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PHARMACOLOGICAL INSIGHTS AND PHARMACEUTICAL FORMULATIONS OF *PANDANUS ODORATISSIMUS* PEDUNCLE AND *CURCUMA LONGA*: A NARRATIVE REVIEW OF THERAPEUTIC APPLICATIONS FROM 2010 TO 2025

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ABSTRACT

Background: Natural products remain a cornerstone of pharmaceutical development, with *Pandanus odoratissimus* and *Curcuma longa* representing significant sources of bioactive compounds for inflammatory, urological, hepatoprotective, and oncological applications. **Objective:** This narrative review synthesizes pharmacological evidence and formulation advancements for *P. odoratissimus* peduncle and *C. longa* rhizome extracts from 2010 to 2025, identifying therapeutic potentials and pharmaceutical development strategies. **Methods:** A comprehensive literature search was conducted focusing on pharmacological studies and formulation research published between 2010 and 2025. Studies were selected based on relevance to therapeutic applications, methodological rigor, and formulation innovation. Data were synthesized narratively to identify trends, mechanisms, and clinical translation potential. **Results:** *P. odoratissimus* peduncle demonstrates significant anti-inflammatory (68% edema inhibition), anti-enuretic (35% bladder capacity increase), and hepatoprotective (59% ALT reduction) activities with favorable safety profiles (up to 5 g/kg). Multiple formulations including oral solutions, orodispersible tablets, and capsules have been developed with 95-98% potency retention. *Curcuma longa* exhibits multitargeting capabilities through NF-κB inhibition, epigenetic modulation, and enhanced bioavailability via nanoparticle systems (40-185-fold increase). Advanced delivery systems including PLGA nanoparticles, solid lipid nanoparticles, and nanoemulsions address bioavailability limitations while improving therapeutic indices in cancer, arthritis, and metabolic disorders. **Conclusion:** Both botanicals demonstrate substantial pharmaceutical potential supported by mechanistic studies and formulation innovations. Standardized extracts and optimized delivery systems represent viable pathways for clinical translation, particularly in pediatric urology, hepatoprotection, and integrative oncology. Future research should prioritize clinical validation and regulatory-compliant manufacturing.

KEYWORDS: *Pandanus odoratissimus*, *Curcuma longa*, pharmacology, pharmaceutical formulations, natural products, drug delivery, anti-inflammatory, hepatoprotective, bioavailability.

1. INTRODUCTION

Natural products have historically provided essential therapeutic agents, with approximately 35% of modern medicines derived directly or indirectly from botanical sources.[1] The integration of traditional medicine knowledge with contemporary pharmaceutical technology offers promising avenues for addressing unmet medical needs, particularly in chronic

inflammatory conditions, metabolic disorders, and cancer supportive care.[2] Among medicinal plants gaining scientific validation, *Pandanus odoratissimus* L. (family Pandanaceae) and *Curcuma longa* L. (family Zingiberaceae) represent distinct yet complementary therapeutic modalities with established ethnopharmacological foundations.

Pandanus odoratissimus, commonly known as kewda or screw pine, has been utilized in traditional Yemeni and Indian medicine for treating dysuria, nocturnal enuresis, kidney stones, and inflammatory conditions.[3] The peduncle (flower-bearing stalk) contains bioactive flavonoids, alkaloids, and phenolic compounds that have demonstrated pharmacological activities in preclinical models. Conversely, *Curcuma longa* (turmeric) and its principal curcuminoid, curcumin, have been extensively investigated for anti-inflammatory, antioxidant, anticancer, and neuroprotective properties, though clinical translation has been hampered by bioavailability limitations.[4]

Despite growing research interest, comprehensive synthesis of formulation strategies addressing the pharmaceutical challenges of these botanicals remains limited. This narrative review aims to critically evaluate pharmacological evidence and formulation advancements for *P. odoratissimus* peduncle and *C. longa* from 2010 to 2025, providing insights for future drug development and clinical applications.

2. Sources and Selection Criteria

This narrative review was conducted following established guidelines for narrative synthesis in pharmaceutical sciences.[5] Literature searches were performed using PubMed, Scopus, Web of Science, and Google Scholar databases for the period January 2010 to March 2025. Search terms included "*Pandanus odoratissimus*," "*Curcuma longa*," "curcumin," "pharmacology," "formulation," "nanoparticles," "bioavailability," and "clinical trials."

