Formulation and Evaluation of Herbal Medicated Lozenges Containing Embelia Ribes Ethanolic Extract for Treating Helminthiasis

Mr. Rishikesh Sidram Nadiwade[1], Dr. Kavaljit Satish Birajdar[2], Mr. Dasrao Ashok Patil[3]
Nishigandha Sachin Chopade[4], Pooja Shivaji Shep[5], Niranjan Sidram Nadiwade[6]
[1,2,3,4,5,6]*Dept. of Pharmaceutics, BSS's Tatyaraoji More College of Pharmacy, Omerga, Maharashtra, India*

***Abstract*—Intestinal helminth infections represent a significant global health burden, predominantly affecting tropical and subtropical regions with limited access to healthcare. This study reports the formulation and evaluation of medicated hard candy lozenges as a novel therapeutic modality utilizing the anthelmintic properties of Embelia ribes (Vidanga) ethanolic extract. Six formulations (F1–F6) were prepared by the heat congealing method using sucrose, dextrose or mannitol, HPMC K100 or HPMC E5 as polymers, citric acid, mint flavour, and amaranth. The active compound embelin, characterized at λmax 289 nm in phosphate buffer pH 6.8, demonstrated Beer–Lambert linearity ($R^2 = 0.9963$) across 10–90 µg/mL. FTIR analysis confirmed no drug–excipient interaction. All formulations were evaluated for hardness, thickness, weight variation, friability, drug content, disintegration time, and in vitro drug release. Formulation F5 (HPMC E5, 23 mg) showed optimal characteristics: hardness 10.50±0.28 kg/cm², drug content 97.12±1.50%, disintegration time 10.18 min, and cumulative drug release of 94.02% in 30 minutes in phosphate buffer pH 6.8. Accelerated stability studies conducted at 40°C/75% RH for three months as per ICH guidelines confirmed formulation stability without significant changes in physical or chemical parameters. These results demonstrate that sucrose-based Embelia ribes medicated lozenges offer an effective, patient-friendly, and compliant therapeutic alternative for helminthiasis, particularly suited for pediatric and dysphagia patients.**

***Index Terms*—Embelia ribes, Helminthiasis, Hard candy lozenges, HPMC K100, HPMC E5, Anthelmintic activity, In vitro drug release, Heat congealing method**

I. INTRODUCTION

Helminthiasis, caused by parasitic worms (helminths), remains a major public health concern worldwide, especially in low-income regions with inadequate sanitation. The primary helminthic groups infecting humans include nematodes (roundworms), trematodes (flukes), and cestodes (tapeworms). Infections lead to morbidity ranging from mild discomfort and malnutrition to severe complications such as anemia, organ damage, impaired cognitive development, and growth retardation in children [1,2,3].

Conventional anthelmintic drugs (albendazole, mebendazole, praziquantel, ivermectin) face challenges of drug resistance, side effects, and limited access in resource-limited settings. This has prompted research into herbal alternatives with anthelmintic potential [4,5,6].

Embelia ribes Burm. F. (family Myrsinaceae), commonly known as Vidanga or false black pepper, is a large scandent shrub found across India and in tropical Asia. Its principal bioactive compound, embelin (2,5-dihydroxy-3-undecyl-1,4-benzoquinone; mol. wt. 294.39 g/mol), has demonstrated anthelmintic activity through interference with helminth energy metabolism and mitochondrial function. Additional bioactives include quercetin and gallic acid, conferring antioxidant and anti-inflammatory properties [4,5,6].

Lozenges are solid medicated dosage forms designed to dissolve or disintegrate slowly in the oral cavity. Their advantages include avoidance of first-pass metabolism, improved bioavailability, bypassing gastrointestinal degradation, ease of administration without water, and high patient compliance especially in pediatric and geriatric populations [7,8,9,10]. Hard candy lozenges, prepared by the heat congealing

method, are particularly suitable for thermostable herbal extracts.

The aim of this study was to formulate and evaluate medicated hard candy lozenges of Embelia ribes ethanolic extract employing HPMC K100 and HPMC E5 as release-modifying polymers, and to identify an optimized formulation through comprehensive physicochemical evaluation and stability testing.

II. MATERIALS AND METHODS

A. Materials

Embelia ribes crude powder was procured from Kshipra Biotech Pvt. Ltd., Indore, Madhya Pradesh. Sucrose, dextrose, mannitol, HPMC K100, HPMC E5, citric acid, mint flavour, and amaranth (food grade) were obtained from analytical-grade commercial suppliers. All reagents and solvents used were of analytical or HPLC grade.

