RESEARCH PAPER

Unlocking Nature's Anti-Inflammatory Arsenal: An Extensive Overview of Bioactive Compounds in *Coccinia Grandis* and their Therapeutic Potential

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ABSTRACT
Inflammation is a key underlying factor in numerous chronic diseases, and the search for safe, effective anti-inflammatory agents from natural sources is ongoing. Coccinia grandis, a medicinal plant widely used in traditional medicine, has shown promising anti-inflammatory potential in preclinical studies. Various extracts from its leaves, stems, and whole plant, particularly methanolic and aqueous preparations, have demonstrated significant inhibition of chemically and physically induced inflammation in animal models. Phytochemical investigations suggest that flavonoids, phenolics, and other bioactive compounds contribute to these effects through modulation of pro-inflammatory mediators and antioxidant mechanisms. This review comprehensively summarizes the current evidence on the anti-inflammatory activity of Coccinia grandis, highlighting its therapeutic potential and highlighting the necessity for additional mechanistic investigations and clinical evaluations to develop plant-based anti-inflammatory interventions.
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1. INTRODUCTION

1.1 Global Burden of Inflammatory Diseases and Limitations of Current Therapies

Inflammation is a simple and complex biological response, the immediate defence of the body in reaction to detrimental stimuli like pathogens, injured cells, or irritants. Although acute inflammation is helpful for healing and defence, its dysregulation or prolongation serves as the foundation of the pathogenesis of a vast array of debilitating human diseases. Chronic inflammation is increasingly recognized as a mover and shaker behind diseases as diverse as autoimmune conditions including rheumatoid arthritis and inflammatory bowel disease to metabolic syndromes, neurodegenerative disorders, and even certain cancers. This global participation of inflammation in modern pathology underscores the demand for efficient and safe therapeutic interventions. However, while most conventional anti-inflammatory drugs, although highly efficacious, have formidable side effects and are best used in a very short-term therapeutic regimen, this has generated a renewed world-wide interest in seeking natural product-derived alternatives.[1-2]

Even with major advances in therapeutic modalities, like the introduction of biologics, a large percentage of patien are still found to have poor responses or suffer from profound, debilitating side effects. Traditional anti-inflammatory medications, like Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), often face limitations. These consist of low bioavailability, lack of specificity, slow onset of therapy, and a significant tendency for systemic toxicities. Such specific issues related to the usage of NSAIDs include intestinal haemorrhage, hematologic, and nephrotoxicity, as well as increased cardiovascular event risks. Moreover, their application necessitates caution among susceptible individuals, such as elderly patients, and for use during the third trimester of pregnancy. The continued difficulties in safely and effectively managing chronic inflammatory conditions further highlight the critical unmet medical need. This urgent need for both alternative or complementary therapies with proven efficacy as well as a safer profile accounts for much of the motivation for investigating new therapeutic entities, particularly those of botanical or natural origin. The inherent complexity of chronic inflammation, characterized by intricate networks of mediators and pathways, often renders single-target

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pharmaceutical interventions insufficient. The limitations observed with conventional drugs, which frequently aim for high specificity to a singular molecular target, highlight this challenge. This situation suggests that therapeutic agents capable of modulating multiple targets simultaneously might offer a strategic advantage. Such multi-target approaches could lead to more comprehensive and potentially safer therapeutic outcomes by acting synergistically on various pathological processes involved in inflammatory conditions. This perspective sets the stage for investigating natural products, which, by their very nature, often contain a broad array of bioactive molecules capable of engaging multiple biological pathways.[2-3]

In this pursuit of new anti-inflammatory agents, medicinal plants, with their intricate richness of bioactive compounds, present a promising field to explore. Of these, *Coccinia grandis (L.)* Voigt, or Scarlet Gourd or Ivy Gourd, stands out as a plant of considerable therapeutic potential. An annual climber from the family Cucurbitaceae, *Coccinia grandis* grows commonly in the tropical and subtropical parts of Asia and Africa. Aside from its culinary uses as a common vegetable, *Coccinia grandis* has a sacred status in other indigenous systems of medicine, specifically Ayurveda and Unani medicine. For centuries now, various parts of the plant, its leaves, fruits, roots, and stem, have empirically been used to treat a range of diseases characterized by inflammatory signs and symptoms such as arthritis, skin rashes, fevers, and respiratory ailments. [2-4]

This review paper will strive to integrate the existing scientific knowledge on the anti-inflammatory potential of *Coccinia grandis* in a holistic manner. We shall explore its rich phytochemical biodiversity, listing the principal classes of phytoconstituents identified from various plant components and developmental stages, and examining how different extraction techniques affect their quantity and quality. Then, the review will critically discuss the molecular pathways by which *Coccinia grandis* extracts and isolated compounds inhibit their anti-inflammatory activities in vitro, particularly their modulation of inflammatory mediators, interference with essential signaling pathways (NF-κB, MAPKs), and strong antioxidant activities. In addition, we shall move on to pre-clinical in vivo investigations, testing the efficacy of the plant in both acute and chronic inflammatory animal models, including related human conditions such as diabetic and liver inflammation, along with pharmacokinetic and initial safety profiles.

