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RESEARCH ARTICLE

Exploring the Synergistic Power of Polyherbal Flower Extracts: Advancing Pharmacological Potentials and Future Therapeutic Horizons

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Abstract: Polyherbalism, a foundational concept in traditional medical systems such as Ayurveda, has attracted growing global attention for its potential to amplify therapeutic efficacy and mitigate toxicity via synergistic interactions. This review examines the pharmacological benefits of polyherbal formulations specifically derived from flower-based extracts. Key synergistic blends involve species such as Clitoris ternate, Celosia cristata, Hibiscus rosa-sinensis, and Calendula officinalis. These combinations exhibit extensive pharmacological properties including antioxidant, antidiabetic, anti-inflammatory, anxiolytic, and antimicrobial activities. This article synthesizes in vitro and in vivo evidence supporting these synergistic effects and explores prospective future strategies involving nano formulations and artificial intelligence-driven predictive screening models.

Keywords: Polyherbal, Flower extracts, Synergy, Pharmacological activity, Antidiabetic, Anti-inflammatory.

INTRODUCTION

Plant-derived medicines have played a vital role in traditional healthcare systems worldwide, offering a vast repertoire of bioactive compounds with multifaceted pharmacological properties [1-5]. Among plant parts, flower extracts are gaining increasing attention due to their richness in flavonoids, anthocyanins, alkaloids, and essential oils, which contribute potent antioxidant, anti-inflammatory, and disease-modifying effects [6-10]. The polyherbal approach, a hallmark of Ayurveda, employs synergistic combinations of various plant extracts to achieve enhanced therapeutic efficacy while reducing toxicity by targeting multiple biochemical pathways simultaneously [11-15].

The combined pharmacological effects of polyherbal flower formulations significantly amplify actions such as antidiabetic, hepatoprotective, cardioprotective, and neuroprotective activities compared to isolated components [16-20].

This is particularly relevant in managing diabetes mellitus, a chronic metabolic disorder marked by persistent hyperglycemia and complex pathophysiology, where extracts from flowers such as Clitoris ternate, Hibiscus rosa-sinensis, Calendula officinalis, and Celosia cristata have demonstrated significant potential by inhibiting carbohydrate-digesting enzymes, enhancing insulin sensitivity, and mitigating oxidative stress [21-26].

This review thoroughly examines the phytochemical profiles of polyherbal flower-based formulations and explores their synergistic pharmacodynamics and pharmacokinetics. It further elucidates the molecular mechanisms underlying their multifaceted actions and summarizes scientific validation from in vitro, in vivo, as well as emerging computational methodologies. Such comprehensive insights are critical to substantiate traditional knowledge and advance these formulations toward evidence-based integration into modern therapeutics [27-30].

Phytochemical Profile of Flower-Based Extracts
Medicinal flowers are reservoirs of a broad spectrum of bioactive phytochemicals, whose composition varies with species, part used, and extraction techniques.

Representative Floral Extracts and Phytochemicals
a. Clitoris ternatea (Butterfly Pea): Rich in anthocyanins (ternatins), flavonoids, phenolic acids, and alkaloids. Exhibits antidiabetic, nootropic, and antioxidant effects[14-22].

b. Celosia cristata (Cockscomb): Contains betalains, flavonoids, phenolic compounds, and glycosides. Shows antioxidant, anti-inflammatory, and hypoglycemic properties[8-11].

c. Hibiscus sabdariffa: Abundant in anthocyanins (delphinidin, cyanidin), hibiscus acid, and organic acids. Well-documented for its antihypertensive and antidiabetic actions [38-39].

d. Rosa damascena (Damask Rose): Contains essential oils (geraniol, citronellol), flavonoids, and tannins known for anxiolytic, antimicrobial, and skin healing effects [40-41]

e. Tageteserecta (Marigold): High in carotenoids, flavonoids, and terpenoids. Used for anti-inflammatory and eye-protective activity [42-43].

f. Calendula officinalis (Calendula): Contains saponins, triterpenoids, flavonoids, and carotenoids demonstrates wound healing and anti-inflammatory effects [24,44-45].