Table I: Materials and Sources

Sr. No.	Chemical	Source
1	Embelia Ribes Extract	Kshipra Biotech Pvt. Ltd., Indore, M.P.
2	Sucrose	DIPA Chemicals Industries, Mumbai
3	Mannitol	Meher Chem Pvt. Ltd., Mumbai
4	Dextrose	Meher Chem Pvt. Ltd., Mumbai
5	HPMC K100	Research Lab Fine Chem, Mumbai
6	HPMC E5	Ozone International, Mumbai
7	Citric Acid	Himedia Lab Pvt. Ltd., Mumbai
8	Mint Flavour	Cosmo Chem, Pune
9	Amaranth	Meher Chem Pvt. Ltd., Mumbai

B. Preformulation Studies

Ethanolic extraction of Embelia ribes crude powder was carried out in a Soxhlet apparatus using ethanol as solvent. The extract was concentrated by rotary evaporation. Preformulation studies performed included: (i) organoleptic property assessment (color, odour, taste, texture); (ii) melting point determination by capillary method; (iii) solubility profiling in water, methanol, ethanol, and acetone; (iv) UV spectrophotometric determination of λmax and calibration curve construction in phosphate buffer pH 6.8; (v) FTIR compatibility studies of pure drug with individual excipients and all excipients combined using a Perkin Elmer IR spectrometer (400–4000 cm^{-1}); and (vi) phytochemical screening for alkaloids, tannins, glycosides, flavonoids, saponins, steroids, and terpenoids.

C. Formulation of Hard Candy Lozenges

Six formulations (F1–F6) were developed by the heat congealing method. Sugar (sucrose) and water were heated to dissolve completely, followed by addition of dextrose or mannitol (dissolved separately at 110°C). The combined mixture was heated to 160°C until a golden-yellow color developed. The temperature was reduced to 90°C, after which Embelia ribes extract (100 mg/lozenge), polymer (HPMC K100 or HPMC E5 at varying concentrations: 15, 23, or 30 mg), citric acid, mint flavour, and amaranth were incorporated with continuous stirring. The molten mass was poured into molds, allowed to cool, and the lozenges were wrapped in aluminum foil and stored in desiccators. Each lozenge had a target weight of 1500 mg.

Table II: Formulation Composition (mg/lozenge)

Ingredient	F1	F2	F3	F4	F5	F6
Embelia 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
Mint Flavour	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Amaranth	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

D. Evaluation Parameters

All six formulations were evaluated for: weight variation (20 lozenges, % deviation = (individual – average)/average × 100); thickness using Vernier calipers; hardness using Monsanto hardness tester (kg/cm^2); friability using Roche friabilator (25 rpm, 4 min, n=20); drug content by UV spectrophotometry at 289 nm after dissolution in phosphate buffer pH 6.8; disintegration time in artificial saliva (pH 5.8, 37±0.5°C) by USP method; and in vitro drug release

using USP Type II dissolution apparatus (paddle, 100 rpm, 37±0.5°C, 900 mL phosphate buffer pH 6.8, sampling at 5-minute intervals up to 30 min).

E. Stability Studies

The optimized formulation (F5) was subjected to accelerated stability studies at 40°C ± 2°C and 75± 5% RH for three months as per ICH Q1A(R2) guidelines. Samples were withdrawn at 0, 1, 2, and 3 months and evaluated for physical appearance, hardness, thickness, weight variation, friability, drug content, disintegration time, and in vitro drug release.

III. RESULTS AND DISCUSSION

A. Preformulation Studies

Organoleptic evaluation revealed that Embelia ribes extract was dark brown to black in color, with a strong, slightly pungent odour, bitter and astringent taste, and fine crystalline powder texture. Melting point was determined at 383–387°C. Solubility studies demonstrated that the extract was soluble in methanol and ethanol, moderately soluble in acetone, and partially soluble in water.

The UV spectrum of embelin in phosphate buffer pH 6.8 showed maximum absorbance (λmax) at 289 nm. The calibration curve was linear over 10–90 µg/mL with the regression equation $y = 0.0963x – 0.0193$ ($R^2 = 0.9963$), confirming adherence to Beer–Lambert law.

Phytochemical screening of the ethanolic extract gave positive results for alkaloids (Wagner's test, iodine test), tannins (Braymer's test, 10% NaOH, lead acetate, picric acid), and glycosides; amino acids were absent.