Inclusion criteria encompassed: (1) peer-reviewed pharmacological studies using standardized extracts; (2) formulation development research with physicochemical characterization; (3) clinical and preclinical safety evaluations; and (4) mechanistic studies elucidating molecular targets. Priority was given to studies demonstrating rigorous methodological approaches, including appropriate controls, validated analytical methods, and reproducible formulations. Non-English publications, abstracts without full-text availability, and studies lacking quantitative data were excluded. The reference list was supplemented with seminal reviews and cross-referenced citations to ensure comprehensive coverage.

3. Pharmacology of *Pandanus odoratissimus* Peduncle

3.1 Anti-inflammatory Activity

The anti-inflammatory potential of *P. odoratissimus* peduncle has been demonstrated in both acute and chronic experimental models. Londonkar and colleagues evaluated ethanolic peduncle extracts (50-100 mg/kg) in Wistar rats using carrageenan-induced acute inflammation and formalin-induced chronic inflammation protocols.[6] The 100 mg/kg dose achieved 68% inhibition of edema in acute models and 64.2% inhibition by day 7 in chronic models, comparable to diclofenac sodium (10 mg/kg) control. Phytochemical screening identified flavonoids, alkaloids, and phenolics as active constituents. Histopathological examination revealed reduced leukocyte infiltration and fibrosis, supporting the traditional use of this botanical in inflammatory conditions. Notably, acute toxicity studies showed no adverse effects up to 2000 mg/kg, indicating a favorable therapeutic index.[6]

A systematic review by Adkar and Bhaskar compiled ethnopharmacological data from over 50 studies (1980-2014), confirming consistent anti-inflammatory effects with 60% edema reduction across compiled investigations.[3] The review highlighted phenolics and lignans as characteristic phytochemicals contributing to these activities and emphasized the need for pharmaceutical standardization to ensure reproducible clinical outcomes.

3.2 Urological Applications

Nocturnal enuresis represents a significant therapeutic application for *P. odoratissimus* peduncle in traditional medicine systems. El-Shaibany investigated methanolic peduncle extracts (200-400 mg/kg) in rabbit models, demonstrating a 35% increase in bladder capacity and 40% reduction in urine volume without compromising detrusor muscle contractility.[7] These findings suggest a unique mechanism distinct from anticholinergic agents, potentially involving modulation of bladder compliance or sensory pathways. The extract exhibited antioxidant activity with IC_{50} of 45 µg/mL and 83% DPPH scavenging at 100 µg/mL, alongside antimicrobial zones of 15-20 mm against Gram-positive and Gram-negative bacteria (MIC: 125-250 µg/mL).[7] Safety profiling revealed no toxicity up to 5 g/kg, supporting traditional dosing regimens and pharmaceutical development for pediatric urological disorders.[7]

3.3 Hepatoprotective Effects

Hepatoprotective activity was evaluated by El-Shaibany and colleagues using methanolic peduncle extracts (200-400 mg/kg) against acetaminophen-induced liver damage in guinea pigs.[8] The 400 mg/kg dose produced significant reductions in hepatic enzymes: AST decreased by 42%, ALT by 59%, ALP by 50%, and bilirubin by 45%, comparable to silymarin reference standards. Histological examination confirmed reduced hepatocyte necrosis and inflammatory infiltration, while antioxidant enzyme systems (SOD, GSH) increased by

30-40%. These findings indicate hepatoprotection through antioxidative mechanisms and membrane stabilization, with no observed toxicity up to 4 g/kg.[8]

4. Pharmacology of *Curcuma longa*

4.1 Anti-inflammatory and Antiarthritic Properties

Curcumin, the principal bioactive constituent of *C. longa*, modulates multiple inflammatory pathways, particularly NF-κB signaling. Daily and colleagues conducted a meta-analysis of eight randomized clinical trials (>600 participants) evaluating turmeric extracts and curcumin for joint arthritis.[9] Results demonstrated a 15-point reduction in Visual Analog Scale pain scores with improved joint mobility and 20% reduction in malondialdehyde (MDA) oxidative stress markers. Dosing regimens of 500-2000 mg/day over 4-12 weeks showed no significant adverse events, validating curcumin as an adjunct therapy for osteoarthritis and rheumatoid arthritis.[9]

Hewlings and Kalman reviewed curcumin data from 2000-2017, documenting 40% prostaglandin E_2 reduction via COX-2 inhibition and 25% increased superoxide dismutase levels.[10] Human trials (n=100, 500 mg/day) confirmed improved joint mobility and 20% C-reactive protein reduction. These anti-inflammatory effects extend to gastrointestinal applications, with 60% *Helicobacter pylori* inhibition observed, suggesting potential for peptic ulcer management.[10]

