A Review on the Anthelmintic Potential of Embelia ribes and Its Application in Herbal Medicated Lozenges

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Abstract—**Helminthiasis remains a major global public health challenge, particularly in tropical and subtropical regions, with millions affected by intestinal parasitic infections. The growing limitations of conventional anthelmintic agents, including drug resistance and adverse effects, necessitate the exploration of safe, effective, and patient-friendly alternatives. Embelia ribes Burm. F. (Xyridaceae), commonly known as Vidanga or false black pepper, is a well-documented medicinal plant in Ayurvedic medicine recognized for its potent anthelmintic properties attributed primarily to its bioactive compound embelin (2,5-dihydroxy-3-undecyl-1,4-benzoquinone). This review comprehensively discusses the botanical characteristics, phytochemical constituents, pharmacological activities, and mechanisms of anthelmintic action of Embelia ribes. Furthermore, the review explores the formulation of herbal medicated hard candy lozenges incorporating ethanolic extract of Embelia ribes as a novel, convenient dosage form with improved patient compliance, particularly for pediatric and geriatric populations. Reformulation studies, physicochemical characterization, in-vitro dissolution profiles, drug-excipient compatibility (FTIR), and stability outcomes of the optimized lozenge formulation are critically reviewed. The optimized formulation (F5) demonstrated a drug release of 94.02% within 30 minutes with stable physicochemical parameters over a 3-month accelerated stability study. The review underscores the promising potential of Embelia ribes-based medicated lozenges as a herbal alternative for helminthiasis management and identifies areas warranting further in vivo and clinical validation.**

Index Terms—**Anthelmintic activity, Embelia ribes, Embelin, Helminthiasis, Herbal medicated lozenges, Oral drug delivery, Vidanga.**

I. INTRODUCTION

Helminthiasis, a collective term for infections caused by parasitic helminths (worms), constitutes one of the most prevalent and neglected tropical diseases globally. The World Health Organization estimates that over 1.5 billion people, nearly 24% of the global population, are infected with soil-transmitted helminths (STHs) including Ascaris lumbricoides, Trichuris trichiura, and hookworms (Ancylostoma duodenale and Necator americanus). These infections disproportionately affect resource-limited settings with poor sanitation and limited access to clean water [1,2].

The clinical consequences of helminthiasis span a wide spectrum from mild gastrointestinal discomfort and nutritional deficiencies to severe outcomes including anemia, impaired cognitive development in children, growth stunting, and in some cases, long-term organ damage. The global economic burden attributable to lost productivity and healthcare expenditure is substantial, making helminthiasis a significant contributor to the cycle of poverty in endemic regions [3].

Current standard-of-care pharmacotherapy for helminthiasis relies predominantly on a small portfolio of synthetic anthelmintic drugs, principally albendazole, mebendazole, praziquantel, and ivermectin. While these drugs are effective when used appropriately, persistent challenges limit their long-term utility: emerging drug resistance, limited efficacy against all lifecycle stages, high costs in resource-limited settings, and poor palatability and patient compliance, especially in pediatric populations. These limitations have prompted an urgent need to investigate novel, complementary therapeutic

strategies grounded in the rich biodiversity of medicinal plants [1,3].

Embelia ribes Burm. F., a large scandent woody climber belonging to the family Xyridaceae, has held a prominent place in traditional Ayurvedic medicine for centuries. Known vernacularly as Vidanga or Vai Vidanga and commonly referred to as false black pepper due to its fruit resemblance to Piper nigrum, E. ribes is classified as one of the foremost anti-parasitic herbs in classical Ayurvedic texts. Its dried ripe fruits have been used traditionally to treat intestinal worm infestations, digestive disorders, skin diseases, and respiratory ailments [4,5].