1.2 Traditional Medicinal Plants as a Source of Anti-Inflammatory Agents

Medicinal herbs have historically played an essential and foundational role in human health and cultural development across civilizations. For millennia, these botanical resources have served as a primary mode of healthcare for approximately 80-85% of the world's population, particularly in vast rural areas of developing countries. This enduring reliance underscores their perceived efficacy and accessibility within traditional medical systems. The profound influence of medicinal plants extends into modern pharmacology, with a significant number of contemporary drugs either directly derived from plant compounds or inspired by their structures. For instance, approximately 100 plant-derived new drugs were introduced to the U.S. drug market between 1950 and 1970, including well-known examples like vincristine and reserpine.

Traditional plant medicines continue to hold a significant position in modern drug discovery due to several inherent advantages. These include their often-minor side effects compared to synthetic counterparts and the potential for synergistic actions among their combined compounds. This inherent complexity is a key differentiator. Herbal medicines are not single-molecule entities but instead consist of complex mixtures comprising multiple major and minor constituents, each with potential targets and mechanisms. This multi-target nature is particularly well-suited for addressing complex chronic diseases, which often involve multiple interacting pathological pathways. This contrasts sharply with the reductionist approach traditionally applied to conventional single drugs, which may struggle to address the multifactorial nature of such conditions. The emerging fields of network pharmacology and systems biology provide appropriate conceptual frameworks for analysing these intricate interactions, offering a more comprehensive view of drugs as multi-target molecules. [2-3]

The strategic advantage of polypharmacology inherent in natural products is increasingly recognized. The ability of complex plant extracts to modulate multiple targets simultaneously, through the synergistic action of various compounds, can lead to more comprehensive and potentially safer therapeutic outcomes for multifactorial inflammatory conditions. This provides a sophisticated theoretical underpinning for exploring plants as a rich "arsenal" of therapeutic agents, capable of addressing complex pathologies more effectively than single-target drugs.

1.3 *Coccinia grandis*: Botanical Description, Distribution, and Traditional Uses [4-5]

Coccinia grandis (L.) Voigt, commonly known as ivy gourd or scarlet gourd, is a perennial herbaceous vine belonging to the Cucurbitaceae family. This fast-growing plant can reach lengths of up to 9 feet (2.7 meters) and grow as much as 4 inches per day. Its morphology is characterized by mostly glabrous stems produced annually from a tuberous rootstock, simple axillary tendrils, and alternate, simple leaves with a broad ovate shape with 5 lobes. The plant produces five-petaled white flowers and smooth, bright red, ovoid to ellipsoid berries when ripe. It is a dioecious species, meaning equally male and female plants must be present to ensure fruiting.

The native range of *C. grandis* extends broadly stretching from Africa to Asia, encompassing countries such as India, Cambodia, Malaysia, China, Indonesia, the Philippines, Myanmar, Thailand, and Vietnam. Its widespread cultivation and transportation by humans have obscured its precise origin. However, its adaptability has also led to it being considered an invasive species in certain introduced regions, including Hawaii, Florida, and Australia, where it can grow in dense blankets, smothering native vegetation.

Historically, various parts of *C. grandis* have been extensively utilized in traditional medicine systems across its natural range for a wide spectrum of ailments. The plant has traditionally been used for conditions such as jaundice, leprosy, bronchitis, asthma, burns, earache, skin eruptions, indigestion, eye infections, nausea, insect bites, tongue sores and fever. Furthermore, it has been used for diabetes mellitus, gonorrhoea, gastrointestinal disturbances, dysentery, vomiting, chronic cough, liver weakness, rheumatism, eczema, syphilis, wound healing, ulcers, and stomach pain. The leaves are particularly prominent in Ayurvedic medicine and other traditional systems for diabetes management, while the fruit juice has traditionally been used for the treatment of urinary stones. The extensive list of traditional uses, particularly for conditions with an underlying inflammatory component (e.g., rheumatism, skin eruptions, asthma, bronchitis), provides a strong historical and observational foundation for its purported anti-inflammatory properties. This empirical knowledge has frequently guided modern scientific investigations, demonstrating a clear correlation between traditional use and modern scientific validation. Traditional knowledge systems thus serve as invaluable "libraries" for modern drug discovery, indicating plants with a high likelihood of containing biologically active compounds relevant to human health. This directly supports the overarching theme of "Unlocking Nature's Anti-Inflammatory Arsenal" by demonstrating that *C. grandis* has been a recognized component of this "arsenal" for centuries, with modern science now providing the tools for deeper validation and mechanistic understanding.

