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Review Article

UNLOCKING NATURE'S PHARMACY: A COMPREHENSIVE REVIEW OF PHARMACOLOGICAL PROPERTIES IN THE CUCURBITACEAE FAMILY

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ABSTRACT

The Cucurbitaceae family, also referred to as the gourd family, is a varied collection of plants that have been utilised for their therapeutic attributes for many years. This article provides a thorough examination of the pharmacological characteristics of the Cucurbitaceae family, focusing on the molecular composition and bioactive substances found in different species of the family. The text discusses the chemical contents of different species, specifically focusing on dimeric furocoumarins, volatile oil, cucurbitine, resin, proteins, myosin, vitelin, shatavarin, saponins, glycosides of quercetin, and carbohydrates. The review also encompasses an examination of the aamayika prayoga (therapeutic applications) of several plant components, including the roots, root stock, fruits, leaves, and seeds. The review emphasises the potential of the Cucurbitaceae family as a reservoir of natural medicines, specifically highlighting its anticonvulsant, anti-inflammatory, and antioxidant characteristics. The paper also examines the possible difficulties and constraints associated with utilising the Cucurbitaceae family as a reservoir of natural remedies, such as the requirement for additional investigation and the likelihood of unfavourable consequences. In summary, this review offers a thorough examination of the pharmacological characteristics of the Cucurbitaceae family, emphasising their potential as a reservoir of natural remedies and the necessity for additional investigation to completely comprehend their therapeutic capabilities.

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Introduction

The Cucurbitaceae species may have the greatest diversity of plants and the widest range of uses among all plant families. On one end of the spectrum, the family consists of bottle gourds, scientifically known as Lagenaria siceraria. These gourds have been transported across the world's oceans and have successfully adapted to various oceanic civilizations, comprising to the advancement of numerous local varieties. Simultaneously and with varying degrees of overlap, cucumbers, melons, squashes, and pumpkins coexist with gourds, forming an essential component of meals in temperate climates worldwide [1]. Another distinct subgroup of Cucurbitaceae consists of ivy gourds, namely Coccinia species like as Coccinia grandis. Those plants are cultivated in Asia and Africa mainly for their palatable fruits and leaves [2]. On the opposite end, there are plants known as colocynth, scientifically called Citrullus colocynthis, and desert gourds. These plants belong to the diverse group of species, primarily from the genus Cucumis. They possess bitter and purgative qualities, often being toxic. Those plants are considered as weeds and are found in desert regions in warm temperate to tropical parts of the world [3]. The Bryonia species, which belong to another temperate zone Old World group of Cucurbitaceae, often have toxic roots. The aboriginal individuals of the America have discovered countless medicinal and tasty utilization for the various plants specified in the assignment [4]. Several local races have been cultivated for certain cucurbits. In addition, there are plants with horticultural significance, in particular, the diverse range of decorative gourds. Rarely a few numbers of cucurbits have been cultivated or utilised exclusively for the formulation of body-care items, such as sponges. These diverse members belong to Cucurbitaceae family are available in many subsistence and agriculture systems [5]. In certain instances, they act as a crucial role in comprehending a small-scale traditional agriculture with limited horticultural practices, while in other circumstances, they are linked to a significant and advanced form of agriculture. Due of its extensive variety, the family provides a fascinating viewpoint on higher plants and a diverse range of connections to human societies [6].

The Cucurbitaceae family, derived from the Latin word "cucurbita" meaning gourd, comprises approximately 90 genera and 700 species. This family holds significant importance in terms of human nutrition and medicine. Most species in this family are origin to the tropical along with subtropical regions of both the northern and southern hemispheres [7]. The family comprises the four cultivated species of Cucurbita, Cucumis, Citrullus, and Lagenaria. This

family is significant because of the fact that, its members possessing fruits, those are appropriate for consumption, and recently, they have been identified for their medicinal characteristics [8]. The fruit of plants belonging to this family is typically a pepo, berry, or occasionally a capsule. Several wild species are having a critical role in the diet of wild animals including peccaries, parrots, and iguanas because of the regular consumption of their fruits [9-11]. Plants belonging to the Cucurbitaceae family can be either annual or perennial herbs, vines, or occasionally shrubs. They frequently have rough or glandular hair. The leaves have an alternating arrangement and are either palmately lobed or palmately compound [12]. Tendrils are typically present and have a spiral or bifurcate shape. The plants are often monoecious, but occasionally dioecious, and produce unisexual blooms. These flowers have actinomorphic symmetry and are frequently huge and conspicuous [13]. The hypanthium is fused to the base of the ovary, and the corolla often consists of fused petals forming a single structure with five lobes. There are typically five stamens that are located on the corolla tube [14]. The twinning or three-dimensional development movements of plants are a result of the differential growth of different regions, which is regulated by hormones [15].