FTIR analysis of the pure drug showed characteristic peaks: O–H stretch (3225 cm^{-1}), N–H stretch (3402 cm^{-1}), N–H bend (1600 cm^{-1}), C–N stretch (1278 cm^{-1}), and C–Cl stretch (568 cm^{-1}). All characteristic peaks were retained in the FTIR spectra of drug–HPMC K100, drug–HPMC E5, and the complete drug–excipient mixture without any disappearance or significant shift, confirming compatibility and the absence of chemical interaction.

B. Physical Characterization

Physical appearance evaluation showed that F5 (HPMC E5, 23 mg) produced smooth, red-colored lozenges that were easily removed from the mold with hardness meeting specifications. F1 was sticky and difficult to demold; F3 exhibited post-molding melting; F6 showed brittleness after a while.

C. Physicochemical Evaluation

Table III: Physicochemical Parameters of All Formulations (n = 3, mean ± SD)

Batch	Hardness (kg/cm^2)	Thickness (mm)	Avg. Wt. (mg)	Disint. (min)	Friability (%)	Drug Content (%)
F1	9.26±0.37	7.12±0.08	1500±0.12	9.02±0.75	0.62	96.02±0.88
F2	10.29±0.43	7.11±0.07	1498±0.24	9.20±0.43	0.78	96.16±2.52
F3	10.07±0.06	7.13±0.09	1500±0.09	10.02±0.28	0.72	95.55±1.56
F4	10.29±0.43	7.11±0.07	1501±0.14	9.12±0.31	0.50	94.46±2.65
F5	10.50±0.28	7.20±0.04	1500±0.10	10.18±0.51	0.71	97.12±1.50
F6	10.69±0.50	7.15±0.02	1499±0.32	10.56±1.25	0.76	96.10±2.32

Thickness of all formulations ranged from 7.11±0.07 to 7.20±0.04 mm, indicating uniformity. Weight variation ranged from 1498±0.24 to 1501±0.14 mg, within acceptable limits. Hardness ranged from 9.26±0.37 to 10.69±0.50 kg/cm^2, with F5 providing adequate mechanical strength. Friability was 0.50–0.78% (within the ≤1% limit), confirming mechanical stability. Drug content ranged from 94.46±2.65 to 97.12±1.50%, indicating uniform drug distribution. All formulations showed disintegration times of 9.02–10.56 min.

D. In Vitro Drug Release

Table IV: Cumulative Drug Release (%) in Phosphate Buffer pH 6.8

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

In vitro drug release studies conducted for 30 minutes in phosphate buffer pH 6.8 showed cumulative release ranging from 86.20% (F3) to 94.02% (F5). Formulation F5 (HPMC E5, 23 mg) demonstrated the highest release of 94.02% at 30 minutes, attributed to the favorable viscosity and hydration characteristics of HPMC E5 at this concentration. F4 and F6 (HPMC E5 at 15 and 30 mg) showed releases of 91.08% and 86.29%, respectively. HPMC K100-based formulations (F1–F3) showed lower release rates, consistent with its higher viscosity grade creating a denser polymer network. Based on optimal physicochemical parameters and maximum drug release, F5 was selected as the optimized formulation.

E. Stability Studies (Optimized Formulation F5)

Table V: Stability Study Data for F5 (40°C/75% RH)

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 Content (%)	97.12±1.50	97.10±1.20	97.06±1.32	97.05±1.20
% Release at 30 min	94.02	93.80	93.52	93.20

Accelerated stability studies over three months at 40°C/75% RH showed no significant changes in any evaluation parameter. Minor decreases in hardness (10.50 to 10.12 kg/cm²) and drug release (94.02% to 93.20%) were within acceptable limits. Friability remained below 1% throughout. Drug content was stable at approximately 97%. These results confirm that formulation F5 is physically and chemically stable under ICH Zone IVb accelerated conditions.

IV. CONCLUSION

Six formulations of medicated hard candy lozenges incorporating Embelia ribes ethanolic extract (100 mg/lozenge) were successfully developed by the heat congealing method using HPMC K100 and HPMC E5 as polymers. Preformulation studies confirmed the compatibility of the drug with all excipients. Formulation F5, containing HPMC E5 at 23 mg, emerged as the optimized formulation with superior drug content (97.12±1.50%), hardness (10.50±0.28 kg/cm²), and maximum cumulative drug release (94.02% in 30 minutes). Stability studies demonstrated that F5 maintained all physicochemical properties within acceptable limits over three months at accelerated conditions. These sucrose-based medicated lozenges represent a viable, patient-friendly, and effective alternative dosage form for helminthiasis treatment, offering particular advantages for pediatric, geriatric, and dysphagia patients who have difficulty swallowing conventional solid oral dosage forms.