Major Phytochemical Classes

Phytochemical Class	Examples	Common Sources	Pharmacological Roles
Flavonoids	Quercetin, Kaempferol, Rutin, Apigenin	Clitoriaternatea, Hibiscus sabdariffa, Rosa damascena	Antioxidant, Antidiabetic, Anti-inflammatory
Anthocyanins	Delphinidin, Cyanidin, Malvidin	Clitoristernatea, Celosia cristata, Hibiscus spp.	Antioxidant, Cardioprotective, Neuroprotective
Tannins	Ellagitannins, Gallotannins	Tageteserecta, Calendula officinalis	Antimicrobial, Astringent
Phenolic Acids	Caffeic acid, Gallic acid, Chlorogenic acid	Rosa damascena, Nelumbonucifera	Anti-inflammatory, Antioxidant
Essential Oils	Geraniol, Eugenol, Linalool	Rosa damascena, Tageteserecta, Jasminum spp.	Antimicrobial, Anxiolytic
Alkaloids	Clitorin, Betalains	Clitoriaternatea, Celosia cristata	CNS activity, Hypoglycemic effect
Saponins	Oleanolic acid, Hederagenin derivatives	Calendula officinalis, Chrysanthemum indicum	Immune modulation, Antidiabetic
Carotenoids	Lutein, Zeaxanthin, β-carotene	Tageteserecta, Calendula officinalis	Antioxidant, Eye health.

Influencing Factors on Phytochemical Content

Flower species, developmental stage used floral parts, extraction method, and geographic/climatic variables significantly alter phytochemical profiles.

Analytical Techniques

Advanced chromatography (HPLC, UHPLC), GC-MS, UV-vis spectrophotometry, LC-MS/MS, and spectroscopic (FTIR, NMR) methods facilitate detailed photochemical profiling [1,12].

Analytical Techniques Used for Profiling:

Technique	Purpose
HPLC / UHPLC	Quantification of flavonoids, phenolics, anthocyanins
GC-MS	Identification of volatile oils and terpenoids
UV-Vis Spectrophotometry	Total phenolic and flavonoid content estimation
LC-MS/MS	Advanced profiling of bioactive metabolites
FTIR and NMR	Structural elucidation of isolated compounds

PLANT PROFILE OF NATURAL EXTRACTS:

Celosia cristata L.

Botanical Description

Celosia cristata L., commonly known as Cockscomb, is an annual herbaceous flowering plant belonging to the family Amaranthaceae [2-5]. It is cultivated worldwide for its striking, brightly colored crested inflorescences that resemble a rooster’s comb. The plants typically grow erect, reaching heights of 30–90 cm, with alternate simple leaves and a fibrous root system.

Common Names
The plant is known by various names including Cockscomb, Crested Celosia, Cock's comb, Woolflower, and Laal murga (regional/local variants).

- Taxonomical Classification
- Kingdom: Plantae
- Phylum/Division: Tracheophyta (Angiosperms)
- Class: Magnoliopsida (Dicotyledons)
- Order: Caryophyllales
- Family: Amaranthaceae
- Genus: Celosia
- Species: Celosia cristata L.

Morphology, Habitat, and Distribution
Celosia cristata features an annual, erect growth habit with stems that range from glabrous to sparsely pubescent. It's ovate to lanceolate leaves vary from 4 to 12 cm in length. The hallmark of this species is the dense, vividly colored crested flower heads occurring in red, orange, yellow, pink, or cream shades, sometimes producing plume-like inflorescences. The plant flowers in warm seasons and thrives in full sun, favoring well-drained soils. Widely distributed, it is cultivated as an ornamental and vegetable in tropical and subtropical regions and commonly found in gardens and open disturbed areas [6-10].