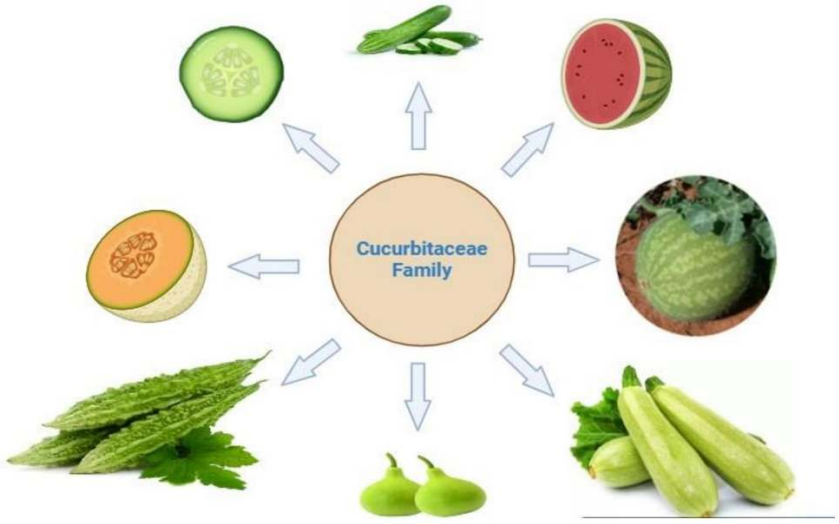

Figure 1. Pictorial interpretation of Cucurbitaceae family

The pharmacological characteristics of the Cucurbitaceae family are of great importance in the field of medical research. The family, which consists of plants such as Citrullus colocynthis, Cucumis sativus, and Cucurbita pepo, is a significant provider of secondary metabolites, specifically triterpenoids, that display a wide variety of biological properties involving anti-inflammatory, cytotoxic, hepatoprotective,

and antiparasitic properties. Natural chemicals have a crucial role in drug discovery, resulting in the creation of novel medications [16-19]. The Cucurbitaceae plants have been utilised in conventional medicine for the treatment of different ailments from longer period. Their medicinal significances are being searched to be nearly associated with their nutritional along with phytochemical makeup, which includes tocopherols, terpenoids, saponins, carotenoids, sterols, phenols, fatty acids, along with polysaccharides and functional carbohydrates [20-21]. The therapeutic attributes of Cucurbitaceae plants rely on the chemical compounds they contain, which have demonstrated distinct physiological impacts on the human body, including blood detoxification, elimination of harmful substances, facilitation of digestion, and provision of vital nutrients for enhanced well-being [22]. Cucurbitaceae family is highly significant in medicinal research as a reason of its diverse range of bioactive chemicals, having the potency to be utilized as therapies for a wide variety of health disorders [23].

Historical Significance of Cucurbitaceae Family in Traditional Medicine

The Cucurbitaceae family has considerable historical significance in traditional medical techniques. Plants from this family have played a crucial role in traditional medicinal practices worldwide for many years [24].

In Africa, these plants have been utilised to cure a diverse array of illnesses. The various species within the Cucurbitaceae family have had important roles in ensuring food security and traditional medicine (Fig 1). Some species are produced specifically for food, while others are obtained from their natural habitats [25]. These plants have been recorded for their medicinal significance in treating different illnesses, emphasising their essential role in offering healthcare options to populations, particularly in rural areas where dependence on traditional medicine is widespread [26]. The Cucurbitaceae family has a significant historical importance due to its extensive use as a natural remedy source, which highlights the valuable ethnopharmacological history linked to these plants [27].