ACKNOWLEDGMENT

The authors acknowledge the support of BSS's Tatyaraoji More College of Pharmacy, Umerga, affiliated to DBATU, Lonere, for providing research facilities and guidance throughout this work.

REFERENCES

[1] McSorley H.J., Maizels R.M., "Helminth infections and host immune regulation," Clin. Microbiol. Rev., vol. 25, no. 4, pp. 585–608, 2012.

[2] Al Amin A.S.M., Wadhwa R., "Helminthiasis," in StatPearls [Internet], Treasure Island, FL: StatPearls Publishing, 2023.

[3] Rennie C., Fernandez R., "The Impact of Helminth Infection on the Incidence of Metabolic Syndrome: A Systematic Review and Meta-Analysis," Front. Endocrinol., vol. 12, 2021.

[4] Asadulla S., Ramandang, "Pharmacognosy of Embelia ribes Burm F," Int. J. Res. Pharm. Chem., vol. 1, no. 4, 2011.

[5] Rout S., Sahoo G., "Embelia ribes Burm F. (Vai Vidanga)—An Overview," Int. J. Mod. Agric., vol. 10, no. 2, 2021.

[6] Swarnkar C.P., Singh D., "Anthelmintic potential of Embelia ribes seeds against Haemonchus contortus of sheep," Indian J. Anim. Sci., vol. 79, no. 2, pp. 167–170.

[7] Nagoba S.N., Purushotham R.K., Zakaullah S., "Formulation of clotrimazole as lozenge tablet for improved delivery to oral thrush," J. Pharm. Biomed. Sci., 2011.

[8] Lakshmi B.M., Brahma K., Swathi G., et al., "Formulation and evaluation of domperidone candy lozenges," World J. Pharm. Pharm. Sci., vol. 6, no. 12, pp. 1167–1175, 2017.

[9] Pothu R., Yamsani M.R., "Lozenges formulation and evaluation: A review," IJAPR, 2014.

[10] Choursiya S., Andheriya D., "Review on lozenges," J. Drug Delivery Ther., 2018.

[11] Rao T., et al., "Preparation and evaluation of sugar based medicated Tramadol hydrochloride hard lozenges for pediatrics," 2018.

[12] Khaladkar A., et al., "Formulation and evaluation of Adhulsa lozenges for pediatric patients," 2019.

[13] Sohal T., et al., "Medicated lozenges," 2018.

[14] Chandrawanshi M.J., Nagoba S.N., et al., "Lozenges: formulation and evaluation," 2019.

[15] Siham Abdoun A., et al., "Formulation and evaluation of metronidazole lozenges for oral thrush," 2017.

[16] Lavanya N., et al., "Formulation and evaluation of lozenges for sore throat using Loratadine," 2020.

[17] Yamsani S.K., et al., "Formulating Doxofylline lozenges to provide slow release for management of asthma," 2018.

[18] Fathima S., et al., "Formulation of paracetamol, diclofenac and domperidone combination lozenges," 2017.

[19] Manasa A., et al., "Formulation and evaluation of Cetirizine sweetened tablet lozenges," 2017.

[20] Lakshmi M., et al., "Formulation and evaluation of Domperidone lozenges," 2022.

[21] Majekodunmi S., et al., "Review on lozenges as solid dosage forms," 2016.

[22] Ramya T., et al., "Structural and qualitative analysis of Embelia ribes extract," 2014.

[23] Chaudhary V., et al., "Development of analytical profile of Embelia ribes extract," 2021.

[24] Harri H., "Zinc lozenges may shorten the duration of colds: A systematic review," Open Respir. Med. J., vol. 5, pp. 51–58, 2011.

[25] Kamath J., et al., "Formulation and evaluation of candy based medicated lollipops of Levamisole for pediatrics," 2014.

[26] Bhati R., Nagrajan R.K., "A detailed review on oral mucosal drug delivery system," IJPSR, vol. 3, no. 3, pp. 661–681, 2012.

[27] Rowe R.C., Sheskey P.J., Quinn M.E., Handbook of Pharmaceutical Excipients, 6th ed. London: Pharmaceutical Press, 2009.

[28] Indian Pharmacopoeia, Ghaziabad: Indian Pharmacopoeia Commission, vol. I & II, 2014.

[29] Patel D.M., et al., "Formulation and evaluation of Diphenhydramine hydrochloride lozenges," World J. Pharm. Pharm. Sci., vol. 3, no. 5, pp. 822–844, 2014.

[30] Hearnden V., et al., "New developments and opportunities in oral mucosal drug delivery," Elsevier, vol. 64, pp. 16–28, 2012.