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A Review on Phytopharmaceutics Profile of Cyperus Rotundus; A Natural Excipient and Bioenhancer in Modern Drug Delivery Systems

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Abstract: *Historically valued for its therapeutic qualities, Cyperus rotundus is now more widely acknowledged in contemporary pharmaceutics as a natural excipient and bioenhancer. Its functional role in improving drug stability, solubility, and permeation is supported by its rich phytochemical profile, which includes sesquiterpenes, flavonoids, alkaloids, and essential oils. Cyperus rotundus, a naturally occurring excipient, helps to improve formulation properties in topical, transdermal, and nanocarrier systems, allowing for the controlled and prolonged release of active ingredients. Its inherent bioactivity acts as an efficient bioenhancer by modifying enzymatic pathways and membrane permeability, which further increases drug bioavailability. The plant is useful for wound healing, skin care, and certain drug delivery applications because of its antimicrobial, anti-inflammatory, and antioxidant qualities. The plant is useful for wound healing, skin care, and certain drug delivery applications because of its antimicrobial, anti-inflammatory, and antioxidant qualities. Recent developments include incorporation into hydrogels, liposomes, and nanoparticles—nanostructured systems that maximize drug penetration and therapeutic efficacy. This integration not only enhances the efficacy of existing medications but also paves the way for innovative treatment options that align with modern healthcare demands. As research continues to unveil the diverse applications of Cyperus rotundus, it could very well transform the future of integrative medicine.*

Keywords: Cyperus rotundus, natural excipient, bioenhancer, drug delivery systems, phytopharmaceutical, Herbal formulation

I. INTRODUCTION

Cyperus rotundus, sometimes referred to as purple nutsedge or nutgrass, has a long and rich ethnopharmacological history that dates back thousands of years. In traditional medical systems like Ayurveda, Traditional Chinese Medicine (TCM), and Islamic medicine, it has been widely used to treat a variety of illnesses, such as pain, inflammation, fever, menstrual irregularities, and digestive disorders. Because of their medicinal qualities as analgesic, antispasmodic, anti-inflammatory, antimicrobial, and antioxidant agents, the plant's rhizomes and tubers are especially prized [(1)].Its documented use by ancient physicians like Dioscorides and Pliny the Elder emphasizes its longstanding significance in healing practices, while evidence from archaeological discoveries points to its use by early human populations for nutritional and medicinal purposes[(2)].Out of more than 3000 species in the Cyperaceae family, around 220 are classified as weeds. In India, there are about fifty-two species of Cyperus that do well in wet or marshy places. The nut sedges come from tropical and subtropical areas [(3)]. Numerous phytochemicals, including flavonoids, alkaloids, sesquiterpenes, and essential oils, are responsible for its wide range of pharmacological effects. Cyperus rotundus is currently receiving more attention as a natural excipient and bioenhancer in contemporary drug delivery systems because of its diverse therapeutic potential and naturally occurring bioactive composition. This status encourages the creation of efficient, biocompatible, and sustainable drug formulations by bridging its historical roles with modern

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pharmaceutical applications [4]. Nagarmotha (Cyperus rotundas), also called "Mutha," is a common plant found all over India. Its name comes from the Greek word Cypeiros (Cyperus) and the Latin word rotundus, meaning "round," which refers to its tubers. This plant grows underground structures like rhizomes, tubers, bulbs, and roots, while above the ground it produces leaves, stems, and flower clusters [5]. This plant's roots and rhizomes are used to treat a variety of additionally; it contains anthelmintic, antihistaminic, antiemetic, antipyretic, antiestrogenic, antibacterial, and antidiabetic properties. [6]

