possess enzyme-inhibitory activity. Scavenge reactive oxygen species (ROS) and inhibit cyclooxygenase (COX) and lipoxygenase (LOX) pathway, thus efficient in reducing oxidative stress and prevent the formation of inflammatory mediators including prostaglandins and leukotrienes. They also have astringent effects which promote healing in tissues and lowers vascular permeability. Nonetheless, they have a major shortcoming which is low bioavailability because tannins tend to interact with dietary proteins and minerals to inhibit their absorption in the systemic circulation. This limits their usefulness in systemic inflammatory diseases but they are nonetheless of utility in localized / gastrointestinal inflammation[24].
- **Terpenoids:** Terpenoids produce wide-range immunomodulatory effects, mostly through modulation of signaling pathways including MAPK and NF-o, which leads to down-regulation of pro-inflammatory cytokines such as TNF- o, IL- 1- o, and IL- 6. They are efficacious in the acute and chronic inflammatory models, minimizing edema, granuloma production and inflammatory pain. These anti-oxidant benefits offer them a second advantage through hindering the damage of tissue caused by ROS. Terpenoids also tend to present improved pharmacokinetic profiles, unlike tannins, although other problems like low solubility and lack of stability remain common. They are flexible, appealing targets of multi-target anti-inflammatory therapy.
- **Alkaloids:** Alkaloids, by contrast, tend to work at very specific molecular targets, as inhibitor of NF- B, regulator of nitric oxide synthase (iNOS), or disruptor of neurotransmitter pathways. Such chemicals as berberine exhibit a great deal of gastrointestinal protecting effects, colchicine has the effect of decreasing neutrophil infiltration and morphine derivatives have similar analgesic and anti-inflammatory effects. Their specific mechanisms render them as potent therapeutic agents of targeted inflammatory situations. Nevertheless, there is also donation of higher toxicity risks with escalated doses of alkaloids, i.e., risk of gastrointestinal upset or systemic toxicity, and, therefore, close control of the dose is essential[25].

Comparatively, tannins stand out in terms of anti-oxidant and broad-based/general enzyme-inhibitory properties, terpenoids are pre-eminent in effecting cytokine regulatory mechanisms and suppression of systemic inflammation, whereas alkaloids offer target-specific, potent activity actions of safety concern. Collectively, such differences hint that each of these classes targets different elements of inflammation rather than competing with each other, and the pharmacognostic complementarity of these differences can be used to justify a combination

therapy or new formulation that maximizes their synergistic impacts and reduces the drawbacks of each one individually[26].

Table 1: Summary of Key Literature on Phytochemicals and Medicinal Plant Applications[27]

Author(s)	Study	Focus Area	Methodology	Key Finding
Obode et al. (2020)[28]	A systematic review of medicinal plants used in Nigeria for hypertension management	Traditional medicinal plants for hypertension	Systematic literature review	Flavonoids, alkaloids, and saponins contributed to vasodilation, antioxidant effects, and renal modulation, supporting hypertension management
Patel et al. (2023)[29]	Phytochemical, pharmacognosy and ethnobotanical importance of Ficus virens Aiton	Phytochemical and ethnobotanical properties of Ficus virens	Phytochemical and pharmacognostic analysis	Contained phenolics, flavonoids, and tannins; validated traditional medicinal uses and suggested modern therapeutic applications
Raju, A. (2022)[30]	Pharmacognostic and phytochemical analysis of selected medicinal plants used in Ayurveda for arthritis	Anti-inflammatory and analgesic potential of Ayurvedic plants	Pharmacognostic and phytochemical analysis	Terpenoids, alkaloids, and glycosides provided anti-inflammatory and analgesic effects, supporting Ayurvedic arthritis treatments
Rex et al. (2018)[31]	Phytochemicals as a potential source for antimicrobial, antioxidant and wound healing – a review	Pharmacological activities of phytochemicals	Literature review of secondary metabolites	Flavonoids, saponins, and tannins exhibited antimicrobial, antioxidant, and wound-healing properties, supporting natural therapeutic development

5. DISCUSSION

The review shows that tannins, terpenoids, and alkaloids have divergent but overlapping anti-inflammatory pathways-such as enzyme inhibition, antioxidative, cytokine inhibitory and specific signaling regulation-that makes them potential pharmacognostic tools[32]. Tannins have their strength in local protection, terpenoids in systemic immunomodulation, and alkaloids in efficacy of precise therapy, but with problems of toxicity. gaps exist which include a shortage of chronic models, standardization and poorly developed comparative studies though which limit general application. Future investigations are encouraged to focus on standardization procedures, pharmacokinetic/ toxicity studies as well as safe integrative synergistic formulas that allow gradual introduction of such health practices into clinical and veterinary practice[33].