4.2 Anticancer Mechanisms

Curcumin exhibits multitargeting chemopreventive efficacy through epigenetic modulation and signaling pathway interference. Hatcher and colleagues explored PI3K/Akt pathway targeting, demonstrating that curcumin (10-50 μM) reduced cancer cell proliferation by 50% through Akt phosphorylation inhibition and mTOR suppression.[11] Apoptosis induction occurred via increased Bax/Bcl-2 ratio and cytochrome c release, with xenograft models showing 40% tumor inhibition at 200 mg/kg oral dosing.[11]

Kunnumakkara and colleagues reviewed curcumin's cancer prevention capabilities through DNA methyltransferase inhibition, histone modification, and microRNA regulation.[12] In vitro models demonstrated restoration of silenced tumor suppressor genes (CDKN2A, MLH1), while animal models showed 50-60% reduced tumor incidence in colon, breast, and lung cancers. These epigenetic modifications complement direct cytotoxic effects, highlighting curcumin's potential as a chemopreventive agent.[12]

Soleimani and colleagues analyzed over 100 studies (2010-2018), confirming NF-κB inhibition with reduced TNF-α and IL-6 expression (DPPH IC_{50} 20 μM).[13] In vivo studies demonstrated 30% blood glucose reduction in diabetic rodents and p53-mediated apoptosis in breast cancer models. Clinical trials (n=50) showed 50% osteoarthritis pain reduction with 1 g/day dosing, with no toxicity observed up to 8 g/day, though bioavailability limitations necessitate enhanced formulations.[13]

4.3 Cardiovascular and Neuroprotective Applications

Ghandadi and Sahebkar examined cardiovascular benefits, documenting 25% reduced lipid peroxidation and improved left ventricular function in myocardial infarction models.[14] Human trials (200 mg/day, 8 weeks) demonstrated 30% improved endothelial function via flow-mediated dilation, with reduced arterial stiffness and enhanced nitric oxide bioavailability. These cardioprotective effects correlate with anti-inflammatory and antioxidant mechanisms.[14]

Neuroprotective potential was investigated by Zheng and colleagues in APP/PS1 transgenic Alzheimer's rats.[15] Curcumin (100 mg/kg/day, 12 weeks) inhibited beta-amyloid aggregation by 40% and reduced tau hyperphosphorylation. Morris water maze testing revealed improved spatial memory with increased brain-derived neurotrophic factor expression and reduced neuroinflammation, suggesting therapeutic potential for neurodegenerative disorders.[15]

4.4 Antimicrobial and Immunomodulatory Activities

Sharifi-Rad and colleagues evaluated antimicrobial properties, reporting MIC values of 50 μg/mL against *Staphylococcus aureus*/MRSA and 75 μg/mL against *Escherichia coli*, with 18-22 mm *Candida* inhibition zones.[16] HIV-1 replication decreased 70% through viral enzyme interference. Immunomodulatory effects included 35% increased T-cell proliferation and 28% enhanced NK cell activity in murine studies. Human trials (1 g/day, 8 weeks) reduced TNF-α by 45% and CRP by 38%, with no serious adverse events up to 6 g/day.[16]

5. Pharmaceutical Formulations

5.1 Formulation Strategies for *Pandanus odoratissimus* Peduncle

Recent advances have addressed the pharmaceutical development of *P. odoratissimus* peduncle extracts through systematic formulation approaches. Alburyhi and colleagues (2024) developed an oral solution containing sorbitol (10% w/v), sodium benzoate (0.1% w/v), and citric acid (pH 6.0±0.2, viscosity 50 cP) with extract concentration of 100 mg/5 mL.[17] Stability testing at 25°C/60% RH and 40°C/75% RH for 6 months demonstrated 98% potency retention with stable physicochemical properties, supporting liquid formulations for pediatric and geriatric populations.[17]

Preformulation studies characterized the extract's physicochemical properties critical for dosage form design.[18] Total phenolic content was 15% with 8% moisture content by Karl Fischer titration. Solubility profiles showed 20 mg/mL in ethanol versus 5 mg/mL in water, with poor flowability (45° angle of repose) indicating granulation requirements for solid dosage forms. Excipient compatibility studies using differential

scanning calorimetry and Fourier-transform infrared spectroscopy confirmed no interactions with lactose, starch, or magnesium stearate, enabling flexible formulation options.[18]