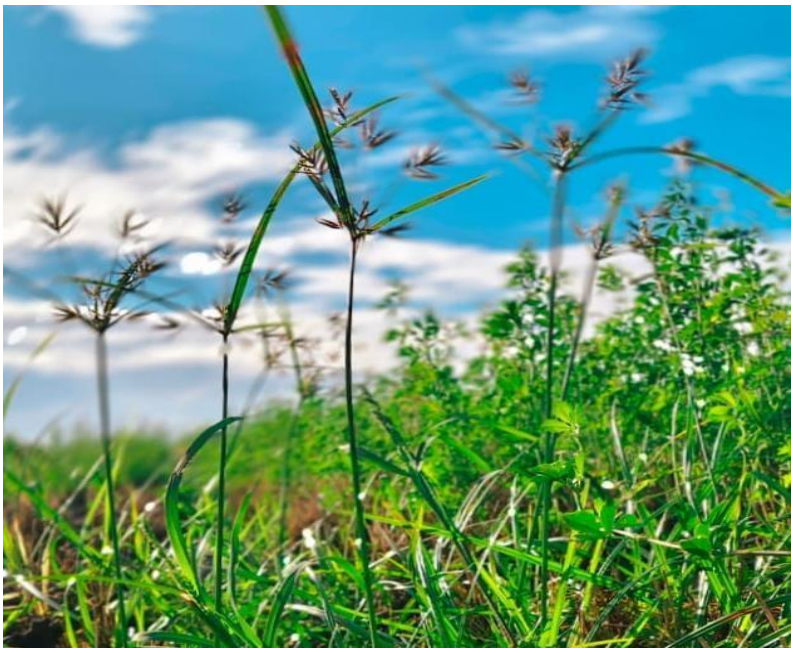

FIG 1: cyperus rotundus plant

pharmaceutical formulations, an excipient is an inactive ingredient that helps with manufacturing, improves stability, and enhances drug delivery without having a therapeutic effect. In pharmaceutical formulations, an excipient is an inactive ingredient that helps with manufacturing, improves stability, and enhances drug delivery without having a therapeutic effect.[7]A bioenhancer is a natural or artificial substance that improves a drug's pharmacokinetic profile and absorption while having negligible pharmacological activity at the dosage, thereby increasing the drug's bioavailability and effectiveness.[8]A formulation or technological advancement intended to safely deliver a pharmaceutical compounds to the body as needed to produce the intended therapeutic effect is known as a drug delivery system. A formulation or technological advancement intended to safely deliver a pharmaceutical compound to the body as needed to produce the intended therapeutic effect is known as a drug delivery system. [9]

PLANT PROFILE OF CYPERUS ROTUDUS

SYNONYMS:-

Blue Nut Grass
Nagarmotha
Musta
Chlorocyperus rotundus (L.)
PallaCyperus olivaris Targioni
BoeckelerCyperus stoloniferum pallidus BoeckelerCyperus
Tetrastachyos Desf.Cyperus tuberosus Roxb.
Pycreus rotundus (L.) Hayek [10]

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Table 2: Taxonomic Classification of Cyperus rotundus

Kingdom	Plantae
Subkingdom	Tracheobiont
Class	Liliopsida
Order	Cyperales
Family Cyperaceae	Cyperaceae
Genus	Cyperus
Species	C .rotundus
Binomial name	Cyperus rotundus linn

Morphology of Cyperus Rotundus :

Purple nutsedge, or Cyperus rotundus L., is perennial sedge that is a member of the Cyperaceae family and is distinguished by its unique growth form and reproductive organs. With solitary or sparsely tufted culms (stems) that are three-angled and upright, the plant usually reaches a height of 10 to 75 cm. The stems are smooth and green, with swollen basal bulbs (tubers) that range in diameter from 1 to 2.5 mm. The tubers are dark reddish-brown, globose-ovoid, hard, fragrant, and roughly 1.2 cm long with a diameter of 0.3-0.7 cm. The linear-lanceolate leaves, which measure 5-30 cm in length and 1-8 mm in width, are grouped in ranks of three at the base. Usually, they are shorter than the culms [(11).]

The base of the stem is encased in green to reddish-brown, membrane-based leaf sheaths. Grey-green or pale underneath, the major ribs and leaf margins are scabrid (rough). Cyperus rotundus's inflorescence is a compound umbel made up of two to eight rays, each of which has clusters of sessile or short peduncle-borne spikelets. Spikelets range in length from 2 to 13 mm and in width from 1.5 to 2 mm. They are crowded with 6 to 24 flowers each, narrowly linear, and erect to spreading. Their coloring ranges from reddish-brown to purplish-brown. Usually bisexual, the tiny, minute flowers have one seeded ovary and one to three stamens[(12).]