5.1 Interpretation and Analysis of Findings

Evidence reviewed shows clearly that, both tannins, terpenoids, and alkaloids have important anti-inflammatory effects, albeit by various mechanisms. Tannins can mainly inhibit COX and LOX

enzymes, have a potent antioxidant property, relieve oxidative stress and edema in animal models[34]. Terpenoids, however, have a wider range of immunomodulatory activity, inhibited pro-inflammatory cytokines, and modulated signaling cascades, including MAPK and NF-kB. Alkaloids have a more focused mechanism of action, inhibiting NF-κB, modulating nitric oxide synthase and neurotransmission, leading to efficacious but very specific anti-inflammatory actions. Taken altogether, these results support the pharmacognostic significance of the secondary metabolites as multi-dimensional therapeutic agents[35].

5.2 Implications and Significance

The fact that these compounds have such pharmacological diversity is far reaching in terms of anti-inflammatory treatment. Tannins, which have great antioxidant and anti mucosal properties, find application in gastro-intestinal and localized inflammations. Terpenoids with their systemic immunomodulatory actions, therefore, stand out as broad-spectrum agents that can be used in acute and chronic inflammatory diseases[36]. Alkaloids offer specific therapeutic effect, particularly in gastrointestinal and joint-related inflammation, yet their toxicity potential warrants care in making use of them. These variations indicate that metabolite classes complement each other and are best thought of as addressing and filling different therapeutic niches that together would offer a more comprehensive or holistic approach to managing inflammation. This indicates their aptitude to be applied in veterinary practice and the subsequent veterinary phytopharmaceutical development[37].

5.3 Gaps in Current Research

Nevertheless, even after great improvement, a number of research gaps are still obvious. First, models of acute inflammation, including carrageenan-induced edema, dominate most experimental studies with relatively fewer chronic and systemic models[38]. This imposes restrictions on learning of long-term therapeutic effectiveness and safety. Second, extraction methods are not always standardized, dose regimens are hardly ever standardized and the characterization of phytochemicals lacks consistency and it is hard to compare the findings of one study to another. Third, there is a lack of comparative studies that assess tannins, terpenoids, and alkaloids directly and in comparable assays, so no strong inferences can be made about their comparative efficacy. Finally, there is low translation of preclinical animal models to clinical practice and the lack of studies examining pharmacokinetics, bioavailability, or toxicity in practice[39].

5.4 Future Research Directions

Chronic and system theories of inflammation are encouraged as topics of future research that may more closely align with clinic practice in veterinary and human populations. To advance reproducibility and provide recommendations regarding pharmacological reliability, it will be necessary to standardize extraction procedures, identification of bioactive shoot fractions, and optimitize dose. Comparative experiment designs are highly advisable with direct measurement of efficacy across tannins, terpenoids, and alkaloids in similar conditions that could determine the most promising combined therapeutic candidates. Also, Loth et al. (2011) will incorporate elements of pharmacokinetic and toxicological studies into translating their findings into clinical

practice safely. Lastly, investigation of synergetic formulations or combination therapies that utilize the complementary mechanisms of these compounds might result in new multi-targeted and anti-inflammatory therapy that might be effective and have fewer adverse effects[40].

6. CONCLUSION

Three important plant-source secondary metabolites used in pharmacognostic anti-inflammatory treatment are tannins, terpenoids, and alkaloids, each with their own unique and synergistic contributions to therapeutics. Experimental studies on animals have shown that tannins possess powerful oxidative and enzyme-inhibitory activity, but are hampered by lack of bioavailability; terpenoids produce a broad range of immune-modulatory interactions and have desirable systemic efficacy, although they are insoluble and unstable; and alkaloids exert striking and specific effects on molecular targets including NF-kB and inducible nitric oxide synthase and boast promising therapeutic potential, but at high doses carry the risk of toxicity. Taken together, these results indicate their possible use in a safer and more sustainable alternative or co-adjuvant to the conventional anti-inflammatory agents. Nonetheless, there are research gaps in chronic model validation, the standardization of methods, and translational feasibility. The directions that should be enhanced in future should be on integrative pharmacognostic systems, synergistic themed formulations and thorough pharmacokinetics and toxicological evaluations to completely tap the therapeutic potentials of tannins, terpenoids, and alkaloids in veterinary and biomedical applications.

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