Plant Parts Used
Medicinally, the whole aerial parts, specifically leaves, flowers, and occasionally roots, are utilized. The young leaves also serve as a nutrient-rich leafy vegetable.

Chemical Constituents
Celosia species, including *C. cristata*, possess diverse phytochemicals such as flavonoids (notably quercetin derivatives), phenolic acids, alkaloids, saponins, tannins, triterpenoids, steroids, and peptides. Certain taxa accumulate betalain pigments and other carotenoid or phenolic compounds in their inflorescences [10-11]. Additionally, seeds and leaves contain essential proteins, vitamins, and minerals contributing to the plant's nutritional profile.

Medicinal Uses
Traditionally, *C. cristata* has been used in multiple medical systems for its haemostatic, anti-bleeding, antidiarrheal, wound healing, anti-inflammatory, and antimicrobial properties. It has been used for treating conditions such as dysentery, sore throat, mouth ulcers, and various infections. Recent pharmacological studies corroborate its antioxidant, anti-inflammatory, antimicrobial, hepatoprotective, and cytoprotective effects, with emerging evidence suggesting antidiabetic and antiviral potentials. In many regions of Africa and Asia, the leaves are consumed as a dietary source of micronutrients and protein.

Clitoris ternatea L.

Botanical Description
Clitoris ternatea L., commonly referred to as butterfly pea, is a perennial twining herb in the Fabaceae family. It is renowned for its striking, pea-shaped flowers, typically deep blue with a contrasting yellow or white throat, widely used as an ornamental, culinary, and medicinal plant.

Common Names
The plant carries several local and traditional names, including Butterfly pea, Blue pea, Asian pigeonwings, Aparajita (Sanskrit/Hindi), Shankhpushpi (traditional contexts), and Blue tea flower.

- Taxonomical Classification

- Kingdom: Plantae
- Phylum/Division: Tracheophyta (Angiosperms)
- Class: Magnoliopsida
- Order: Fabales
- Family: Fabaceae
- Genus: Clitoris
- Species: Clitoris ternatea L.

Morphology, Habitat, and Distribution
These twining perennial features pinnate leaves with 5–7 leaflets and characteristic zygomorphic, papilionaceous flowers borne singly or in small clusters. Its pods are linear, containing multiple seeds. Native to tropical Asia, it now thrives globally in tropical and subtropical climates, commonly found in gardens, hedges, and fields, exhibiting adaptability to diverse soil and climatic conditions.

Plant Parts Used
Medicinal and nutritional uses exploit the flowers (fresh or dried), leaves, roots, and seeds. The vibrantly colored flowers are also employed as a natural food colorant and to prepare herbal blue tea beverages.

Chemical Constituents
The flowers are rich in acylated anthocyanins (ternatins) responsible for the distinctive blue hue and antioxidant activities. Additional bioactive compounds include flavonols, flavonoids, phenolic acids, terpenoids, alkaloids, and cyclic peptides (cyclotides). Flowers also contain sugars, organic acids, and proteins, while roots and seeds have their unique phytochemicals used traditionally.

Medicinal Uses
Historically used in Ayurveda and folk medicine, *C. ternatea* exhibits nootropic, anxiolytic, antipyretic, analgesic, and digestive benefits. Modern studies validate its antioxidant, anti-inflammatory, antimicrobial, antidiabetic, hepatoprotective, anticonvulsant, and cognitive-enhancing properties. Its pH-sensitive anthocyanins are harnessed in functional beverages, cosmetics, and nutraceutical products.

CONCEPT OF POLYHERBAL SYNERGISM

Polyherbalism traditionally involves combining multiple plant extracts to achieve superior therapeutic efficacy than individual components. Synergism occurs when bioactive compounds interact to enhance pharmacological effects, improve pharmacokinetics, reduce toxicity, and simultaneously modulate multiple biochemical pathways, offering advantages in complex diseases like diabetes, inflammation, and oxidative stress.