Orodispersible tablets were developed for pediatric enuresis using direct compression with superdisintegrants: crospovidone (5%), sodium starch glycolate (3%), and croscarmellose sodium (4%).[19] Each tablet contained 200 mg extract with mannitol as diluent. Evaluation parameters included hardness 5 kg/cm², friability <1%, wetting time 25 seconds, and disintegration time 45 seconds (pH 6.8). Dissolution studies demonstrated 95% release within 15 minutes, with accelerated stability (40°C/75% RH, 3 months) showing <5% degradation. Palatability testing confirmed acceptable taste masking, successfully addressing compliance challenges in pediatric populations.[19]

Hard gelatin capsules for hepatoprotective applications utilized wet granulation with PVP K-30 binder, containing granulated peduncle extract (300 mg, equivalent to 45 mg phenolics).[20] Granule characterization showed 500 µm particle size, improved flowability (32° angle of repose), and 4% moisture content. Dissolution testing in simulated gastric and intestinal fluids revealed biphasic release: 30% in 15 minutes (SGF) and 80% cumulative by 45 minutes (SIF). Stability at 30°C/65% RH for 6 months showed <3% moisture gain. Pharmacokinetic studies in rats demonstrated sustained 6-hour plasma levels, confirming suitability for twice-daily administration.[20]

5.2 Advanced Delivery Systems for *Curcuma longa*

Curcumin's clinical utility has been limited by poor aqueous solubility, rapid gastrointestinal metabolism, and low systemic bioavailability. Nanotechnology-based approaches have significantly enhanced pharmacokinetic profiles and therapeutic efficacy.

Bisht and colleagues developed PLGA nanoparticles (80 nm, polydispersity index 0.15, 85% encapsulation efficiency) demonstrating 60% sustained release over 48 hours.[21] Against PANC-1 and MiaPaCa-2 pancreatic cancer cells, IC_{50} values improved to 5-7 µM versus 25-30 µM for free curcumin. Fluorescent microscopy confirmed rapid 2-hour cellular internalization with 60% caspase-3-mediated apoptosis, providing effective pancreatic cancer targeting.[21]

Targeted delivery was advanced by Yallapu and colleagues using PLGA nanoparticles functionalized with A10 RNA aptamer (110 nm, 78% encapsulation) for prostate-specific membrane antigen (PSMA)-positive LNCaP cells.[22] This targeted system achieved 5-fold higher cellular uptake, with cytotoxicity showing 70% reduction at 20 µM versus 40% for non-targeted nanoparticles and 15% for free curcumin. Xenograft biodistribution demonstrated 3-fold tumor accumulation with 60% volume reduction versus 25% for non-targeted formulations, advancing prostate cancer nanomedicine applications.[22]

Solid lipid nanoparticles (SLNs) utilizing glyceryl monostearate (180 nm, 80% encapsulation, -28 mV zeta potential) showed biphasic release: 25% burst release followed by sustained delivery over 72 hours.[23] Caco-2 cellular uptake increased 4-fold compared to free curcumin, while MCF-7 breast cancer cytotoxicity improved significantly (IC_{50} 8 µM vs. 30 µM). Six-month stability at 4°C showed no aggregation, demonstrating SLNs as effective carriers for cancer chemotherapy.[23]

Liposomal formulations using phosphatidylcholine vesicles (150 nm, 90% encapsulation) achieved 6-fold higher plasma levels (AUC 450 vs. 75 µg·h/mL) and 3-fold tumor accumulation in murine models.[24] HT-29 colon cancer xenografts showed 50% tumor reduction versus 20% for free curcumin after 4 weeks, with decreased Ki-67 proliferation and increased apoptosis. Notably, no hepatic or renal toxicity was observed, supporting liposomal formulation safety.[24]

Nanoemulsion technology has addressed solubility limitations, with Feng and colleagues developing curcumin nanoemulsions (50 nm) using medium-chain triglycerides showing 500-fold solubility improvement (50 mg/mL) with 6-month stability.[25] In vitro lipolysis released 90% in mixed micelles, while rat pharmacokinetics demonstrated 7-fold bioavailability increase (Cmax 280 ng/mL at 3h vs. 40 ng/mL at 6h). Colitis models showed 60% disease activity reduction with decreased inflammatory markers.[25]

Recent innovations include polyvinyl alcohol-stabilized nanoparticles (100 nm, PDI <0.2, -25 mV zeta potential) prepared by high-pressure homogenization.[26] In vitro dissolution increased 10-fold compared to crude extract (85% vs. 15% in 30 minutes), with rat pharmacokinetics showing 8-fold bioavailability increase (Cmax 320 ng/mL at 2 hours). Carrageenan-induced paw edema inhibition was 75% versus 40% for conventional extract, confirming enhanced anti-inflammatory delivery.[26]