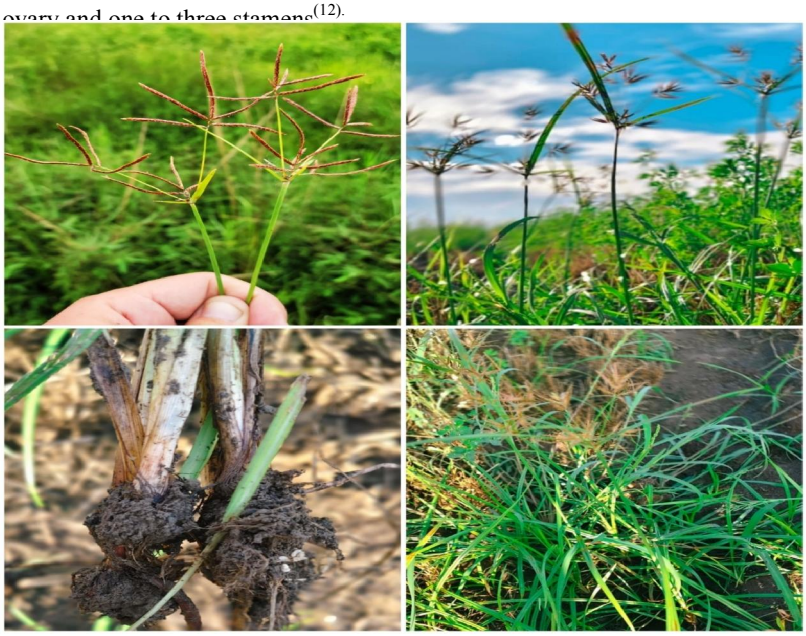

FIG 2 : Cyperus Rotundus plant a) flower ,b)stem , c) rhizomes d) leaves

Usually bisexual, the tiny, minute flowers have one seeded ovary and one to three stamens. Trigonous (three-angled), the fruit is an oblong to ovate-oblong nutlet that is 1.3-1.5 mm long and 0.5-0.7 mm wide. As it ages, it turns dark or

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brown. Woody, branching chains of rhizomes and tubers make up the plant's vast underground network of propagation. Because of its intricate rhizomatous system, Cyperus rotundus is extremely invasive and challenging to remove[13].

MEDICINAL USE

Ayurveda states that C. rotundus rhizomes are regarded as diuretic, analgesic, antispasmodic, astringent, and diaphoretic aromatic, litholytic, carminative, antitussive, emmenagogue, stimulant, tonic, vermifuge, stomachic, sedative, and antimicrobial. Given that it might be an effective treatment for indigestion,components found in it, such as the numerous enzymes for minerals and carbohydrates, which serve as catalysts for a number of aids in indigestion and biochemical reactions[15]

FIG 3: Cyperus rotundus seed root

Additionally, it is helpful for Dietary treatment of metabolic disorders and psychotic illnesses.They are used to treat dyspepsia, nausea, vomiting,intestinal parasites, fever, diarrhea, dysentery, flatulence, and colic renal and vesical calculi, bronchitis, malaria, cough, and urinary wounds, tenesmus, skin conditions, amenorrhea, dysmenorrhea,inadequate lactation, memory loss,

food poisoning, insect bites,cervical cancer, bronchitis, nausea, dysuria, and infertility menstrual irregularities and cancer, and the fragrant oils are composed of scentsplashessplash[15].

Phytochemical profile of Cyperus rotundus

Cyperus rotundus's proximate composition and physicochemical profile the phytochemicals identified in Cyperus rotundus fall into one of the following general categories: solvent's proximate constituents, volatile and non-volatile compounds extract. Cyperus rotundus rhizome's physicochemical characteristics and extractive values include total ash, sulfated ash, water-soluble ash, acid-insoluble ash, and loss upon drying extractive, alcohol-soluble extractive, and

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subsequent extractive methods were identified. Values with various solvent systems, such as benzene,n-hexane, petroleum ether, water, alcohol, methanol, acetone, chloroform, and ethyl acetate. [16]

Flavonoids:

Such as luteolin and quercetin, which are well-known for their antioxidant and enzyme-modulating properties that can enhance the stability and absorption of medications [17].

Essential Oils:

A complex mixture that helps improve drug penetration and skin penetration, mostly made up of mono- and sesquiterpenes. Glycosides, tannins, alkaloids,

Starches:

By stabilizing formulations and enhancing drug release profiles, these substances enhance the excipient's qualities[18].