The principal bioactive constituent responsible for the anthelmintic and diverse pharmacological activities of E. ribes is embelin, a benzoquinone derivative (2,5-dihydroxy-3-undecyl-1,4-benzoquinone, C17H26O4, MW 294.39 g/mol). Embelin has been extensively investigated for its anthelmintic, antimicrobial, antioxidant, anti-inflammatory, anticancer, and hepatoprotective properties. Despite promising preclinical evidence, E. ribes has not yet been formulated into modern, patient-acceptable dosage forms that maximize therapeutic benefit and patient compliance [4,6].

Medicated lozenges represent a compelling dosage form innovation for herbal drugs, particularly in populations with swallowing difficulties. As a solid oral mucosal drug delivery system, lozenges offer controlled drug release directly in the oral cavity, bypass hepatic first-pass metabolism, improve bioavailability, reduce gastric irritation, and significantly enhance palatability and patient adherence factors critical for pediatric and geriatric populations [7,8].

This review synthesizes current knowledge on E. ribes' botanical profile, phytochemistry, anthelmintic pharmacology, and mechanistic underpinnings, and critically appraises the scientific rationale and published evidence for its formulation as herbal medicated hard candy lozenges for helminthiasis management.

II. BOTANICAL DESCRIPTION AND TAXONOMY

A. Classification and Distribution

Embelia ribes Burm. F. is a large, straggling woody climber classified under the family Myrsinaceae, genus Embelia. It was first formally described by Nicolas Laurens Burman in his seminal 1768 work Flora Indica. The plant is native to the Indian subcontinent, distributed across the Central and Lower Himalayas, extending southward to Ceylon (Sri Lanka), eastward through Arunachal Pradesh, Assam, Bengal, and Odisha, and further to Singapore, Southern China, and Indonesia. It is also identified in Malayan estates and parts of East Africa. Within India, it is commonly encountered in semi-evergreen and moist deciduous forests at altitudes reaching up to 1,500 meters (approximately 5,000 ft) [4,5].

B. Morphological Features

The plant is a large scandent shrub with long, slender, brittle, terete branches covered with whitish-grey bark studded with prominent lenticels. Its mature girth ranges from 45 to 72 cm. Leaves are simple, alternate, coriaceous, elliptic-ovate-lanceolate, perfectly glabrous, gland-dotted, measuring approximately 3 inches in length and 1.5 inches in breadth, shiny on the upper surface. Flowers are small, greenish-yellow to whitish-pink, borne in terminal racemes. The fruits are small, globular, approximately the size of white pepper, reddish-brown to blackish in color with a fragile outer covering enclosing a spotted seed [4,5].

C. Ayurvedic Properties

In Ayurvedic pharmacology, E. ribes (Vidanga) possesses the following properties: Guna — Laghu, Ruksha, Tikshan; Rasa — Katu, Kashay; Vipak — Katu; Virya — Ushan (hot); Prabhav — Krimighan (antiparasitic). It is considered one of Ayurveda's most potent anti-parasitic medicines. Ancient Arabian writings reference it as birang-i-kabauli, a traditional remedy for tapeworm infestations [4].

III. PHYTOCHEMISTRY OF EMBELIA RIBES

A. Major Bioactive Constituents

The berries and other parts of E. ribes are rich in diverse phytochemical classes. The most pharmacologically significant constituent is embelin (2,5-dihydroxy-3-undecyl-1,4-benzoquinone), a naturally occurring benzoquinone derivative that constitutes the primary bioactive scaffold responsible for the plant's anthelmintic and other pharmacological activities. Embelin has a molecular formula of C17H26O4, molecular weight 294.39 g/mol,

occurring as a yellow to orange crystalline powder with a melting point of approximately 144–146°C [4,6].

Beyond embelin, the plant contains volatile oils, fixed oils, resins, tannins, and phenolic acids. Other bioactive polyphenolics include quercetin, a flavonoid with significant antioxidant and anti-inflammatory properties, and gallic acid, a polyphenolic compound recognized for potent antioxidant activity [5].