Common Traditional Remedies and Practices

The treatments have been inherited across multiple generations and remain applicable in the present day. The Cucurbitaceae family, comprising plants such as cucumbers, melons, pumpkins, and watermelons, has historically been utilised in traditional medicine to address various health conditions [28]. Common traditional practices involving Cucurbitaceae plants include their use in the treatment of

illnesses such as diabetes, inflammation, cytotoxicity, liver protection, and parasite infections. Moreover, these plants have played a crucial role in ensuring food security and nutrition in various places, highlighting their significant value in both traditional medicine and dietary customs [29]. The historical importance of the Cucurbitaceae family in traditional medicine underscores the profound cultural and medicinal worth linked to these plants in many communities.

Cultural Perspectives on Medicinal Plants

The cultural viewpoints of medicinal plants in the Cucurbitaceae family are firmly established in diverse traditions and practices throughout numerous regions. West Africa extensively use the Cucurbitaceae species for both dietary and medicinal purposes, highlighting the interconnectedness of culture, health, and the natural environment [30]. These plants play a major role in traditional medicine systems, where species like Momordica charantia, Lagenaria breviflora, and Citrullus colocynthis are utilised for treating disorders like diabetes and other illnesses. These plants are having cultural importance that goes beyond their medical benefits, as they are also crucial for ensuring food security and nutrition in various cultures [31]. Furthermore, the use of Cucurbitaceae species in traditional medicinal systems exemplifies the intricate relationship between cultural beliefs, knowledge, and the natural environment. This demonstrates the long-standing appreciation and incorporation of these plants into local restorative traditions across many generations [32].

Phytochemical Composition

The Cucurbitaceae family encompasses a diverse array of crops such as cucumbers, melons, and other vegetables that possess therapeutic significance. The plants belonging to this botanical family, referred to as cucurbits, are a unique and isolated group that do not have any closely related species. They possess numerous advantageous properties in terms of both medicinal and nutritional value. The primary phytochemicals found with respect to this family including glycosides, terpenoids, saponins, tannins, steroids, carotenoids, and resins, with terpenoids being the most prevalent [33]. The family is renowned for its elevated protein content and diverse biological properties, encompassing anti-bacterial, anti-viral, anti-tumor, anti-fungal, anti-diabetic, & anti-AIDS actions. Cucurbit plants have long been utilised as traditional herbal medicines for a range of ailments and have shown notable effectiveness in reducing inflammation, inhibiting tumour growth, protecting the liver, promoting cardiovascular health, and regulating the

immune system [34]. The family possesses a significant amount of bioactive chemicals, including cucurbitacins, triterpenes, sterols, and alkaloids. An evaluation of the chemical constituents found in plants belongs to the Cucurbitaceae family has confirmed the existence of several types of phytochemicals, including cardiac glycosides, terpenoids, carotenoids, polysaccharides, tannins, resins, phytosterols, & saponins. Glycosides are having diverse and significant functions in living beings, with cardiac glycosides primarily employed for the management of heart illness or cardiac disease [35]. Cucurbitacins, a class of triterpenoids, exhibit diverse biological properties such as anti-inflammatory, antioxidant, antimalarial, antibacterial, hepatoprotective, and anticancer effects.

Bioactive Compounds in Cucurbitaceae Family

The primary bioactive components found in plants belonging to this family are saponins, tannins, flavonoids, alkaloids, and phenolic compounds. Cucurbitaceae family is comprising of approximately 800 species along with 130 genera. Notable genera within this family include Trichosanthes, Lagenaria, Luffa, Benincasa, Momordica, Cucumis, Citrullus, Cucurbita, Bryonopsis, and Corallocarpus. Cucurbit plants have long been utilised in traditional medicine for their therapeutic properties, which include anti-inflammatory, anticancer, hepatoprotective, cardiovascular, and immunoregulatory effects. They contain a wide variety of proteins that possesses different biological activities, comprising anti-bacterial, anti-viral, anti-fungal, anti-diabetic, anti-AIDS, & anti-tumor properties [36]. Cucurbits contain a variety of phytochemicals, including glycosides, terpenoids, saponins, tannins, steroids, carotenoids, and resins. Among them, terpenoids such as cucurbitacins are the most prevalent.