Table 1: Phytochemical profile of Cyperus rotudus

Phytochemical Class	Key Chemical Constituents/ Structures.	Functional Role in Drug/Formulation Enhancement
Flavonoids	Luteolin, Quercetin	Properties that modulate enzymes and antioxidants prevent oxidative degradation to improve drug stability and absorption.
Essential Oils	Mono- and sesquiterpenes, including α-pinene, β-pinene, limonene, 1,8-cineole, bornel, verbenone	Complex mixtures that increase the effectiveness of dermal delivery by improving drug and skin penetration through lipophilic action.
Starches	Polysaccharides	Enhance formulation consistency and excipient qualities by stabilizing formulations and adjusting drug release profiles.
Glycosides	Iridoid glycosides (Rotunduside A & B), steroidal glycosides	Interact with receptors to enhance bioavailability or targeted delivery and contribute to pharmacological effects.
Tannins	Afzelechin, Catechin	Indirectly promoting drug stability, they offer anti-inflammatory and antioxidant qualities.
Alkaloids	Rotundine A and B, Octopamine	Alter physiological processes and can function as active pharmaceutical ingredients or bioenhancers in formulations.

METHOD OF EXTRACTION OF CYPERUS ROTUDUS

Hydro distillation and steam distillation:

The processes of steam distillation and hydrodistillation are mainly used to extract essential oils that are high in monoterpenes and sesquiterpenes, which naturally increase permeation. The volatile compounds in the plant material (such as rhizomes or tubers) are vaporized by steam or water vapor, then condensed and gathered.

Extracting Solvents:

Flavonoids, phenolics, and fatty acids are obtained through extraction using solvents such as ethanol, methanol, hexane, or ethyl acetate. The yield and profile of bioactive compounds are influenced by the solvent selection.

SFE or supercritical fluid extraction:

Enhancing bioactivity and suitability for pharmaceutical formulations, supercritical CO2 is a clean and effective way to extract thermolabile compounds with little solvent residue.

Extraction Assisted by Ultrasound (UAE):

Increases compound yield and decreases extraction time by employing ultrasonic waves to improve the extraction efficiency of bioactive.

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Microwave-Assisted Extraction (MAE):

Enhances phytochemical release and maintains bioactivity by heating the plant matrix using microwave energy. As natural bio enhancers, these extraction techniques produce bioactive compounds with permeation-enhancing qualities that can be added to topical or transdermal delivery systems. The target compound, the intended use, and the production scale all influence the decision . [19]

Role as Natural Excipient in Modern Drug Delivery Systems:

Natural excipients are compounds derived from natural sources, such as minerals, plants, or animals that are used in pharmaceutical formulations to help deliver drugs safely. Compared to synthetic excipients, they are more cost-effective, environmentally sustainable, biocompatible, and safe. They lessen toxicity while improving solubility, stability, and bioavailability and altering drug release. Natural excipients are compounds derived from natural sources, such as minerals, plants, or animals that are used in pharmaceutical formulations to help deliver drugs safely. Compared to synthetic excipients, they are more cost-effective, environmentally sustainable, biocompatible, and safe. They lessen toxicity while improving solubility, stability, and bioavailability and altering drug release. [20]

Extracts from Cyperus rotundus can be used as natural binders, emulsifiers, and suspending agents in pharmaceutical formulations because they contain mucilaginous polysaccharides, flavonoids, tannins, and essential oils that significantly increase viscosity and emulsification. While the emulsification properties stabilize drug suspensions and emulsions, the viscous nature of the mucilage aids in controlled drug release. Additionally, these characteristics enhance the solubility and bioavailability of drugs. [21]

Examples of Formulations Incorporating Cyperus Rotundus as

Topical herbal ointments and gels, where its extract improves absorption and has calming properties.

Liposomal formulations and nanoparticles for better bioavailability and regulated drug release.

Suspensions and emulsions that are stabilized by their inherent emulsifiers.

Its mucilaginous extracts are used as matrix formers and binders in sustained-release tablets. Several formulations have included Cyperus rotundus, including:

Topical herbal ointments and gels, where its extract improves absorption and has calming properties.