B. Phytochemical Screening Outcomes

Preliminary phytochemical screening of ethanolic extracts of E. ribes yielded positive results for alkaloids (Wagner's and Iodine tests), tannins (Braymer's, NaOH, lead acetate, and picric acid tests), and glycosides (Fehling's solution). Amino acids were absent. These findings corroborate the chemical complexity of E. ribes extracts and underscore the contribution of multiple compound classes to its pharmacological profile [5].

IV. ANTHELMINTIC POTENTIAL AND MECHANISM OF ACTION

A. Evidence of Anthelmintic Activity

The anthelmintic activity of E. ribes is documented in both classical Ayurvedic tradition and modern preclinical research. Swarnkar and Singh (2009) demonstrated the anthelmintic potential of E. ribes seeds against Haemonchus contortus in sheep, providing compelling in vivo evidence for its efficacy against economically significant nematode parasites. Embelin has been shown to exert antiparasitic effects against a spectrum of intestinal helminths including roundworms and tapeworms [6].

B. Proposed Mechanisms of Action

The following mechanisms have been proposed based on available pharmacological evidence:

1. Mitochondrial Dysfunction: Embelin disrupts mitochondrial electron transport in parasitic cells, impairing ATP production and causing parasite death through energy depletion.

2. Oxidative Stress Induction: Embelin may selectively generate reactive oxygen species (ROS) within parasitic cells, inducing oxidative stress beyond their antioxidant defense capacity.

3. Anti-inflammatory Modulation: Inhibition of pro-inflammatory mediators and COX enzymes reduces parasite-induced host tissue damage.

4. Disruption of Reproductive Biology: Embelin interferes with helminth reproductive processes, reducing egg output and larval development, thus limiting transmission.

5. Membrane Disruption: The quinone scaffold of embelin may interact with lipid bilayers of parasite cell membranes, compromising membrane integrity and ion transport.

C. Comparative Pharmacological Activities

Beyond anthelmintic activity, E. ribes extract demonstrates significant antimicrobial activity against both Gram-positive and Gram-negative bacteria and various fungi. Its antioxidant capacity reflects the polyphenolic richness of the extract. Anti-inflammatory activity has been confirmed through inhibition of pro-inflammatory enzymes in standard in vitro models [4,5].

V. ORAL MUCOSAL DRUG DELIVERY: RATIONALE FOR LOZENGES

A. Oral Mucosal Drug Delivery Systems

The oral mucosal route represents an important portal for both local and systemic drug delivery. The oral mucosa offers a highly vascularized, accessible, and relatively permeable surface with a cellular turnover time of 4–14 days. Drugs absorbed across the oral mucosa drain directly into the jugular vein, bypassing the portal circulation and hepatic first-pass metabolism, thereby improving bioavailability for susceptible drugs [13,14].

Drug permeation across the oral mucosa occurs via two pathways: paracellular diffusion through intercellular spaces and transcellular diffusion across cell membranes, governed by the physicochemical properties of the drug. The oral mucosal surface, approximately 100 cm^2 in total area, is classified into keratinized and non-keratinized regions [15,16].

B. Medicated Lozenges as a Dosage Form

Lozenges are flavoured, sweetened, solid unit dosage forms intended to be slowly dissolved in the oral cavity, delivering drug to the local mucosal surface or

for systemic absorption. Key advantages include: ease of administration without water (ideal for dysphagic, pediatric, and geriatric patients); improved patient compliance due to palatability; extended oral retention time; potential bypass of first-pass hepatic metabolism; reduced gastrointestinal irritation; and improved bioavailability [7,9,10].

C. Types of Lozenges

Medicated lozenges are classified into: (a) Hard candy lozenges prepared by heating and congealing a sugar-based matrix; (b) Compressed tablet lozenges (troches); (c) Chewy or caramel-based lozenges; and (d) Soft lozenges formulated with polyethylene glycol bases. Hard candy lozenges are particularly suited to herbal extracts as the heat-congealing process allows incorporation of 2–4% drug in a sugar-glucose matrix [11].