Table 1: Traditional Uses of *Coccinia grandis* [6-11]

Plant Part Used	Traditional Ailments Treated	Geographical Region
Whole Plant	Cystitis, fever, snake bites, urinary tract infections, ringworm, chickenpox.	India, Sri Lanka, Thailand, Australia, Egypt, South Africa, Malaysia, UK, USA, Europe, Asia Minor, Bangladesh
Leaves	Jaundice, bronchitis, skin eruptions, earache, indigestion, nausea, insect bites, fever, diabetes mellitus, burns, gonorrhoea, gastrointestinal disturbances, dysentery, asthma, vomiting, chronic cough, eye infections, tongue sores, liver weakness, rheumatism, eczema, syphilis, wound healing, ulcers, stomach pain, insomnia, headache, nervous debility, giddiness, anti-spasmodic, expectorant, anti-malarial, anti-inflammatory, anti-oxidant, anti-ulcer, anti-pyretic, analgesic.	India, Sri Lanka, Thailand, Australia, Egypt, South Africa, Malaysia, UK, USA, Europe, Asia Minor, Bangladesh
Fruit	Leprosy, fever, asthma, bronchitis, jaundice, eczema, tongue sores, cerebral oxidative stress, urinary stones, helminths infections, anti-inflammatory, anti-oxidant, anti-pyretic, analgesic, hepatoprotective.	India, Indonesia, Southeast Asia, Pakistan, Bangladesh
Stem	Skin diseases, asthma, bronchitis, joint pains, expectorant, anti-spasmodic, gastrointestinal disturbances, urinary tract infection.	India, Pakistan, Bangladesh
Root	Skin diseases (Tenia), arthritis, mouth ulcers, wheezing, phlegm, joint pain, urinary tract infection, diabetes, jaundice, uterine discharge.	India, Peru, Pakistan, Bangladesh, Western Europe, temperate forests of India and Pakistan, Egypt, Europe, Asia Minor
Seeds	Industrial and edible purposes (oil, protein source).	India, Venezuela, USA, Italy

1.4 Rationale and Scope of the Review

The scope of this review is to address this critical knowledge gap by systematically integrating detailed phytochemical characterization with the nuanced molecular mechanisms underlying *C. grandis*'s anti-inflammatory action. The aim is to move beyond a mere compilation of studies to provide a critical scrutiny of the evidence, identify the specific bioactive compounds accountable for its effects, and elucidate the cellular and molecular pathways they modulate. Furthermore, this review will critically assess the current state of research, including *in vitro* and *in vivo* models used, and discuss the challenges inherent in translating preclinical findings into clinical applications. By providing a holistic perspective on *C. grandis* as a natural anti-inflammatory agent, this review seeks to offer a significant contribution to the field, guiding future research towards more targeted investigations, potential drug development, and ultimately, harnessing the full therapeutic potential of this remarkable plant.

2. PHYTOCHEMICAL PROFILE OF *COCCINIA GRANDIS* [12-14]

2.1. Overview of Major Bioactive Compound Classes

Coccinia grandis is widely recognized for its rich and diverse array of secondary metabolites, which are largely responsible for its extensive pharmacological activities. Phytochemical screening across numerous parts of the plant has consistently revealed the existence of several major bioactive compound classes, including alkaloids, flavonoids, saponins, phenols, tannins, terpenoids, and glycosides. This robust chemical profile inherently supports the concept of polypharmacology, where multiple compounds work in concert to produce a therapeutic effect, rather than a single molecule targeting a specific pathway. The observed synergistic effects in some studies are likely a direct consequence of the intricate interplay among these diverse compounds, allowing for simultaneous modulation of multiple biological pathways. This multifaceted approach is particularly advantageous for addressing complex inflammatory conditions, which often involve a cascade of interconnected molecular events.[12]

Specific examples of identified compounds within these classes further illustrate the plant's chemical richness. Flavonoids, a prominent group of polyphenolic compounds, are abundant, with identified examples including kaempferol glycosides, rutin, quercetin-3-O-neohesperidoside, kaempferol-3-O-rutinoside, kaempferol-3-O-neohesperidoside, kaempferol-3-O-glucoside, kaempferol-hexoside, apigenin, and quercetin. Notably, young leaves of *C. grandis* have been reported to contain particularly high levels of total flavonoids and tannins, suggesting that the biological activity may vary with the maturity of the plant material. Terpenoids constitute another significant class, with compounds such as lupeol, β-amyrin, cucurbitacin B, taraxerone, taraxerol, and cephalandrol consistently isolated from various plant parts. Saponins, specifically coccinoside, have also been identified in the roots. Phenolic acids, including vanillic acid, gallic acid, protocatechuic acid, gentisic acid, salicylic acid, syringic acid, ellagic acid, m-coumaric acid, and caffeine acid, contribute to the plant's antioxidant and anti-inflammatory properties. Furthermore, various alkaloids such as 1-tert-Butyl-5,6,7-trimethoxyisoquinolene, Lukianol, Senecionine, Cathinone, Camptothecin, (S) Norlaudanosoline, Trachelogenin, and (6S)-Hydroxyhyoscyamine have been identified in leaf and fruit extracts. The presence of these diverse secondary metabolites is unswervingly responsible for the observed biological characteristics and extensive range of pharmacological activities of *C. grandis*, underscoring its potential as a comprehensive "anti-inflammatory arsenal".[13]

2.2. Isolation and Characterization Techniques

The rigorous identification and structural elucidation of compounds from complex plant matrices like *Coccinia grandis* are paramount for validating their therapeutic potential and understanding their mechanisms of action. This process heavily relies on the application of advanced spectroscopic and chromatographic techniques. Nuclear Magnetic Resonance (NMR) spectroscopy, including both 1D and 2D techniques, is a powerful tool for structural elucidation, providing detailed information on molecular structure, functional groups, and stereochemistry. Mass Spectrometry (MS) is indispensable for determining molecular weight and fragmentation patterns, offering insights into molecular formula and structural features. Additionally, Ultraviolet-Visible (UV-Vis) spectroscopy is employed to study electronic transitions, while Fourier Transform Infrared (FTIR) spectroscopy provides information on functional groups existing in the compounds.