Liposomal formulations and nanoparticles for better bioavailability and regulated drug release. [22]

Role as Bioenhancer Properties in Cyperus Rotundus as Exipient

Bioenhancers are compounds that, when taken with medications, increase the drugs' bioavailability and effectiveness through a variety of mechanisms, including synergistic action, enzyme inhibition, and drug transporter modulation. By enhancing drug absorption, lowering dosage requirements, and minimizing adverse effects, they are essential to contemporary drug delivery. Evidence for Cyperus rotundus's bioenhancer qualities primarily comes from its diverse phytochemical composition, which includes flavonoids, sesquiterpenes, alkaloids, and essential oils. These substances improve the bioavailability of co-administered medications by inhibiting enzymes and modifying drug transporters. [23]

For example, elements in C. rotundus have the ability to block metabolic enzymes that normally break down medications, increasing the amount of the drug in the blood. Additionally, its phytochemicals' synergistic effects can intensify the effects of medications, improving therapeutic results overall. Mechanistically, compounds from Cyperus rotundus may affect P-glycoprotein, which is crucial for drug efflux, inhibit enzymes like cytochrome P450, which is essential for drug metabolism, and have anti-inflammatory and antioxidant properties that enhance the pharmacokinetics and pharmacodynamics of medications. Studies demonstrating enhanced mitochondrial protection, modulation of enzyme activity, and decreased drug metabolism resulting in increased drug efficacy support these bioenhancer properties. In conclusion, Cyperus rotundus enhances drug delivery and therapeutic efficacy by acting as a natural bioenhancer through synergistic phytochemical interactions, drug transporter modulation, and enzyme inhibition. [24]

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Cyperus rotundus compounds have been shown to improve oral drug absorption and potency by inhibiting metabolic enzymes (like cytochrome P450), increasing intestinal membrane permeability, and reducing drug efflux. These findings provide evidence that these compounds are bioenhancers. Cyperus rotundus phytoconstituents, for instance, have been found to greatly improve pharmacokinetic profiles when combined with bioenhancers such as BioPerine® (piperine), which lowers the need for drug dosages while preserving efficacy. This demonstrates how useful Cyperus rotundus phytochemicals are for lowering the effective dose and improving therapeutic results in drug delivery applications. [25]

The Mechanism of Cyperus Rotundus Act as Bioenhancer:

Flowchart of Bioenhancement Mechanisms by Cyperus rotundusPhytochemicals
(kaempferol, quercetin, sesquiterpenes, β-sitosterol)

Enzyme Inhibition
↓
Reduced First-Pass Metabolism
↓
Modulation of Drug Transporters (P-gp inhibition)
↓
Increased Drug Absorption
↓
Synergistic Effects (antioxidant, anti-inflammatory)
↓
Improved Bioavailability & Therapeutic Efficacy
↓

Enzyme Inhibition:

Cyperus rotundus contains bioactive compounds like kaempferol and quercetin, which exhibit enzyme inhibition properties.

These flavonoids inhibit drug-metabolizing enzymes such as cytochrome P450, reducing the first-pass metabolism of co-administered drugs and thereby enhancing their bioavailability.

This inhibitory action helps in increasing the concentration of drugs in systemic circulation, improving their therapeutic efficacy.

For example, kaempferol has been shown to interact with signaling proteins like AKT1 that regulate cellular processes, suggesting a broader regulatory role that complements its enzyme inhibition activity.

Quercetin similarly exhibits potent antioxidant and antiviral activities, supporting its function as a bioenhancer. [26]

Modulation of Drug Transporters:

Cyperus rotundus modulates drug transporters by interacting with important proteins like P-glycoprotein (P-gp) and other intestinal epithelial-expressed efflux transporters through its bioactive compounds. Usually, these transporters limit absorption and bioavailability by pumping medications back into the gut lumen.

Quercetin, beta-sitosterol, and sesquiterpenes are among the compounds found in C. rotundus that have demonstrated the capacity to inhibit or modify these transporters, thereby decreasing drug efflux and improving oral drug absorption.

For instance, network pharmacology and molecular docking studies show that components of C. rotundus bind strongly to targets linked to drug metabolism and diabetes, such as AKT1 and MMP9, which are involved in pathways involving cellular uptake and transporter regulation.

By promoting increased cellular drug uptake and decreasing transporter-mediated drug resistance, this modification increases bioavailability. This action encourages the use of phytochemicals from C. rotundus to enhance drug delivery effectiveness and pharmacokinetic profiles in therapeutic applications. [27]

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Synergistic Action:

By combining its anti-inflammatory, antioxidant, and signaling modulation qualities, Cyperus rotundus shows synergistic effects. Because they influence several biological pathways at once, these phytochemicals combine to increase the effectiveness of medications.

For instance, elements such as alkaloids and flavonoids help to modulate important signaling pathways involved in immunological responses and cell survival while lowering oxidative stress and inflammation.