Chemical Diversity and Variation within the Family

The Cucurbitaceae family has a wide range of chemical variety and variation, with different species containing various phytochemicals and bioactive substances. Momordica charantia L., also known as bitter melon, is a species of Cucurbitaceae that is abundant in cucurbitacins [37]. It has been the subject of much research due to its notable anti-obesity, anti-inflammatory, and anti-neoplastic characteristics. The family has seen multiple instances of whole-genome duplication (WGD) throughout its evolutionary history [38]. These events have played a role in enhancing its genetic diversity and facilitating the exposure of significant agronomic characteristics, such as fruit quality. The genome sequences belongs to

18 distinct cucurbit species from the tribes Benincaseae, Cucurbiteae, Sicyoeae, Momordiceae, and Siraitieae have been decoded. This breakthrough offers valuable insights for studying gene identification, genome evolution, genetic variation, and molecular breeding of cucurbit crops.

Pharmacological Activities

Antioxidant and Anti-inflammatory Effects

The Cucurbitaceae family, which consists of plants including cucumbers, melons, and bitter melon, demonstrates notable antioxidant and anti-inflammatory properties because of the bioactive components it contains, notably cucurbitacins, terpenoids, saponins, and phytochemicals [39]. Cucurbitacins are naturally occurring compounds that are present in various plant groups, with a particular abundance in the Cucurbitaceae family. These compounds have demonstrated significant potential as antioxidants, anti-inflammatory agents, and immunomodulators. Cucurbitacins, specifically cucurbitacin B and cucurbitacin E, have the ability to regulate the immune response, hinder the activity of COX-2 along with NOS enzymes, decrease the oxidative stress, suppress the proinflammatory cytokines, as well as adjust acquired immunity proteins [40]. This showcases their extensive adaptability in the field of therapeutic advancements. The antioxidant and anti-inflammatory benefits of the Cucurbitaceae family are due to the wide range of bioactive substances found in plants of this family, specifically cucurbitacins, terpenoids, and phytochemicals. Vegetables from the Cucurbitaceae family include natural substances that have the potential to effectively counteract oxidative stress, reduce inflammation, and regulate the immune response. These vegetables are valuable additions to a balanced diet and have the potential to provide medicinal advantages [41].

Antimicrobial and Antiviral Properties

The Cucurbitaceae family, which includes many types of cucurbit plants, has notable antibacterial and antiviral effects due to its bioactive components [42]. Cucurbituril homologues have been shown, possessing wide-ranging extracellular antiviral actions against many viruses, such as herpes simplex, hence highlighting their antiviral characteristics. The antimicrobial and antiviral activities of plants in the Cucurbitaceae family are attributed to the presence of bioactive compounds such as cucurbitacins, terpenoids, saponins, and phytochemicals [43]. These compounds make these plants valuable in traditional medicine and having the potential to be used as novel antimicrobial and antiviral agents.

Antipshycotic Properties

Researchers investigated the leguminous plant Mucuna pruriens (MP) as a potential alternative source of levodopa for those with Parkinson's disease. MP is a plant that grows well in tropical locations and naturally contains levodopa. The presence of polyphenols in herbal medications plays a role in regulating depression. Proinflammatory cytokines found in polyphenols have been shown in clinical investigations to potentially play a role in the development of depression. The phytochemical analysis revealed the presence of many secondary metabolites, including anthraquinone, flavonoids, steroids, tannins, saponins, alkaloids, terpenoids, and cardiac glycosides.

Anticancer and Tumor-Inhibiting Potential

The Cucurbitaceae family, has been thoroughly investigated due to its significant potential in preventing cancer and suppressing tumour growth. Cucurbitacins, a class of biologically active substances included in the Cucurbitaceae plant family, have demonstrated notable anti-cancer properties [44]. These include the capability in hindering the growth of the cancer cells, induce cell cycle arrest along with programmed cell death, additionally diminish the generation of blood vessels in tumours and the spread of cancer to other parts of the body [45]. These chemicals have been discovered to function as STAT3 inhibitors, rendering cancer cells more vulnerable to reactive oxygen species and free radicals, and triggering apoptosis in Sezary cells. Studies have demonstrated that cucurbitacins can work along with chemotherapy drugs, increasing the effectiveness of treatment and potentially preventing the development of drug resistance in cancer cells [46].