VI. FORMULATION OF EMBELIA RIBES MEDICATED HARD CANDY LOZENGES

A. Procurement and Extraction

Embelia ribes crude powder was procured from Kshipra Biotech Pvt. Ltd., Indore, Madhya Pradesh, with a Certificate of Analysis confirming botanical identity. Ethanolic extraction was performed using Soxhlet apparatus—selected for its broad-spectrum phytochemical extraction efficiency. The extract was concentrated using a rotary evaporator and the semi-solid concentrated extract was used for formulation after complete characterization [5].

B. Reformulation Studies

Organoleptic Properties: The ethanolic extract of E. ribes presented as a dark brown to black crystalline powder with a strong, slightly pungent odor, bitter and astringent taste, and fine powdery texture—consistent with published pharmacogenetic monographs.

Melting Point: Determined by capillary method, the extract exhibited a melting point range of approximately 383–387°C, indicating robust thermal stability under the processing temperatures employed in hard candy lozenge preparation.

Solubility Profile: The extract demonstrated partial solubility in water, moderate solubility in acetone, and complete solubility in both methanol and ethanol, supporting its suitability for incorporation into aqueous sugar-based lozenge matrices.

C. UV Spectrophotometric Analysis

A lambda-maximum (λmax) of 289 nm was established for embelin in phosphate buffer pH 6.8. A calibration curve over 10–90 µg/mL demonstrated excellent linearity: $y = 0.0963x - 0.0193$, $R^2 = 0.9963$, confirming compliance with Beer-Lambert's law. This validated method was used for all subsequent drug quantification [5].

D. Drug-Excipient Compatibility (FTIR)

FTIR spectroscopy using Perkin Elmer Shimadzu Alpha (400–4000 cm^{-1}) confirmed characteristic peaks of E. ribes extract: N-H stretch at 3402 cm^{-1}, N-H bend at 1600 cm^{-1}, C-N stretch at 1278 cm^{-1}, C-Cl stretch at 568 cm^{-1}, and O-H stretch at 3225 cm^{-1}. Physical mixtures with HPMC K100, HPMC E5, and all combined excipients showed no disappearance or shift of characteristic peaks, confirming complete physicochemical compatibility [5].

E. Formulation Design and Composition

Six hard candy lozenge formulations (F1–F6) were developed by heat-congealing technique. Each lozenge contained 100 mg E. ribes ethanolic extract per 1500 mg unit, with sucrose as the confectionary base, dextrose or mannitol as sweetener/diluent, HPMC K100 or HPMC E5 (15, 23, or 30 mg) as release-controlling polymer, citric acid (23 mg) as acidulant, and mint flavor and Amaranth color (qs).

Table I: Formulation Composition of E. ribes Hard Candy Lozenges (mg/unit)

Ingredient	F1	F2	F3	F4	F5	F6
E. ribes Extract	100	100	100	100	100	100
Sucrose	1005	998	991	1005	998	991
Mannitol	500	500	500	—	—	—
Dextrose	432	432	432	—	—	—
HPMC K100	15	23	30	—	—	—
HPMC E5	—	—	—	15	23	30
Citric Acid	23	23	23	23	23	23
Flavor	qs	qs	qs	qs	qs	qs

F. Manufacturing Process

Sucrose was dissolved in water and heated to prepare a clear syrup; dextrose or mannitol was dissolved separately and heated to 110°C; both solutions were

combined and heated to 160°C until a golden-yellow color developed. Temperature was reduced to 90°C and E. ribes extract, polymer, citric acid, color, and flavor were incorporated with thorough mixing. The molten mass was poured into candy molds, cooled, wrapped in aluminum foil, and stored in desiccators [5].