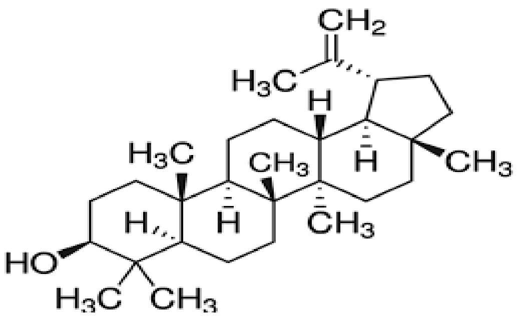
For the separation and purification of individual compounds from crude plant extracts, various chromatographic techniques are essential. These include traditional column chromatography, Thin-Layer Chromatography (TLC), and more sophisticated hyphenated techniques such as Liquid Chromatography-Mass Spectrometry (LC-MS) and Gas Chromatography-Mass Spectrometry (GC-MS). LC-MS and GC-MS are particularly valuable for their ability to combine separation power with mass analysis, enabling rapid identification of known natural products and the elucidation of structures for novel compounds within complex mixtures. This capability is crucial for moving beyond studies of crude extracts to pinpoint specific active molecules.

"Functional chromatography," for instance, represents a cutting-edge approach that deploys biological affinity as the matrix for compound isolation, allowing for the purification of compounds based on their affinity to specific target proteins. This methodological advancement is critical for achieving a deeper mechanistic understanding, as it enables researchers to identify and isolate the exact components of *C. grandis*'s "arsenal" that interact with specific biological targets, thereby accelerating the drug discovery process. The continuous refinement and application of these sophisticated analytical methods are fundamental to dissecting the plant's complex phytochemical composition and validating its therapeutic potential at a molecular level.[15-16]

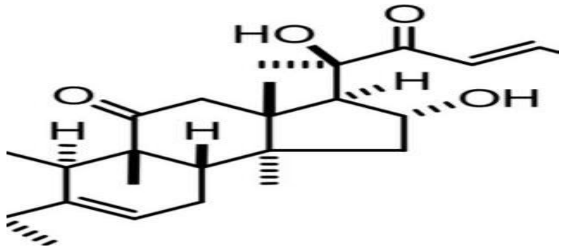
2.3. Specific Compounds Identified with Anti-Inflammatory Potential

The anti-inflammatory potential of *Coccinia grandis* is intricately linked to the presence of specific bioactive compounds, primarily belonging to the flavonoid, phenolic acid, and triterpenoid classes. These compounds are consistently highlighted across various studies for their significant anti-inflammatory and antioxidant activities. Their presence provides a strong chemical basis for the traditional usages of the plant in treating inflammatory conditions.

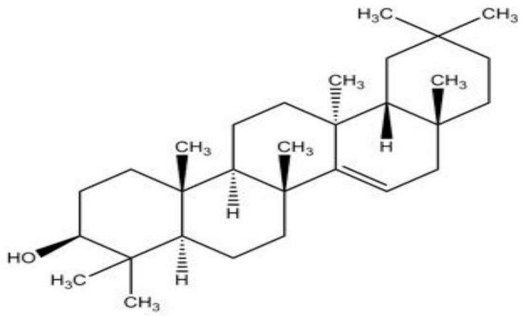
Among the triterpenoids, lupeol has been specifically identified in *C. grandis* and has demonstrated significant *in vitro* anti-inflammatory activity, with an IC50 value of 9.63±1.10 mg/mL. This finding provides concrete evidence for the direct anti-inflammatory action of a purified compound from the plant. Other triterpenoids like β-amyrin, cucurbitacin B, taraxerone, taraxerol, and cephalandrol are also present and contribute to the overall pharmacological profile.[17-19]