Immunomodulatory Effects

Moreover, studies on cucurbitacins, a category of organic compounds commonly found in the Cucurbitaceae plant family, have emphasised their ability to modulate the immune system. Cucurbitacins, specifically cucurbitacin B & cucurbitacin E, have been identified as crucial substances that have the ability to modify the immune system, affecting both the innate and adaptive immune responses [47]. This demonstrates their versatility in regulating the immune system.

Cardiovascular and Metabolic Benefits

The Cucurbitaceae family is notable for its cardiovascular advantages in comparison to other plant families [48]. This is because they contain a high concentration of bioactive chemicals such as saponins, terpenoids, flavonoids, phenolic acids, and terpenes, which contribute to their medicinal characteristics. These chemicals have a significant impact on the cardiovascular system, providing

antioxidant, antiplatelet, anti-hyperlipidemic, and anti-inflammatory properties that promote cardiovascular well-being. Furthermore, many species belong to family Cucurbitaceae have been explored to possess antioxidant and antiplatelet properties, which are crucial for preventing and treating cardiovascular disorders. The varied physiological characteristics of vegetables belong to this family, such as their capability to reduce high levels of lipid in the blood, capability to prevent obesity, and ability to regulate body weight, emphasise their positive effects on cardiovascular health and make them valuable components of a diet that promotes heart health [49].

Mechanism of Action

Cellular Targets and Molecular Pathways

Cucurbitacins have been discovered to interact with various cellular targets, including Bcl-2/Bax, caspases, STAT3, fibrous-actin, cyclooxygenase-2, and Janus kinase (JAK). These interactions have an impact on significant physiological events such as apoptosis, cell cycle regulation, and signal transmission [50]. These interactions result in the adjustment of signalling pathways such as PI3K/AKT/mTOR, JAK/STAT, MAPK, and others, which have crucial functions in the growth, survival, and spread of cancer cells. Cucurbitacins possess the capability to specifically target cellular components and pathways, hence contributing to their beneficial effects in terms of anticancer, anti-inflammatory, antioxidant, and immunomodulatory properties [51]. Consequently, they hold great potential as candidates for cancer therapy and other therapeutic uses.

Pharmacokinetics and Bioavailability

Pharmacokinetic studies have been carried out on various cucurbitacins, such as CuB, CuIIa, CuD, CuE, CuI, and CuIIb, mainly using rat models. Despite their structural similarities, cucurbitacins exhibit variations in absorption, distribution, metabolism, and excretion. For example, the oral bioavailability of cucurbitacin B is around 10%, and it reaches its highest concentration in the blood within 0.5 to 1 hour after adjusting for the dosage [52].

Potential Applications in Drug Development

The Cucurbitaceae family is having the potential for be utilised in pharmaceutical research since it contains cucurbitacins, group of triterpenoids that have shown strong anticancer properties by modifying different molecular targets and signalling pathways [53]. These chemicals have notable biological activity, including anti-inflammatory, antioxidant, antimalarial, antibacterial, hepatoprotective, and anticancer properties. The Cucurbitaceae family, specifically the Cucurbita genus,

has been employed in traditional medicine to address gastrointestinal disorders, intestinal parasites, hypertension, and urinary disorders, among other medical issues [54-57]. The pharmacological effects of these plants have been searched to be closely connected with their nutritional and phytochemical content, which includes tocopherols, phenols, carotenoids, terpenoids, sterols, fatty acids, saponins, and useful carbohydrates along with polysaccharides. Recently, cucurbitacins, a kind of triterpenoids, have gained considerable attention because of their well-known biological properties [58]. These chemicals have demonstrated antibacterial, antioxidant, and anticancer properties, which make them highly viable contenders for therapeutic development.

Drug Discovery and Development Strategies

Drug development efforts utilising the Cucurbitaceae family aim to use the pharmacological significance of these natural chemicals, which possess antidiabetic, anti-inflammatory, cytotoxic, hepatoprotective, and antiparasitic properties, in order to create novel pharmaceuticals [59]. These elements have undergone substantial research to understand the molecular mechanisms along with biological activities, particularly their ability to combat cancer. As an outcome, they have emerged as very promising candidates for the advancement of new medications.