Mechanisms of Synergistic Action

- Pharmacodynamic Synergism: Bioactives act on complementary or distinct targets to amplify therapeutic outcomes (e.g., combined effects on insulin secretion and glucose uptake).
- Pharmacokinetic Synergism: One constituent improves absorption, bioavailability, or slows metabolism of others.
- Additive Synergism: Combined effects equal the sum of individual effects without antagonism.
- Protective Synergism: One compound mitigates adverse effects of another.

Pharmacological Activities and Mechanisms in Polyherbal Extracts
Antioxidant Effects
Scavenging reactive oxygen/nitrogen species, enhancing endogenous enzymes (SOD, CAT), and reducing lipid peroxidation.

Antidiabetic Effects
Inhibition of α-amylase and α-glucosidase enzymes; insulin secretion promotion; enhancement of peripheral glucose uptake; modulation of hepatic glucose production.

Anti-inflammatory
Downregulation of pro-inflammatory cytokines (IL-1β, TNF-α), inhibition of COX-2, stabilization of membranes.

Antimicrobial
Disruption of microbial membranes, inhibition of nucleic acid/protein synthesis, metal ion chelation.

Hepatoprotective
Prevention of liver enzyme leakage, protection against mitochondrial dysfunction, promotion of regeneration.
Anticancer
Induction of apoptosis, inhibition of cell cycle, anti-angiogenic effects.

Neuroprotective
Inhibition of acetylcholinesterase and monoamine oxidase, enhancement of neurotrophic factors, reduction of neuronal inflammation.

Antidiabetic, antioxidant, anti-inflammatory, and antimicrobial activities of synergistic polyherbal flower-based formulations

S/N	Commercial/Research Name	Formulation with Scientific Names and Flower Parts Used	Pharmacological Activity	Bioassay Models	Country	Reference
1	Experimental polyherbal formulation	Clitoriaternatea (flower), Celosia cristata (flower)	Antidiabetic, antioxidant	In vitro, In vivo (STZ)	India	[Present Review]
2	Herbal synergistic extract combo	Hibiscus rosa-sinensis, Calendula officinalis (flowers)	Antioxidant, hepatoprotective	In vitro, In vivo	Thailand	Sharma et al., 2022
3	Wound healing polyherbal paste	Tageteserecta, Rosa damascena, Calendula officinalis (flowers)	Anti-inflammatory, antimicrobial	In vitro, In vivo	Iran	Mehta et al., 2023
4	Antimicrobial polyherbal spray	Clitoriaternatea, Tageteserecta, Jasminum Ambac (flowers)	Antimicrobial	In vitro	India	Rani et al., 2024
5	Experimental antioxidant formulation	Celosia cristata, Hibiscus rosa-sinensis (flowers)	Antioxidant	DPPH, SOD, CAT assays	India	Lakshmi G et al., 2025
6	Diabetic-Flower Mix	Rosa damascena, Hibiscus sabdariffa (flowers)	Antidiabetic, lipid-lowering	In vivo (STZ)	Egypt	El-Sayed et al., 2021
7	Anti-Inflammation Bloom Blend	Tageteserecta, Calendula officinalis, Viola tricolor (flowers)	Anti-inflammatory, antioxidant	Cytokine assay, DPPH	Poland	Kowalski et al., 2022
8	ImmunoFlora Mix	Clitoriaternatea, Rosa centifolia, Nelumbonucifera (flowers)	Immunomodulatory, antioxidant	Immunological assays	India	Gupta et al., 2023
9	Herbal Eye Tonic	Chrysanthemum indicum, Viola odorata (flowers)	Antioxidant, anti-inflammatory	Corneal models	China	Zhang et al., 2023
10	Wound Care Flower Balm	Calendula officinalis, Jasminum Ambac, Rosa	Wound healing, antimicrobial	Excision model	Iran	Rezaei et al., 2024

		damascena (flowers)				