Lupeol

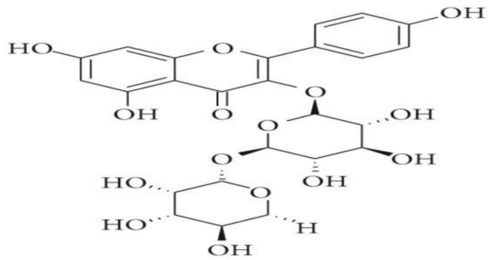


Cucurbitacin B

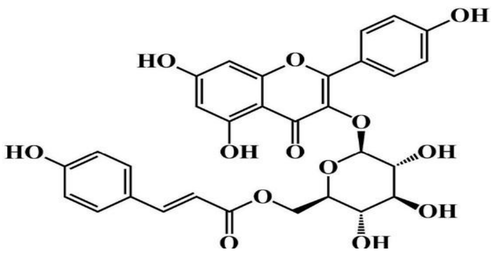


Taraxerol

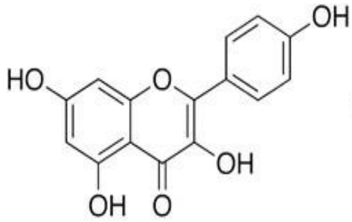
Some of the most well-investigated groups are the flavonoids, a ubiquitous family of polyphenols that are known for their very strong antioxidant and anti-inflammatory capacities. Some of the flavonoids found in *Coccinia grandis* are rutin (quercetin-3-O-rutinoside), a glycoside commonly known for its very strong free radical scavenging and anti-inflammatory activities via numerous mechanisms, such as the inhibition of phospholipase A2 and cyclooxygenase. Tiliroside is another important flavonoid present, which has shown strong anti-inflammatory and hepatoprotective activities. Other flavonoids that are identified, including kaempferol and quercetin, which are commonly found in glycosidic forms, also play their part in the overall antioxidant defense mechanism of the plant, which indirectly protects against inflammation through lessening oxidative stress. Flavonoids, known for their potent antioxidant and anti-inflammatory properties, are abundant in *C. grandis*. Kaempferol glycosides, for example, have been isolated and characterized from the plant. While primarily studied for their α-glucosidase inhibitory activity, which is relevant to diabetes management, their presence suggests broader metabolic influences that can indirectly impact inflammatory pathways. Other identified flavonoids include rutin, quercetin, and apigenin, all of which are well-documented for their anti-inflammatory effects in the broader scientific literature. [19-20]



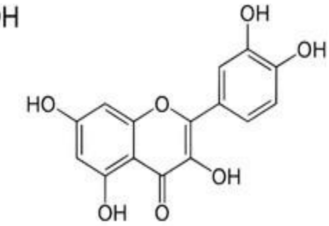
Rutin



Tiliroside

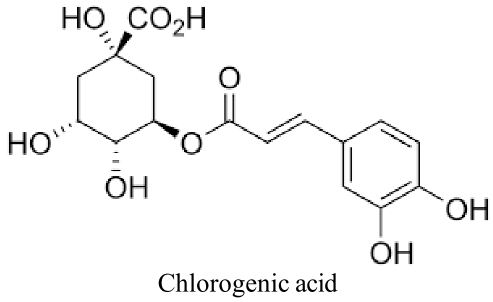


Kaempferol

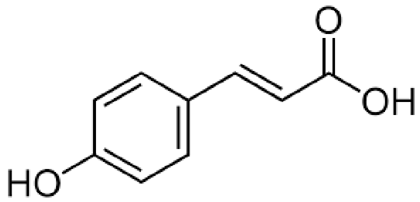


Quercetin

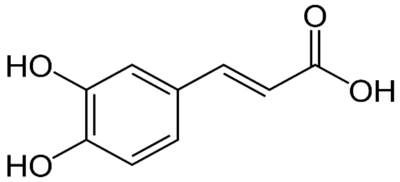
Phenolic acids are another essential category of compounds of *Coccinia grandis*. These are simple aromatic acids that are good antioxidants and have direct anti-inflammatory effects. Chlorogenic acid, a major ester of caffeic and quinic acid, is rich in occurrence and has been extensively known for its strong anti-inflammatory, antioxidant, and antidiabetic activity. Some other phenolic acids such as p-coumaric acid, caffeic acid, and gallic acid may also be found, frequently contributing to the free radical scavenging ability of the plant and influencing inflammatory mechanisms.[21]



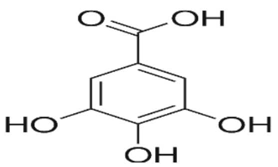
Chlorogenic acid



p-coumaric acid



Caffeic acid



Gallic acid

The terpenoids are a class of chemically diverse compounds and the cucurbitacins are particularly significant in *Coccinia grandis*. The highly oxygenated tetracyclic triterpenoids cucurbitacin B and cucurbitacin D are typical of the family Cucurbitaceae and are responsible for the bitterness that is characteristic of gourds. Apart from their flavor, cucurbitacins are strong bioactive compounds, recognized for their strong anti-inflammatory, anticancer, and cytotoxic activities, mainly through the interruption of cell signaling pathways such as JAK/STAT and MAPK. Other triterpenoids and diterpenes, although less defined for their unique anti-inflammatory functions in *Coccinia grandis*, would partly be responsible for the plant's overall pharmacological profile.

Alkaloids, nitrogenous compounds with frequently very strong physiological activity, have also been described in *Coccinia grandis*. Although their particular anti-inflammatory actions in this species are not as well described as those of flavonoids or cucurbitacins, their occurrence indicates a contribution to the intricate balance of bioactive compounds. [22-23]

Saponins, another important group of glycosides with soap-like foaming action, are another group. Saponins are identified to have immunomodulatory effects and have been found involved in anti-inflammatory responses by modulating cell permeability as well as enzyme activity.