Nguyen and colleagues (2025) reported novel oil-in-water-in-oil double emulsions for transdermal curcumin delivery using medium-chain triglycerides and Span 80 emulsifier.[27] Internal droplet size was 200 nm with 3-month stability. Franz diffusion cell studies demonstrated 5-fold higher transdermal flux (12 µg/cm²/h) with 40% skin retention after 8 hours. Sustained release occurred over 24 hours with zero-order kinetics, with no irritation in rabbit testing, indicating suitability for topical anti-inflammatory and wound healing applications.[27-33]

Formulating natural sources and herbal extracts as advanced drug delivery systems that have been developed and formulated in different pharmaceutical dosage forms and therapeutic doses appropriate to the

type of diseases such as acute, chronic, or emergency cases and the principles and strategies of treating them, whether direct, auxiliary, or preventive treatment. They are distinguished by their safe and effective natural drug use according to scientific studies determined by pharmacognosy and pharmaceutical formulation Scientists.[34-39]

6. DISCUSSION

This narrative review synthesizes substantial evidence supporting the pharmaceutical development of *P. odoratissimus* peduncle and *C. longa* as therapeutic agents for diverse clinical applications. Both botanicals demonstrate multitargeting pharmacological profiles that align with complex disease pathophysiology, particularly in chronic inflammatory conditions, metabolic disorders, and cancer.

Pandanus odoratissimus peduncle exhibits a unique therapeutic profile combining anti-inflammatory, urological, and hepatoprotective activities with exceptional safety margins. The 59% reduction in ALT and 68% edema inhibition observed in preclinical models, combined with absence of toxicity up to 5 g/kg, position this botanical as a candidate for pediatric enuresis and liver protection indications where conventional therapies carry significant adverse effect burdens. The development of age-appropriate formulations—particularly orodispersible tablets with 25-second wetting times and 95% dissolution within 15 minutes—addresses critical compliance challenges in pediatric populations. However, clinical translation requires standardized extraction protocols ensuring consistent phenolic content (targeting 15% total phenolics) and prospective clinical trials validating efficacy in nocturnal enuresis and drug-induced hepatotoxicity.

Curcuma longa presents a more complex development trajectory. Despite extensive pharmacological validation—including NF-κB inhibition, epigenetic modulation, and antioxidant effects—clinical efficacy has been constrained by bioavailability limitations. The 40-185-fold increase in plasma levels achieved through nanoformulations represents a paradigm shift in curcumin therapeutics. PLGA nanoparticles, solid lipid nanoparticles, and liposomal formulations not only enhance pharmacokinetics but enable targeted delivery to tumor sites, with 3-fold increased accumulation and 50-60% tumor volume reduction in xenograft models. The convergence of enhanced bioavailability with targeted delivery suggests potential for curcumin as an adjunct in cancer chemotherapy, particularly in pancreatic, prostate, and colon malignancies.

Comparative analysis reveals distinct formulation challenges: *P. odoratissimus* requires stability optimization and palatability enhancement for pediatric compliance, while *C. longa* necessitates bioavailability enhancement through nanotechnology. Both botanicals benefit from quality control standardization—*P. odoratissimus* through phenolic content specification and *C. longa* through curcuminoid standardization.

Limitations of current evidence include reliance on preclinical models for *P. odoratissimus* and limited large-scale clinical trials for optimized curcumin formulations. Future research should prioritize randomized controlled trials investigating *P. odoratissimus* in pediatric nocturnal enuresis and drug-induced liver injury, alongside phase II/III trials of bioavailable curcumin in cancer supportive care and inflammatory arthropathies. Regulatory considerations for botanical drug products, including New Drug Application pathways and quality control specifications, require careful navigation to achieve clinical translation.

7. CONCLUSION

The pharmacological and formulation research reviewed herein establishes *Pandanus odoratissimus* peduncle and *Curcuma longa* as viable candidates for pharmaceutical development. *P. odoratissimus* offers a favorable safety profile with demonstrated efficacy in inflammation, urological dysfunction, and hepatoprotection, supported by innovative pediatric formulations. *C. longa*, enhanced through advanced nanodelivery systems, overcomes historical bioavailability limitations to realize its multitargeting therapeutic potential. Integration of traditional medicine knowledge with modern pharmaceutical technology—exemplified by the formulation strategies presented—provides a template for evidence-based botanical drug development. Clinical validation studies and regulatory-compliant manufacturing processes represent the critical next steps toward therapeutic application.

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