Researchers have examined the pharmacokinetic properties of cucurbitacins, such as their absorption, metabolism, distribution, and elimination, in order to gain insight into their biological effects and prospective medical applications [60]. Research has emphasised the significance of combining the pharmacokinetic profiles of cucurbitacins with their biological activities, including their ability to fight cancer, in line to fully explore their potency in therapeutic development. In general, the drug discovery along with advancement approaches regarding Cucurbitaceae family focus on investigating the wide variety of biological impacts of cucurbitacins and other secondary metabolites [61]. The goal is to turn up novel therapeutic agents relating different conditions like cancer, diabetes, inflammation, and parasitic infections.

Formulation and Delivery Systems

There has been an enhancing curiosity in developing new methods to deliver natural plant extracts, especially those from the Cucurbitaceae family, as drugs in recent years. These systems comprise of organic, inorganic, and hybrid nanoparticles, which have demonstrated superiority over traditional delivery methods in terms of solubility, bioavailability, toxicity, and pharmacological activity [62].

For instance, regarding a unique medication delivery system, for a natural plant extract involves the utilization of cubosomes, which are nanoparticles consisting of an aqueous solution & a lipid bilayer. The particles have been utilised to encase achyranthes bidentata polysaccharides, which have demonstrated immunological action in laboratory experiments [63]. Another instance involves the utilisation of biopolymer-based nanoparticles for the objective of delivering drugs or genes, additionally for tissue engineering.

Furthermore, there has been a concerted effort to enhance the composition of conventional delivery techniques, including hydrogels, for the usage of natural plant extracts. These formulations are having the potency to enhance the solubility and stability of the chemicals, while also enabling their regulated release.

Combination Therapy and Synergistic Effects

The Cucurbitaceae family, comprising plants like cucumbers, pumpkins, and gourds, possesses bioactive chemicals that exhibit anticancer, anti-inflammatory, antioxidant, and antibacterial effects. The chemicals, specifically cucurbitacins, have demonstrated potent synergistic anticancer effects when coupled with chemotherapy medicines commonly utilised in clinical practice [64]. Cucurbitacins possess not only anticancer capabilities but also exhibit antidiabetic, anti-inflammatory, cytotoxic, hepatoprotective, and antiparasitic activities. The chemicals in question are primarily triterpenoids, with cucurbitacins being the most renowned and extensively researched category. Cucurbitacins exhibit diverse biological activities, involving antidiabetic, anti-inflammatory, cytotoxic, hepatoprotective, and antiparasitic effects.

The concurrent use of cucurbitacins and other medicinal substances has been discovered to provide synergistic effects [65]. An illustration regarding this, is a discovery that cucurbitacin E synergistically interacts with other therapeutical drugs, such as paclitaxel and doxorubicin, to augment their anticancer properties. The Cucurbitaceae family has been discovered to possess antibacterial and antiviral characteristics [66-69].

Cucurbitacins have shown promise as anticancer drugs in the field of drug research, with recent discoveries shedding light on their molecular targets and methods of action. Moreover, cucurbitacins have demonstrated synergistic anticancer properties when coupled with chemotherapeutic medicines commonly used in clinical practice, thereby making them highly viable candidates for combination therapy.

Conclusion

The Cucurbitaceae family is a varied and significant group of plants that encompasses numerous foods and medicinal plants. The family is renowned for its secondary metabolites, specifically triterpenoids, that exhibit a diverse array of pharmacological properties, such as antidiabetic, anti-inflammatory, cytotoxic, hepatoprotective, and antiparasitic actions. Cucurbitacins, a specific class of triterpenoids, have demonstrated synergistic properties when used in conjunction with other medicinal chemicals. For instance, cucurbitacin E has been observed to collaborate with other drugs, thereby augmenting their therapeutic effects. The vast research conducted on the family is due to its genetic richness and global distribution. Genome sequencing and resequencing have been particularly useful in giving excellent data for genome-wide investigations of significant Cucurbitaceae plants. Research has focused on studying the molecular mechanisms that control significant characteristics in order to enhance the quality of fruits and the breeding of cucurbit crops.

Conflict of Interest

The writers state they have no competing interests.

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