Lastly, phytosterols, structurally identical to cholesterol, are found in plants. Beta-sitosterol is the standout here, thoroughly documented for its anti-inflammatory, immunomodulatory, and cholesterol-lowering action. Its presence in *Coccinia grandis* further solidifies the plant as a natural anti-inflammatory therapy. [23-24]

Table No. 2 bioactive compounds of *Coccinia grandis* and its activity

Bioactive Compound	Source/Part of Plant	Type of Extract	Pharmacological Activity
Flavonoids (e.g., Quercetin)	Leaves, fruits	Methanol, Ethanol	Anti-inflammatory, antioxidant
Alkaloids	Leaves, roots	Aqueous, Ethanolic	Anti-inflammatory, analgesic
Tannins	Leaves, bark	Ethanol	Antioxidant, anti-inflammatory
Saponins	Leaves, fruits	Methanol, Aqueous	Anti-inflammatory, immune-modulatory
Terpenoids	Leaves, fruits, stems	Methanol, Hexane	Anti-inflammatory, antimicrobial
Phenolic acids (e.g., Gallic acid)	Leaves, fruits	Ethanol, Aqueous	Antioxidant, anti-inflammatory
Beta-carotene	Fruits	Ethanol	Antioxidant, anti-inflammatory
Cucurbitacins	Leaves, fruits	Methanol, Aqueous	Anti-inflammatory, anticancer
Ascorbic acid (Vitamin C)	Fruits	Aqueous	Antioxidant, anti-inflammatory

2.4 Variation in Phytochemical Content [25]

The therapeutic value of *Coccinia grandis* is not consistent throughout the whole plant; instead, it's considerably impacted by the particular plant part being used, along with its maturity level. This inconstancy of phytochemical content is an important consideration for traditional medicine usage, where certain parts are traditionally preferred for specified conditions, and also for contemporary drug formulation, requiring accurate standardization of starting materials. Knowledge of these differences is crucial for the fine-tuning of extraction procedures and yielding reproducible bioactivity.

Leaf: Leaves of *Coccinia grandis* are perhaps the best studied tissue, and they exhibit uniformly a dense profile of anti-inflammatory constituents. They are rich in flavonoids like rutin, kaempferol, and quercetin derivatives, along with a very high level of phenolic acids like chlorogenic acid, caffeic acid, and p-coumaric acid. The persistent availability and comparably high concentrations of these compounds in the leaves are most likely responsible for their broad traditional application in poultices against swelling and their substantive in vitro and in vivo anti-inflammatory activities seen in scientific research. Leaf extracts tend to be indicated as being highly active antioxidants directly attributable to their content of phenolic and flavonoid compounds.

Fruit: The fruit of *Coccinia grandis* also shows significant phytochemical modification with maturity from green (immature) to red (ripe). Immature fruits have higher contents of cucurbitacins (e.g., cucurbitacin B and D), which are responsible for their bitter taste and strong biological activities, such as anti-inflammatory. As the fruit matures, the content of these bitter triterpenoids tends to diminish, whereas there is an impressive accumulation of carotenoids such as β-carotene and lycopene, which contribute the red hue. The carotenoids are endowed with robust antioxidant activity that indirectly exerts anti-inflammatory action by mopping up reactive oxygen species. The change in composition between unripe and ripe fruit indicates different uses; unripe fruits may be better for their more active cytotoxic and straight anti-inflammatory cucurbitacin content, whereas ripe fruits provide a dense source of dietary antioxidants useful for long-term health and modulation of inflammation.

Roots: The roots of *Coccinia grandis* are less commonly investigated than the leaves and fruits, yet studies show their specific phytochemical profile. They have been reported to contain diverse triterpenoids, saponins, and certain alkaloids which are different in percentage from the rest of the plant. Certain studies propose the occurrence of certain compounds in roots that might contribute to its traditional application in treating certain chronic diseases, with possibly diverse anti-inflammatory pathways than those in the aerial part.

Stem: Like the roots, the stem of *Coccinia grandis* is not as well explored. Preliminary phytochemical screenings indicate the existence of flavonoids, phenolic substances, and some steroids/phytosterols. Stem bark extracts could have a unique set of compounds that contribute to the overall healing potential of the plant if used entirely in traditional herbal remedies.

In short, the particular portion of *Coccinia grandis* chosen for investigation or application significantly determines the resulting phytochemical profile. This not only means the existence of principal classes of compounds but also the individual types and levels of specific bioactive molecules within those classes. This intrinsic diversity has stressed the importance of rigorous phytochemical characterization of the starting material source in any scientific study to make studies reproducible and to safely assign observed biological activity to individual compounds or their mixtures. Such characterization is indispensable for creating standardized extracts with reliable anti-inflammatory activity.

3. ANTI-INFLAMMATORY ACTIVITIES OF *COCCINIA GRANDIS* EXTRACTS

Building on the known medicinal properties of Coccinia grandis (ivy gourd), **Chuchote and et al**. investigated its ethanolic extract to uncover previously unreported pharmacological activities and identify the compounds responsible. The study found that the extract exhibits significant anti-tyrosinase and anti-inflammatory properties, with impressive IC50 values of 0.29 ± 0.06 mg/mL and 9.63 ± 1.10 mg/mL, respectively. Through HPLC profiling, the active triterpenoid compound lupeol was identified and quantified at 18.87 ± 0.79 mg per 100 g of dry extract. These findings suggest that the plant's extract, rich in lupeol, holds promise as a functional ingredient for developing new health-beneficial food and medicinal products.[17]