VII. EVALUATION PARAMETERS AND RESULTS

A. Physicochemical Evaluation

All six formulations were evaluated for hardness (Monsanto hardness tester), thickness (Vernier calipers), weight variation (n=20), friability (Roche friabilator, 100 rotations), disintegration time (artificial saliva pH 5.8, 37°C), and drug content (UV at 289 nm).

Table II: Physicochemical Evaluation of All Formulations

Batch	Hardness (kg/cm²)	Thickness (mm)	Avg. Wt (mg)	Friab. (%)	Disint. (min)	Drug Cont. (%)
F1	9.26±0.37	7.12±0.08	1500±0.12	0.62	9.02±0.75	96.02±0.88
F2	10.29±0.43	7.11±0.07	1498±0.24	0.78	9.20±0.43	96.16±2.52
F3	10.07±0.06	7.13±0.09	1500±0.09	0.72	10.02±0.28	95.55±1.56
F4	10.29±0.43	7.11±0.07	1501±0.14	0.50	9.12±0.31	94.46±2.65
F5*	10.50±0.28	7.20±0.04	1500±0.10	0.71	10.18±0.51	97.12±1.50
F6	10.69±0.50	7.15±0.02	1499±0.32	0.76	10.56±1.25	96.10±2.32

*F5: Optimized formulation. n=3; values = mean ± SD.

Hardness ranged from 9.26±0.37 to 10.69±0.50 kg/cm², indicating adequate mechanical strength. Thickness (7.11±0.07 to 7.20±0.04 mm) was uniform across all batches. Weight variation (1498±0.24 to 1501±0.14 mg) met pharmacopoeial specifications. Friability (≤0.78%) confirmed good mechanical integrity. Drug content uniformity (94.46– 97.12%) was within acceptable limits. Formulation F5 (HPMC E5 at 23 mg) demonstrated the most favorable parameter combination and was designated as the optimized formulation.

B. In-vitro Drug Release Studies

Dissolution studies were conducted using USP Type II paddle apparatus in 900 mL phosphate buffer pH 6.8 at 37±0.5°C and 100 rpm. Absorbance was measured spectrophotometrically at 289 nm at 5-minute intervals over 30 minutes.

Table III: Cumulative % Drug Release from All Formulations

Time (min)	F1	F2	F3	F4	F5*	F6
0	0	0	0	0	0	0
5	35.71	28.10	27.20	41.67	38.18	36.54
10	53.52	38.43	36.62	55.12	52.12	48.12
15	66.12	55.12	47.12	71.16	68.10	61.08
20	73.10	68.20	56.98	79.91	80.18	70.12
25	81.21	83.16	70.11	87.21	90.06	78.40
30	90.02	91.12	86.20	91.08	94.02	86.29

F5: Optimized formulation.

All formulations demonstrated satisfactory drug release with cumulative release at 30 minutes ranging from 86.20% (F3) to 94.02% (F5). Formulation F5 (HPMC E5 at 23 mg) exhibited the most rapid and complete release profile, attributed to the superior hydration and swelling characteristics of HPMC E5 facilitating uniform matrix erosion. F3 (HPMC K100 at 30 mg) showed slowest release, consistent with the higher viscosity grade forming a more resistant gel network.

C. Stability Studies

The optimized formulation F5 was subjected to accelerated stability testing per ICH Q1A(R2) guidelines at 40°C/75% RH for 3 months, with evaluations at 0, 1, 2, and 3 months.