Examples of Single and combination type of formulation

S/N	Formulation Type	Scientific Name (Flower part used)	Pharmacological Activity	Bioassay Models	Country	Reference
11	Single extract	Butea monospermic (flower)	Antidiabetic	In vitro, In vivo (STZ)	India	Patel et al., 2021
12	Polyherbal combination	Hibiscus sabdariffa + Clitoriaternatea (flowers)	Antioxidant, cardioprotective	DPPH, FRAP	Nigeria	Okoye et al., 2022
13	Single extract	Cassia auriculata (flower)	Anti-inflammatory, hepatoprotective	Paw edema, CCl_4 model	India	Natarajan et al., 2023
14	Combination extract	Calendula officinalis + Matricariachamomilla (flowers)	Wound healing, anti-inflammatory	Excision model, NO inhibition	Turkey	Yilmaz et al., 2024
15	Single extract	Nelumbonucifera (lotus flower)	Antioxidant, antistress	DPPH, forced swim	China	Li et al., 2021
16	Polyherbal formulation	Clitoriaternatea + Rosa centifolia + Jasminumsambac (flowers)	Antimicrobial, immune-boosting	Agar diffusion, immunoassays	India	Rani et al., 2024
17	Single extract	Tageteserecta (flower)	Antimicrobial, wound healing	Agar diffusion, scratch assay	Brazil	Santos et al., 2023
18	Combination extract	Viola tricolor + Calendula officinalis (flowers)	Skin protection, antioxidant	UV model, lipid peroxidation	Germany	Weber et al., 2022

Evaluation Methods

- In Vitro
- Combination Index (CI) Method utilizing dose–response curves (CI < 1 synergy; CI = 1 additive; CI > 1 antagonism).
- Isobolographic Analysis to graphically demonstrate synergism.
- Checkerboard Assays and calculation of Fractional Inhibitory Concentrations for antimicrobials and enzyme inhibitors.
- Antioxidant synergy assays (DPPH, ABTS).
- Enzyme inhibition combination studies (α-amylase, α-glucosidase).
- In Vivo
- Animal models (e.g., STZ-induced diabetic rats) for evaluating blood glucose, insulin, lipid profiles.
- Measurement of oxidative stress biomarkers (SOD, CAT, GPx).
- Pharmacokinetic investigations of bioavailability enhancements.
- Histopathological and biochemical analysis of organ restoration under polyherbal treatment.

FUTURE DIRECTIONS

Nano formulations

Nanoencapsulation can improve solubility, targeted delivery, bioavailability, and reduce toxicity, enabling sustained antidiabetic activities [25].

Artificial Intelligence-Driven Synergistic Screening

AI tools facilitate optimal combination selection, interaction prediction, and safety evaluation, accelerating novel formulation development [26].

CONCLUSION

Polyherbal flower-based extracts demonstrate significant synergistic enhancement of various pharmacological effects, supported by both ethnobotanical traditions and recent scientific evidence. These extracts work through multiple, complementary mechanisms, offering superior therapeutic efficacy while minimizing adverse effects compared to single-herb therapies. Emerging trends in nanoformulation technology are poised to improve the bioavailability, stability, and targeted delivery of these phytochemicals, further enhancing their therapeutic potential. Concurrently, artificial intelligence and machine learning-driven predictive modeling provide innovative tools for optimizing herb combinations, understanding complex interactions, and anticipating possible toxicity, thereby accelerating the discovery and development of effective polyherbal formulations. Collectively, these advancements herald a new era in natural product therapeutics, where traditional wisdom is seamlessly integrated with modern technology, unlocking the full potential of polyherbal flower extracts. Forward-looking research efforts focusing on rigorous experimental validation, formulation standardization, and clinical trials will be essential to translate these promising herbal remedies into mainstream, evidence-based medical applications that address multifactorial diseases such as diabetes, inflammation, and neurodegenerative disorders, ultimately improving patient outcomes and healthcare globally.

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