In a study **by Albrahim et al.** (2020), the potential anti-inflammatory and immunomodulatory effects of *Coccinia grandis* crude extract were studied using LPS-stimulated THP-1 cells. The researchers found that treating these cells with the extract significantly downregulated the expression of multiple pro-inflammatory cytokines, including IL-6, IL-1β, and IL-8. Furthermore, the extract was revealed to modulate key molecular signaling pathways involved in inflammation and apoptosis, such as the NF-κB, p38 MAPK, and ERK1/2 pathways, as evidenced by the reduced expression of proteins like ERK5, BAX, and P-NF-κB. This research is a pioneering effort to demonstrate how *C. grandis* extract can affect a wide range of cellular processes in human monocytic cells, including proliferation, inflammation, phagocytosis, migration, and apoptosis, highlighting its potential therapeutic application in inflammatory conditions.[18]

A Study by **Ashwini et al.** (2012) on the fruit extracts of *Coccinia grandis* investigated its antioxidant and anti-inflammatory properties to validate its traditional use in India. The research confirmed the presence of various phytochemicals, including alkaloids, tannins, flavonoids, and diterpenes. Using *in vitro* assays, the study found that the antioxidant activity was most prominent in the methanolic extract, with an IC50 value of 140 µg/ml. Furthermore, all tested extracts exhibited anti-inflammatory activity as measured by their ability to inhibit protein denaturation, with the highest activity observed in the n-hexane extract, which had an IC50 value of 100 µg/ml. These results scientifically support the folkloric use of *Coccinia grandis* fruits for treating conditions related to oxidative stress and inflammation.[20]

According to a study conducted by **Sakharkar and Chauhan** (2017) investigated the antibacterial, antioxidant, and cell proliferation–promoting properties of *Coccinia grandis* fruits. Using various extraction methods, they tested the efficacy of the extracts against several bacteria, including *Staphylococcus aureus* and *E. coli*. The results indicated that both the ethanol and acetone extracts exhibited a certain level of bacterial growth inhibition, with acetone extracts demonstrating superior antibacterial activity. Furthermore, both ethanol extracts demonstrated notable antioxidant activity when compared to a standard. Contrary to a cytotoxic effect, all extracts showed cell proliferative properties on MDA-MB 321 breast cancer cells, with the acetone extracts and cold extracts performing better than their counterparts. These findings confirm the presence of antimicrobial, antioxidant, and cell proliferative properties in *C. grandis* fruits, providing a base for further research to identify and characterize the particular phytochemicals accountable for these biological activities. The findings of this study, when interpreted in conjunction with previous research on the anti-inflammatory properties of *C. grandis*, suggest a broader therapeutic potential for the plant. The antioxidant activity observed in the Sakharkar and Chauhan study is often closely linked to anti-inflammatory effects, as oxidative stress is a key driver of inflammation. The cell proliferative properties also point to a role in tissue repair and wound healing, processes that are closely associated with the body's inflammatory response.[21]

Kondhare and Lade (2017) investigated the phytochemical composition, aldose reductase inhibitory (ARI) potential, and antioxidant activities of *Coccinia grandis* fruit extracts, validating its traditional use in Southeast Asia. Their study found that the methanolic extract had the highest yield of compounds and phenolic content, while the water extract contained the most flavonoids. A GC-MS analysis of these extracts identified the presence of flavonoids, phenolic compounds, alkaloids, and glycosides. The research highlighted the significant bioactive properties of the extracts. The methanolic extract demonstrated a potent ARI activity of 96.6% with an IC50 value of 6.12 µg/mL, followed closely by the water extract. Both methanolic and aqueous extracts likewise demonstrated potent antioxidant activities in various scavenging assays (ABTS, DPPH, and hydroxyl radical). The study concluded that the high flavonoid and phenolic content in the fruit extracts is directly correlated with their ARI and antioxidant properties[16]

The anti-inflammatory properties of *Coccinia grandis* have been scientifically validated through experimental studies using chemically induced inflammation models in rodents. **Deshpande et al.** investigated the aqueous extracts of the leaves (AEL) and stem (AES) of *Coccinia grandis* for their efficacy against carrageenan-induced paw edema in rats. The extracts were prepared and subsequently subjected to acute toxicity evaluation following CPCSEA guideline No. 423, confirming their safety profile. Based on these findings, doses of 50, 100, and 200 mg/kg were selected for in vivo experiments. Both AEL and AES significantly inhibited carrageenan-induced paw edema ($p < 0.001$) in a dose-dependent manner in comparison with the control group, with the leaf extract showing superior activity over the stem extract. The pronounced anti-inflammatory potential of *Coccinia grandis* extracts has been attributed to its bioactive phytoconstituents, particularly polyphenols, flavonoids, and steroidal compounds. These findings support the traditional use of *Coccinia grandis* in the treatment of inflammatory conditions and provide a scientific foundation for its therapeutic potential as a natural anti-inflammatory agent.[26]