This diverse activity not only improves therapeutic results but also bolsters the use of C. rotundus as a useful supplement to treatment plans, such as antimicrobial and anticancer therapies, where synergy with traditional medications has been noted. [28]

Application in Modern Drug Delivery Systems

Cyperus rotundus is used in a variety of contemporary drug delivery systems by being incorporated into topical formulations, tablets, liposomes, and nanoparticles. Compared to chemical enhancers and synthetic excipients, its natural phytochemicals offer benefits like reduced toxicity, improved biocompatibility, and sustainable sourcing.

Nanoparticles and Nanocarriers:

Extracts from C. rotundus are utilized in the environmentally friendly synthesis of nanoparticles (such as iron oxide, zinc oxide, and silver) that exhibit improved antibacterial, antioxidant, and anti-inflammatory qualities. In addition to improving drug stability, solubility, and targeted delivery, these nanoparticles also encourage wound healing while lowering adverse effects

Topical Formulations:

It speeds up skin wound healing and improves antimicrobial efficacy when added to hydrogels and creams. When compared to synthetic capping agents, natural capping agents in C. rotundus lower toxicity risks.

Tablets and Oral Delivery Systems:

By blocking metabolizing enzymes and altering drug transporters, natural excipients derived from C. rotundus increase drug bioavailability, enabling lower dosages and better patient compliance.

Adding C. rotundus bioactives to these drug delivery platforms has been shown to improve drug efficacy, bioavailability, and toxicity, according to preclinical and clinical data. Additionally, the green synthesis approach provides alternatives for pharmaceutical manufacturing that are less harmful to the environment. [29]

Challenges

Chemical Variability

Environmental factors, harvest time, and ecological zones all have a substantial impact on Cyperus rotundus's chemical makeup and profile of bioactive constituents. This variability affects the consistency of pharmacological effects and bioenhancer efficacy, complicating standardization of extracts for pharmaceutical use.

Safety and Toxicity:

Although generally regarded as safe, there are few thorough toxicological and cytotoxicity studies, and possible cytotoxic effects associated with particular compounds must be carefully assessed to guarantee safety, particularly for high-dose and long-term applications.

Extraction and Formulation Challenges:

It is necessary to have effective and scalable extraction techniques that preserve bioactive compounds while retaining functional qualities appropriate for excipient use. Compatibility research and stability evaluations are necessary for incorporation into contemporary dosage forms.

Clinical Validation:

The majority of pharmacological and bioenhancer activity evidence is still found in vitro or animal studies. Thorough clinical research and human trials are required to firmly establish efficacy and safety.[30]

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Future Perspectives

Standardization and Quality Control:

For Cyperus rotundus, pharmacopoeia standards and standardized extraction procedures will improve regulatory acceptability and reproducibility.

Advanced Drug Delivery Technologies:

Utilizing Cyperus rotundus extracts in innovative drug delivery systems like hydrogels, liposome's, or nanoparticles offers chances to take advantage of its excipient and bioenhancer qualities for applications requiring controlled and targeted release.

Sustainable and Green Chemistry:

Utilizing Cyperus rotundus to produce pharmaceutically active nanoparticles in an environmentally friendly manner reduces dependency on artificial chemicals and is consistent with eco-friendly development.

II. CONCLUSION

Cyperus rotundus' varied bioactive compounds and advantageous physicochemical characteristics make it a highly promising candidate for phytopharmaceutical use as a natural excipient and bioenhancer in contemporary drug delivery systems. Because of its abundance in flavonoids, sesquiterpenes, and mucilaginous polysaccharides, Cyperus rotundus is a powerful binder, emulsifier, and stabilizing agent that promote efficient drug formulation and controlled release. Its bioenhancer qualities result from processes like drug transporter modulation, enzyme inhibition, and synergistic interactions that increase drug bioavailability. Nonetheless, issues with clinical validation, safety profiling, chemical composition variability, and standardization still exist.

The Integration of Cyperus rotundus into pharmaceutical applications will be made possible by addressing these issues through thorough human trials, sophisticated formulation technologies, and strict quality control. This plant's natural and sustainable origin fits in nicely with the rising need for biocompatible and environmentally friendly drug delivery excipients. To sum up, Cyperus rotundus is a valuable natural resource with a variety of uses as a bioenhancer and excipient, providing chances to improve contemporary drug delivery while preserving efficacy and safety. For its full therapeutic and formulation potential to be realized, more multidisciplinary research is necessary.

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