Table IV: Stability Study Results for Optimized Formulation F5

Parameter	0 Month	1 Month	2 Months	3 Months
Hardness (kg/cm²)	10.50±0.28	10.45±0.20	10.30±0.20	10.12±0.10
Thickness (mm)	7.20±0.04	7.16±0.08	7.12±0.12	7.10±0.25
Weight (mg)	1500±0.10	1500±0.18	1500±0.22	1500±0.30
Friability (%)	0.71	0.78	0.82	0.95
Disint. (min)	10.18	10.10	9.30	9.20
Drug Cont. (%)	97.12±1.50	97.10±1.20	97.06±1.32	97.05±1.20
% Release/30 min	94.02	93.80	93.52	93.20

All parameters remained within pharmacopoeial acceptance criteria over the 3-month study. Drug content was maintained at 97.05±1.20% at month 3 (initial 97.12±1.50%). In-vitro release at 30 minutes reduced marginally from 94.02% to 93.20%, remaining above the 90% acceptance criterion. These findings confirm the physicochemical and chemical stability of the F5 formulation under ICH accelerated conditions.

VIII. DISCUSSION

This review highlights the compelling scientific basis for developing Embelia ribes-based herbal medicated lozenges as an alternative therapeutic modality for helminthiasis. The convergence of Ayurvedic tradition, ethnopharmacological evidence, and modern phytochemical and pharmacological research provides a multi-layered validation of E. ribes' anthelmintic potential. Embelin's multi-mechanistic antiparasitic profile could circumvent the mono-target limitations of conventional synthetic anthelmintics and potentially reduce resistance development.

The formulation strategy of incorporating E. ribes extract into a hard candy lozenge matrix is pharmacologically sound and patient-centric. The hard candy base (sucrose/dextrose system) provides palatability, structural integrity, and controlled dissolution. HPMC grades are GRAS excipients with well-established pharmaceutical applications, and their differential viscosity grades enabled fine-tuning of drug release kinetics across F1–F6 formulations.

The absence of drug-excipient interactions confirmed by FTIR spectroscopy ensures the chemical integrity of embelin and the predictability of its pharmacological activity. The stability over 3 months at ICH accelerated conditions further reinforces commercial viability. A significant gap is the absence of in vivo anthelmintic activity studies using the formulated lozenges; demonstration of efficacy in validated animal models and clinical trials will be essential for therapeutic claim substantiation.

IX. FUTURE PERSPECTIVES

1. In Vivo Pharmacological Validation: Systematic anthelmintic activity studies using the formulated lozenges in validated animal infection models against diverse helminth species.

2. Standardization: Development of robust phytochemical standardization protocols with embelin as a quantitative marker using HPLC or HPTLC methods.

3. Pharmacokinetic Studies: Characterization of ADME profile of embelin following oral mucosal and oral administration, including bioavailability determinations.

4. Clinical Trials: Rigorous, randomized, double-blind, placebo-controlled clinical trials establishing efficacy, safety, and optimal dosing regimen.

5. Scale-up: Technology transfer from laboratory-scale to industrial-scale manufacturing with validation of process parameters.

6. Pediatric Optimization: Palatability studies, dose-finding, and pediatric clinical trials to formally establish suitability for children the population most burdened by helminth infection

X. CONCLUSION

Embelia ribes (Vidanga) represents a botanically rich, phytochemically validated, and pharmacologically promising source of anthelmintic activity, with embelin as the primary bioactive quinone responsible for its efficacy. This review has critically synthesized the current evidence base supporting both the anthelmintic potential of E. ribes and the scientific rationale for its incorporation into herbal medicated hard candy lozenges.

The developed hard candy lozenge formulations demonstrated satisfactory physicochemical properties, excellent drug-excipient compatibility, controlled drug release (86.20–94.02% at 30 minutes), and robust stability over a 3-month ICH accelerated study. The optimized formulation F5 (HPMC E5 at 23 mg) achieved 94.02% drug release at 30 minutes with stable physicochemical attributes, confirming suitability as a herbal anthelmintic dosage form.

The medicated lozenge dosage form addresses key compliance challenges in helminthiasis treatment, particularly for pediatric and dysphagic populations, offering palatability, ease of administration, and convenience for field use in resource-limited settings. Successful translation through in vivo and clinical validation holds significant promise for integrating traditional herbal knowledge with modern pharmaceutical science to address the persistent global burden of helminth infections.

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