Chandaka Madhu et al. (2023) evaluated the phytochemical profile along with the analgesic and anti-inflammatory effects of the hydroalcoholic extract of *Coccinia grandis* whole plant. In this study, the extract was administered orally at two different doses (200 and 400 mg/kg body weight) in experimental models. The anti-inflammatory effect was assessed using carrageenan-induced paw edema in Wistar albino rats and compared with the standard drug diclofenac (10 mg/kg). The analgesic effect was determined in Swiss albino mice by Eddy's hot plate method and compared with aspirin (25 mg/kg). The hydroalcoholic extract produced a significant reduction in paw edema at both tested doses ($p < 0.01$), showing results comparable to diclofenac. Likewise, the extract demonstrated marked analgesic activity ($p < 0.01$), with 400 mg/kg demonstrating marked reduction in paw licking response comparable to the standard drug. The study concluded that *Coccinia grandis* possesses potent anti-inflammatory and analgesic properties, supporting its traditional therapeutic use in the managing painful and inflammatory disorders.[27]

Chatterjee *et al.* evaluated the anti-inflammatory activity of various solvent extracts of *Coccinia indica* whole plant using the carrageenan-induced rat paw oedema model. Petroleum ether, 60% methanolic, and aqueous extracts were prepared, and phytochemical screening revealed the presence of flavonoids only in the methanolic extract. Among the tested extracts, the 60% methanolic extract exhibited the highest anti-inflammatory activity, producing greater inhibition than diclofenac sodium after three hours of administration. In contrast, the petroleum ether and aqueous extracts exhibited comparatively lower inhibition, supporting the role of flavonoids in mediating the observed pharmacological effect.[28. 29, 30, 31, 32]

Table No 3- Summary of *Coccinia grandis* Extracts and Biological Activities

Author(s)	Extract/Part Used	Model/Assay	Key Findings	Active Compounds/Notes
Chuchote et al.	Ethanolic extract	Anti-tyrosinase & Anti-inflammatory assays	IC_{50}: 0.29 ± 0.06 mg/mL (anti-tyrosinase), 9.63 ± 1.10 mg/mL (anti-inflammatory)	HPLC: Lupeol identified (18.87 ± 0.79 mg/100 g dry extract)
Albrahim et al.	Crude extract	LPS-stimulated THP-1 cells	Downregulated IL-6, IL-1β, IL-8; modulated NF-κB, p38 MAPK, ERK1/2; reduced ERK5, BAX, P-NF-κB	First study showing immunomodulation in human monocytic cells
Ashwini et	Fruit extracts (methanol,	Antioxidant (in	Antioxidant: methan	Alkaloids, tannins, flavonoids, diterpenes

al.	n-hexane, others)	vitro), anti-inflammatory (protein denaturation)	olic extract IC_{50} = 140 µg/mL; Anti-inflammatory: n-hexane IC_{50} = 100 µg/mL	
Sakharkar & Chauhan	Fruit extracts (ethanol, acetone, cold extracts)	Antibacterial, antioxidant, cell proliferation	Acetone extract = best antibacterial (S. aureus, E. coli); Antioxidant activity significant; Extracts promoted MDA-MB 321 cell proliferation	Suggests role in tissue repair and wound healing
Kondhare & Lade	Fruit extracts (methanol, water)	Aldose reductase inhibition (ARI), antioxidant assays (ABTS, DPPH, OH•)	Methanol extract: ARI = 96.6% (IC_{50} = 6.12 µg/mL); Both methanol & water extracts strong antioxidants	GC-MS: flavonoids, phenolics, alkaloids, glycosides
Deshpande et al.	Leaf (AEL) & stem (AES) aqueous extracts	Carrageenan-induced paw edema in rats	Dose-dependent inhibition (50–200 mg/kg); AEL > AES; safe by CPCSEA guideline 423	Attributed to polyphenols, flavonoids, steroids
Chandaka Madhu et al.	Hydroalcoholic whole plant extract	Carrageenan-induced paw edema (rats), Eddy's hot plate (mice)	Anti-inflammatory: significant reduction in paw edema at 200 & 400 mg/kg (comparable to diclofenac 10 mg/kg); Analgesic: reduced paw licking at 400 mg/kg (comparable to aspirin 25 mg/kg)	Supports anti-inflammatory & analgesic traditional uses
Deshpande et al.	Aqueous leaf & stem extracts	Formaldehyde-induced paw edema in rats	Significant inhibition; leaf extract most effective ($p < 0.05 – 0.001$)	Supports folkloric use
Chatterjee et al.	Petroleum ether, 60% methanolic, aqueous extracts (whole plant)	Carrageenan-induced paw edema in rats	60% methanolic extract showed highest anti-inflammatory effect, greater than diclofenac after 3 h; others less effective	Flavonoids (present only in methanolic extract)

CONCLUSION

Coccinia grandis demonstrates significant potential as a source of natural anti-inflammatory agents. Preclinical studies on leaf, stem, and whole-plant extracts consistently show inhibition of chemically and physically induced inflammation in animal models, with methanolic and aqueous extracts often exhibiting the highest activity. Phytochemical analyses indicate that flavonoids, phenolics, and other secondary metabolites are likely accountable for these effects, acting through mechanisms such as inhibition of pro-inflammatory mediators and oxidative stress modulation. While current evidence is largely preclinical, these findings underscore the therapeutic promise of *Coccinia grandis* and provide a strong rationale for future research, including mechanistic studies and clinical trials, to validate its safety and efficacy in human inflammatory disorders. Harnessing the bioactive compounds of *Coccinia grandis* could pave the way for the development of novel, plant-based anti-inflammatory therapeutics with reduced side effects than conventional drugs.

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